

PEDIATRICS

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By
Members of the Pediatric Department
Faculty of Medicine
University of Alexandria

Editor
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DAR AL-MAAREF

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

*To our students and colleagues. To all
physicians dealing with infants and children
who aim at a healthy, happily adjusted
new generation*

This book is dedicated.

PREFACE TO THE FIRST EDITION

Within the various fields of Modern Medicine, «Pediatrics» has rapidly gained its individuality and personality. Pediatrics deals with the young generation, which - in contrast to adults — is continuously growing and developing. In our country, as well as in almost all developing countries, this young generation constitutes about 50% of the total population. Hence, pediatric teaching and training should be considered the keystone of medical education.

To teach or be taught medicine, the «PATIENT» and the «BOOK» are the two indispensable means. The teacher, the different laboratory procedures, the help of the radiology and other investigations are only useful for better understanding of the medical problem and for arriving at the proper diagnosis. The latter necessitates keen observation and complete medical examination, i.e. the «Patient», together with sound knowledge of the various diseases and their clinical picture, i.e. the «Book». Therefore, may I strongly persuade every student of medicine to start by observing his patient, because observation is one form of examination which is always rewarding in pediatrics. This should be followed by detailed history of the complaint, analysis of all the symptoms and eliciting every possible physical sign. The signs are then translated into underlying pathology, which when discussed in the light of the history and symptoms, will rule out many of the possible diseases and point to the most probable one.

On the above assumptions, this book is introduced to the medical body. I feel that it will be a good guide to the undergraduate, a great help to the young pediatrician and general practitioner and a useful companion to the teaching staff who intend to make pediatrics easy as well as interesting for their students.

I wish to thank the different authors for their care and thoroughness in preparing their various sections, and also for permitting me to harmonize the style throughout the entire book. My deep thanks and gratitude are due to Doctor Galal H. Aref and Doctor Shawky El Khateeb for their invaluable help in revising the proofs. I also wish to thank «DAR AL-MAAREF», our publishers, and «MOHARRAM» press for their sincere and continuous efforts to bring this edition in its present form.

January 1970

AHMAD SHAFIK ABBASSY

The Editor

PREFACE TO THE THIRD EDITION

During the last years, enormous developments in the field of diagnosis have been achieved. In spite of that, the practitioner must avoid thinking that data of investigations and radiography can save him from keen observations, careful history taking and a thorough clinical examination of the baby.

Accordingly, in this edition of the book, it will be noticed that the authors have endeavoured to present to the student and pediatrician the available material necessary for bringing up healthy and adjusted adolescents as well as the recent management of pediatric disorders.

With this goal in mind, two new chapters were added; one on social pediatrics, while the other deals with the more common disorders of inborn errors of metabolism.

Description of the full term normal infant, the possible birth injuries and the diseases of the newborn were all amalgamated in a logic and more understandable way in a single chapter.

More attention was given to tropical pediatrics and to diseases of the developing communities especially malnutrition and diarrheal disorders. The latter was re-written in a detailed but simple manner because it is the first killing disease in infants in our country.

I take pleasure in expressing my indebtedness to my colleagues the authors and to our publishers for their cooperation and great help.

November 1977

AHMAD SHAFIK ABBASSY

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Chapter I

SOCIAL PEDIATRICS

The child could be considered as the outcome of multiple interactions, viz : genetic, maternal, paternal and environmental factors playing within and around him, that finally bring him to the state of health, disease or maladjustment.

Social pediatrics is not an independent field or a special technique used in management of infants and children. It is the sum of all the efforts directed for bringing up the child and keeping him in the best possible state of physical and mental health and adapting him to be a useful member of the society. Social pediatrics is thus intimately connected with both the preventive and the curative fields of pediatrics on local, national and international basis.

The Family and Social Development

The first social unit that the child comes to know is that of the family. The family is the keystone of our society, for in it the child is born and within which he grows up. *Family structure* differs greatly between different societies and cultures, from the small urban family in the new industrial cities with no or little experience in caring for children to the large extended and usually rural family comprising many generations and adults to whom the child can turn for affection and guidance after the inevitable separation from an ever present and available being i.e. *his mother* when she goes back to her job or work after weaning the baby. The development of the personality of the child depends on the way he is treated by those around him. The vital role of the mother as the main source of physical security and psychological warmth, and the interactions between the child and the adults surrounding him can be merely protective, or it can be stimulating, warm or frustrating.

In a small family unit, the child's emotional ties are concentrated on a few persons; mother, father and may be older sibling. The former two are usually engaged in work and therefore the child feels frustrated or hurt by his mother's lack of attention. Moreover, as families crowd into cities, living accommodations

become smaller, more compact and frequently the family has less privacy. Play space for children may be limited to restricted playgrounds and frequently to streets. Life becomes more organized and less spontaneous and the opportunities for discovery and exploration, so easily available in the country, are limited for the city child. In the search for adventure the child may express unusual behavior and go beyond the usual limitations.

The impact of *social structure and culture* on the child's development is also shown in the difference in behavior between boys and girls. Psycho-motor development, and even death rate, will change with sex according to whether the society attaches more importance to the boy or the girl.

An awkward situation may arise when a parent has the sole or major responsibility for family affairs and support because of death, desertion, divorce, separation or chronic illness of the other parent. This creates a situation where the child is more exclusively dependent on one adult in his environment, and so more vulnerable to the feelings of anger and aggression directed towards the parent.

Lastly, for children who must, for various reasons, be *deprived of the security and affection* of their families, substitute parents who may be relatives, friends or foster parents, will need to provide for the child warmth, love and acceptance the child misses from his own parents so that he may have the opportunity for normal social and emotional development.

On the whole, the effects of social structure inside and outside the family is linked with the quality of the care the child is given and with the degree of affection and of stimulus he receives from his parents or from the persons who share the parental functions. *Stimulation* considerably influence the development of speech, the personality and the intellectual potentials of the small child; some of these effects are lasting and perhaps permanent.

Social and Economic Factors Influencing Family Life

Beside the family structure, the socio-economic environment of the population reacts on the child through the family group. A detailed analysis of socio-economic factors shows the part played by the parent's profession, income, nutrition, housing, education and other factors which provide a basis for the establishment of sociological classification. If these environmental factors are

unfavorable, they can slow down and change development either temporarily or permanently and thus hinder the expression of the genetic factors, which potentiate development.

Nutritional deficiencies have a very definite influence on the development and behavior of the small child. Studies suggest that the brain may be permanently affected if nutritional restrictions are imposed at a time when it is undergoing its period of fastest growth. In human, this period is mainly concerned with myelination and occurs during the last few months of gestation, and to a lesser extent during the first few months of post-natal life.]

Overcrowded housing and poor sanitation cause the spread of infectious diseases and affect the quality of the care given to the small child especially among country families who have migrated to the big cities. Such infections must be combatted and attempts must be made to prevent them by means of vaccinations.

Education of the parents seems to be at least as important as the economic level especially during the period of infancy. Their wise guidance allows the child to flourish. The family's intrinsic qualities i.e. its ability to meet difficulties is closely related to the child's development. A serious position occurs if the family is unable to meet its basic requirements either due to the big size of the family or to poverty. In such cases there is little choice except for all members of the family to earn what they can. This may put undue pressure on children to earn too early, or at unsuitable occupations, or for too long hours.

In a developing country like ours, priority must be given to the fight against hunger and infections, an indispensable basis for normal economic and social development. In this respect, organization of prophylactic and educational activities is preferable to those concerned with treatment (Chapter II).

Social and Psycho-emotional Development of Children

Through the Various Age Periods.

Neurological, intellectual, behavioral and other functional maturation of systems and gaining of skills follow special order but with many individual variations. These differences are dependent on the child himself i.e. his power of attention and mechanisms of response, and upon his experiences. The later are influenced by the social and emotional situation and the opportunities which

are available to him. Of major importance will be the relationship which he has established with his parents and siblings, the constancy of these relationships especially with the mother, the atmosphere of the home and the regularity of chances and stimuli for development.

A child's development from birth to puberty can be schematically divided into three stages which may be referred to as infancy, early childhood or preschool age and school age.

Period of infancy : During the early stage of infancy, the baby is unable to express himself and incapable of independent movement. The *motor actions* up to the third or fourth month of life are not voluntary but reflex actions such as the rooting, sucking, swallowing, grasping and other reflexes. The stimuli influencing his *emotions* are "intrinsic" i.e. arising inside his body such as hunger, colic etc. which are usually expressed by screaming, the intensity of which differ from infant to infant. By the second month sensory-motor i.e. *adaptive development* starts and the baby tries to discover himself, and then recognizes his mother. Later he starts to show his feelings to those around him and thus "extrinsic" emotions, i.e. stimuli arising outside himself, influence his feelings and responses.

During these critical changes of the infant, the responsibility for care is usually placed on the mother who realizes that she will be evaluated as a mother by her husband, family and friends. Thus, she should give her baby constant physical and psychological warmth. However, with the 24 hour care required by a baby, mothers often feel home bound and isolated, and often need some practical help in order to gain a little leisure. One result of this is that the baby, in his first year of life, may become exposed to several different persons with the effect of confusing the baby in regard to the mother-figure.

During the second year, as the child develops the ability of moving, he tries to discover the little world around showing increasing independence, but he always needs to be able to return to the familiar rhythms of life, habits and people which reassure him and give him the necessary *emotional and physical security*. This is primarily the job of the mother.

The new baby will also affect the relationships of parents with the baby's siblings who usually show resentment and jealousy unless prepared for the new situation beforehand.

Period of early childhood (the preschool years) : Between infancy and the school entry age i.e. six or seven years, there is a special period of rapid transition. The child is then still living with his family—

which constitutes his first environment, but after the separation from his mother, he rapidly acquires more active, emotional, adventurous and social independence. He *loves to explore* but his interest is fleeting and he needs variety for the release of his energy. Usually the father urges his young son to discover things for himself even at some risk, while the mother tends to restrain the child and to limit the scope of his activities. This parental inconsistency may confuse the child who is not sure of what is permitted. To stimulate the development of the child's latent abilities and potentialities an optimal balance should be achieved between satisfying the child's needs on the one hand and frustrating him on the other hand.

In these early years the child shows *negativism* and his reaction to almost every request made by his parents is "no". Through negativism the child gets a sense of himself as a separate individual and gains a feeling of independence. If the child gets constant disapproval, he becomes even more negative. Parents should use suggestions rather than commands, and should avoid threats, especially threats of punishment. Thus, discipline plus affection are needed throughout this age period and both mother and father should share these responsibilities. A child of this age *asks many questions* and wants truthful answers which help him to rely on his parents and develop faith in them. During development of language, he may pick up *naughty words*. Many parents use punishment to discourage the use of such forbidden words, but this may tend to fix them in the child's mind. The proper attitude is to pay little attention to this and the child soon drops them for something newer and more interesting.

The *imaginative child* at this period may imagine that he has playmates with him and tell false stories which in the eyes of the family are *considered lies* and may mistakenly punish children for quite acceptable imaginative projections.

Play is the major business of the child and undoubtedly the most important activity for psycho-motor development at this age period. The child needs playmates of his own age. If these are much younger, the preschool child tends to dominate them, while if older, he has little opportunity to develop his own interests and will try to follow the lead of the older children. The child who has no playmates of his own age will benefit from more supervised play opportunities e.g. at day-care centers or nursery schools. The child devotes practically all his waking hours to play, immerses himself in it completely, forgetting everything around him. Of great concern to the parents is his attitude towards food. The *poor appetite* the child displays alarms the parents, raises hot discussions and they try to persuade or even force the child by all means to eat; so much so that he shows *negativism* and thus become "the little emperor" of the family. Parents should be taught that anorexia is the general attitude at this age period.

Towards the end of this period, the child likes to be included in the family's

social activities and be treated as an active *member of the family* and to be with visitors and identifies strongly with his own family as being the best.

Preschool stimulations of social development through planned play, social activities etc., when well organized and directed, particularly by an educator with technical knowledge, promote adaptability, intellectual curiosity and powers of observation. Therefore, in family circumstances with a high social and economic level, *preschool education* is useful for intellectual training of the child. On the other hand, when family environment, for social or cultural reasons, affords the child neither security nor stimulation, group or nursery *preschool education* is useful if it can be arranged.

On the whole, the social adjustment of the child at this age period will determine his readiness for school because during it the basic pattern of social relationships with his peers and with adults are developed.

Period of school age: At an age varying between six and seven years, according to country, the child, having already acquired complete motor independence and mastered his means of communication, affirmed his personality in relation to his parents and other adults, and being capable of elementary intellectual operations, enters a society organized for him, where he will be a child among other children, namely "the school". Through the school discipline his physical growth, like his emotional, intellectual and social development, will be regular. He begins to learn that in his *group experience* he must conform to what is expected of him, both in the school and in community. He finds that it is not acceptable to be different, and so he wants to be like his peers in actions and dress. Much *self-consciousness* is developed for the child who cannot buy his lunches in school, or dress as the other children dress, or have spending money like the other children. Experiences of *deprivation* and feelings of *restriction* also develop and are especially hazardous for the *handicapped* child or for the child who in some way is so deprived that he is unable to compete.

During the early part of the school age period (7 years-puberty), the child is *very active*. He wants to make use of his body, and exerts his energy ceaselessly. He is always in a *hurry*, he has little time to wash or eat and find it hard to leave his play or playmates. However, children have real *worries* during these years as they take on more responsibilities and begin to react to them with *anxieties* and *tension*. They begin to question the knowledge and authorities of parents who, in the past, they considered all-knowing and all-powerful. The teacher begins to take an important place in their esteem and they begin to build their self-image as *potential adults*. They tend, too, to be concerned about the unfamiliar or the unexplained, and seek answers to these. Some children who feel unwanted

or unloved, or who believe they do not belong at home, may tend to run away as a means of begging for more attention and display of affection. Therefore, parents, teachers and leaders should keep in mind that psychologic development and mental health of the child require that events in all the stages of development be managed in such a way as to keep tension in the child with tolerable limits.

On the other hand, during the first part of this period the child is as soft wax, can register many ideas and acquire the sense of responsibility. A well planned *school health program* is needed, as well as good balance between work, rest and recreation. Throughout the school age period the child needs the steady influence and direct *guidance* of parents and teachers and the *security* of knowing that they are behind him, supporting him and accepting his limitations.

As the child grows older, increasing emphasis is placed by parents on his *school performance*, and the parents tend to compare the success of their child with that of others in his group. If pushed beyond his capacities he will show attitudes of confusion, conflict, and frustration. With failure in school the child experiences a loss of self-esteem and a deep sense of humility. How he succeeds will depend to a large extent on the soundness of his early development and on the readiness of others to help him make his adaptations to fuller life experiences. Thus parents, teachers and leaders in leisure-time activities, working together, can round out the child's needs in his efforts to meet the increasing responsibilities of late childhood and the young adult years. During the school years the foundations are laid for the child's ability to *support himself* and to be ready for the opportunities and obligations of marriage and parenthood.

A. S. ABBASSY

PREVENTIVE PEDIATRICS

The idea of preventive medicine is as old as medicine itself. More than two thousand years ago, a Chinese physician described a good doctor as one "who pays constant attention to keeping people well so there will be no sickness".

The essential aim of preventive pediatrics is the protection of the child, not only from disease but also from malformations, hunger, brutality, bad habits, psychic disorders and any other influence which would tend to prevent the growing organism from reaching maturity in a normal, healthy, happily adjusted manner.

To reach this goal the forementioned factors should be considered in detail by a team of a physician, obstetrician, pediatrician, teachers and care-takers in order to supervise the child from - or even before - conception until adolescence. By doing this many preventable and reversible risks could be avoided or overcome.

The following are the risks and their prevention :-

Pre-natal risks :

- a) *Hereditary factors* : are most serious and therefore honest detailed family history is needed before marriage.
- b) *Before pregnancy* :¹ impairment of health through nutritional deficiency or excess and exposure to X-rays as far as possible must be avoided.
- c) *During pregnancy* : Protect the fetus from the many insults which may lead to its death, injury or malformation such as :-
 - i - Infections (rubella, mumps, syphilis, polio., toxoplasmosis, coxsackie, malaria etc.)
 - ii - Chronic diseases and toxemias of the mother (heart failure, toxemia of pregnancy, malignancy, tuberculosis, etc.)
 - iii - Maternal malnutrition or vitamin deficiency or excess.
 - iv - Endocrine disorders (diabetes, hyperthyroidism etc.)
 - v - Blood disorders (Rh incompatibility, anemias, leukemias etc.)

- vi - Drugs (sulfa, vit K excess, sedatives, hypnotics, hormones etc.)
- vii - Allergic, metabolic and/or neurologic disorders.

Natal risks :

During the process of birth the baby is threatened by :-

- i - Injury especially in difficult births.
- ii - Anoxia (analgesics & anaesthetics)
- iii - Infections especially in prolonged and difficult labour.

Post-natal risks:

The neonatal period (first month of life) is very critical to the mother especially if primipara but much more so to the infant. This is because it is the period of its transition from dependent intra-uterine to independent extrauterine life and during which many adjustments - some of which are vital and urgent - take place. These physiologic changes usually pass peacefully but they may be severe and become pathologic leading to one or more of the particular diseases of the newborn characterized by high mortality rate.

After the neonatal period, post-natal care aims at harmonious development of the child physically, intellectually and socially. This needs consideration of the following :-

- i - Early detection of anomalies and metabolic disorders.
- ii - Diet and prevention of nutritional disorders.
- iii - Prevention and detection of diseases through proper hygienic conditions, clean habits, immunizations, early diagnosis, proper prophylaxis and treatment as well as guidance of parents.
- iv - Prevention of injury, accidents and poisons.
- v - Social life and adaptation (chapter I).

The methods and techniques which have been developed to meet most of these problems are the pre-natal clinics, infant welfare centres, foundling homes, kinder gardens, health program for school age children, development of youth and sports clubs e.c.

Prevention of communicable diseases by routine active immunization became a prominent item of preventive pediatrics. Thanks to the recent studies and new techniques which proved that reasonable antibody formation follows antigenic stimulation even when done at or shortly after birth.

IMMUNIZATION IN INFANCY AND CHILDHOOD

The aim is to build up resistance in the child against certain infectious diseases in advance.

Infant, the newborn possesses some *passive* humoral immunity inherited from the mother having passed to the fetal circulation via the placenta. This type of immunity is lost about the fourth month. *Active* immunity begins slowly to be acquired about the 12th to the 18th month. There exists a critical period (4th -- 18th month) during which the baby is very liable to contract many of the communicable diseases. It is therefore advisable to enable him to build active immunity as early as possible. This is done by means of inoculations. The accompanying table shows the different kinds of immunity which may occur or be induced in the child.

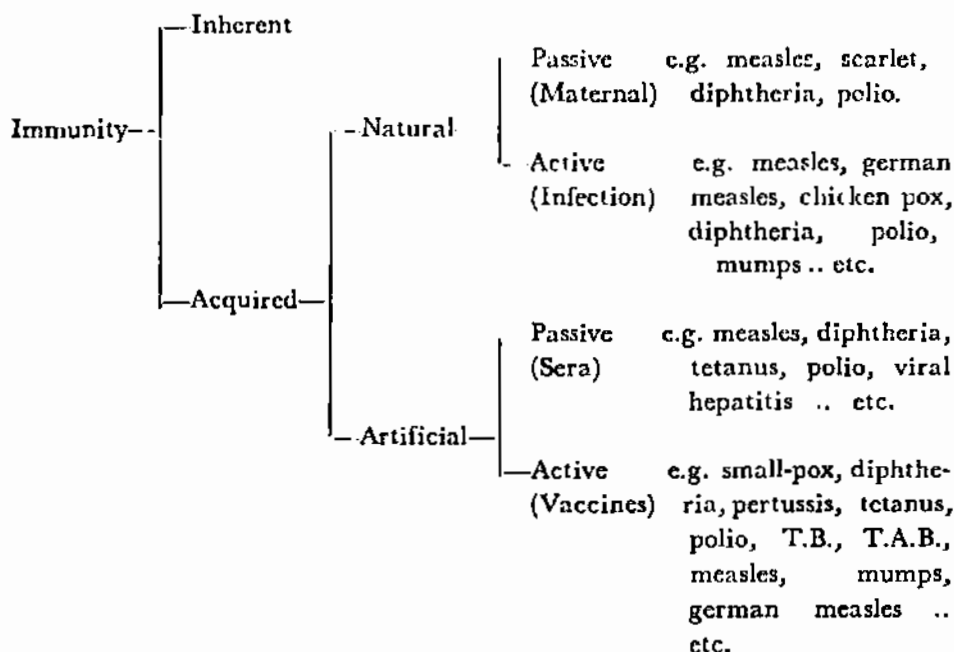


Fig. 1 : Different Kinds of Immunity

Acquired Natural Passive Immunity :

Most of the antibodies in the mother's blood pass to the fetus. In this respect the human placenta acts as a selective filter. While some antibodies may not pass through it to the fetus (e.g. small-pox, pertussis), others appear in the cord-

blood more concentrated than they are in the maternal blood (measles). In general the duration of immunity given, have a direct relation to the concentration of antibodies in the mother's blood. Being passive immunity, it gradually disappears in a few months without formation of new antibodies by the baby.

Acquired Natural Active Immunity :

This is the result of infection either subclinically or by contracting the disease itself. The causative agent acting as antigen and stimulating the *active* production of antibodies against the specific infection. Such antibodies may be anti-viral, anti-bacterial or antitoxic according to the offending antigen. Generally speaking immunity following systemic virus infections is more lasting than that following bacterial ones especially when the agent is of homogeneous antigenicity and single strain (measles, chicken-pox, mumps, german measles etc.), where second attacks are rare. But when more than one immunologic strain exist like in polio., influenza etc. second attacks may occur caused by different strains. Same is the case with common cold with the addition that being of superficial nature (on mucus membrane of respiratory tract), the immunity is also lost rapidly. Other viruses tend to run a prolonged course with relapses (trachoma, lymphogranuloma etc. probably due to failure of developing specific immunity.

Similar classification exists also regarding bacteria and toxins.

Acquired Artificial Passive Immunization :

Susceptible children can be *passively protected* by injection of human or animal sera containing particular antibodies. Such sera may be simple adult serum, convalescent serum, hyperimmune serum or gamma globulins. Again, the antibodies in such preparations may be antiviral, antibacterial or antitoxins either alone or in combination.

Examples for these are :

Measles : Gamma globulin administration within 3 days after first exposure to a known case of measles will avert the attack in most instances or almost certainly modify it. Given between 4 and 6 days after first exposure, there is reasonable chance of modifying the severity of attack and the patient probably will acquire lasting immunity to measles. If given later; little effects is to be expected. The dose is 0.25 ml. per kg. of body weight.

Diphtheria : Contacts below 10 years exposed and not previously immunized with toxoid may be given a prophylactic dose of diphtheria antitoxin 10,000

units. Persons previously immunized should have a reinforcing dose of toxoid (vaccine). Older children and adults, not immunized before should be examined daily for the disease and actively immunized by the vaccin (toxoid) given later.

Tetanus : In the absence of previous active immunization, passive protection of injured persons is indicated through injection of 1,500 to 2,500 units of tetanus antitoxic serum if the patient is seen on the day of injury, otherwise give double this dose.

For children previously actively immunized against tetanus, a single booster injection of tetanus toxoid is administered promptly on the day of injury.

This method of passive immunization allows immediate protection but for a short duration and so is used in emergency cases and in contacts. The drawbacks of this method are :

- a) Gives rise to sensitivity.
- b) May cause homologous serum hepatitis.
- c) Short period of protection.

Acquired Artificial Active Immunization :

The aim here is to lay down sound potential immunity i.e. once well immunized, always potentially immune. Such *active* immunization is done by inoculation with vaccines which may be viral, bacterial or of toxins. The agent used may be :

- Live attenuated (e.g. B.C.G., polio. "Sabin", etc.)
- Killed (e.g. T.A.B., polio. "Salk", etc.)
- Modified toxin (Diphtheria, tetanus etc.)

Solid immunity develops after two or three suitably spaced inoculations. A booster dose is recommended after one or several years because the basal immunity may wane due to rarity of subclinical infections that can raise the immunity. A re-inforcing dose is also needed in face of epidemics or on exposure to infection.

It should be noticed that the response of individuals to produce antibodies is different and is also influenced by many factors chief among which are :

State of antigen : Living or attenuated antigens induce high immunity of longer duration than the killed vaccines.

Amount of antigen : Up to a certain limit, larger doses of stimulation result in quantitatively greater antibody response.

Size of antigen : Large sized antigenic molecules, induce earlier and greater response.

Chemical nature of antigen : Better response is obtained by complex molecules than by simple ones.

Route of administration : The intradermal route which is intralymphatic, gives rapid response. Subcutaneous and intramuscular injections act as depot.

Adjuvant effects : Antigenic stimulation may be enhanced and sustained by incorporating the material with alum, oil etc.

Use of multiple antigens : Good response can occur to the individual components of a mixture of antigens at the same time. But, if a baby who started immunization against one disease, is given the rest of immunization by combined antigens, then the response will be almost exclusively for the first one only.

Presence of passively acquired antibody: This could interfere quantitatively with active immunization (e.g. diphtheria, measles and poliomyelitis.). Such circulating antitoxin or antibody levels may be acquired by the fetus through the placenta or given to the infant by injection.

The following schedule (table 1) may be a working one for routine active immunization both primary (basal) and booster (re-inforcing doses) in our country :

Table 1 : Scheme for active immunization of normal infants and children.

	Age	Vaccine	Route and Remarks
Primary Immunization:	1 st month	B.C.G.	Intradermal or oral
	2 nd „	Small-pox ??	Multiple pressure or scratch
	3½ - 4 „	D.P.T.	Intramuscular
		Polio. (Sabin)	Oral
	5½ - 6 „	D.P.T.	I. M.
		Polio. (Sabin)	Oral
	7½ - 8 „	D.P.T.	I. M.
		Polio. (Sabin)	Oral
Booster Doses :	11 th -15 th „	Measles	Subcutaneous
	12 th „	B.C.G.	If not given before, it should be given only to tuberculin negative.
	15 months	D.P.T.	I. M.
		Polio. (Sabin)	Oral
	3-6 years	D.P.T.	I. M.
		Polio. (Sabin)	Oral
	6-10 „	Diphtheria & tetanus.	„ „ „ „ 10 „

Other vaccines may be used or are needed under certain circumstances such as :

Rubella vaccine : German measles live virus vaccine may be used between the first year and puberty. Vaccination of adult women may also be carried

out, but precautions are necessary to make sure that the woman is not pregnant when vaccinated and will not become pregnant for 3 or more months following vaccination. This is because a short viremia follows immunization and the virus may persist in the nasopharynx for up to 50 days. The vaccine is administered as a single subcutaneous injection. Criteria for possible recall doses remain to be determined.

Mumps vaccine : A live attenuated mumps vaccine is now commercially available. It is efficient and the protection afforded by it appears to be long-lasting. Because mumps is considered a relatively benign disease, its use will probably be limited to adolescent and adult males who have not had the disease. It can be given to children over the age of 12 months. The three-in-one vaccine against measles, mumps, and rubella offer a practical method of acceptance for mumps vaccination.

Typhoid-paratyphoid vaccine : Is recommended in endemic areas or in presence of a known household carrier and similar conditions. The antibody response is not high during infancy. Booster doses are needed every 2 years.

Cholera vaccine : May be given for persons going to endemic areas and in face of threatening epidemics. It is not very effective and should be repeated every 6 months,

Precaution and contra - indications :

Although prevention of communicable diseases by routine active immunization is an important aspect of preventive pediatrics, yet certain precautions and contra-indications must be recognized. Because adequate antibodies against diphtheria, poliomyelitis and to a less extent small-pox are transmitted from the mother to her infants, they are protected against these diseases during the first few months of life and their response to active immunization is interfered with by these antibodies. Therefore, we have either to wait 3 or 4 months or to start early using a potent antigen to be followed by booster doses later on.

—All children to be vaccinated against infectious diseases should have preliminary medical examination for the purpose of discovering any contra-indication such as acute infectious disease, any pyrexia, acute gastroenteritis, nephritis, heart failure, active tuberculosis or rheumatism, diabetes, eczema etc.

— It is recommended that initial vaccination against small-pox be done during the first year of life to avoid the likelihood of encephalomyelitis and severe constitutional reactions. Because of the geographical situation of Egypt, vaccination is done during the first 3 months for fear of possible imported cases. The

site of vaccination should be inaccessible in order to avoid scratching and auto-inoculation vaccinia which is usually seen on the eye lids, cornea, oral cavity, tongue, vulva and/or perineal region. Scratching or neglect may cause contamination giving rise to cellulitis that needs antibiotics. Eczematous babies should not be vaccinated or come in contact with recently vaccinated infants in order to avoid generalized eczema vaccinatum which occurs either by direct contact or through blood. Hematogenous spread or failure to produce antibodies due to agammaglobulinemia may cause also gangrenous vaccinia which affects the skin, mucosa or internal organs. Generalized vaccinia rashes resembling those of measles, scarlet or vaccinia itself are also hematogenous complications. Epilepsy is a contra-indication to vaccination. If it is necessary to vaccinate under such conditions give hyperimmune vaccinal gamma globulin (0.6 ml./ Kg.) or big doses of gamma globulin. These can also be used and repeated as required in treating cases of generalized vaccinia, eczema vaccinatum and lesions due to autoinoculation occurring in dangerous sites. The antiviral agent N-methylisatin B-thiosemicarbazone (marboran), given orally as a 10 per cent suspension, has appeared to be effective in some cases of agammaglobulinemia when the previous measures fail. (This is History now-1983) #

If the child has an active clinical or subclinical enteric virus infection and is given orally an attenuated enteric virus like the live polio. vaccine, interference takes place and no or little antibodies against polio. are thus elaborated. Under such circumstances "Salk" polio. vaccine by the I.M. route should be administered and later on the live oral vaccine may be given. The milk of the mother contains specific circulating antibodies which also interfere with oral polio. vaccine. Therefore, it is recommended to avoid putting the infant to the breast an hour or more before and after giving the oral polio. vaccine.

B.C.G. inoculation is contra-indicated in premature and underweight infants and in children with infectious skin diseases. Complications may follow the administration of this vaccine, chief among which are : a) — Persistent ulcer at the site of vaccination, b) — Regional suppurative lymphadenitis, c) — Marked lymphadenitis with cold abscess and tuberculous sinus, and d) — Generalised B.C.G. infection especially in infants with deficient immune mechanisms.

If a severe reaction or febrile convulsions occur in an infant after the first dose of diphtheria - pertussis - tetanus vaccin, diphtheria and tetanus antigens only should be used for the remainder of immunization.

Infants suffering from cerebral damage should not be immunized during their first year of life. For such babies, fractional doses of single antigens should be employed.

Because patient receiving steroids may not develop good immunity from active immunization, it is important to postpone any immunization until treatment with steroids can be discontinued.

A. S. ABBASSY

Chapter III

GENETICS

THE GENETIC CODE

The genetic material lies within the nucleus and is part of the chromosome of all living cells. It has been identified as desoxyribonucleic acid (DNA). The DNA molecule consists of two coiled strands of polynucleotides. Each nucleotide is composed of phosphate and sugar (*desoxyribose*) linked together by a nitrogenous base (*purine or pyrimidine*). The DNA has two functions. First, it is able to synthesize or replicate itself, by uncoiling. Second, the order of the nitrogenous bases of the DNA acts as the Genetic Code that determines the development and metabolism of cells. DNA accomplishes this by directing the synthesis of ribonucleic acid (RNA). RNA in turn, determines the amino acid composition of the proteins, and hence, their function.

NORMAL CHROMOSOMAL PATTERN

Chromosomes are composed of thousands of genes, which are the basic units of heredity. The number of chromosomes is species specific. In man, the normal somatic cell contains two similar sets of chromosomes (*diploid number*), while the gamete contains a single set (*haploid number*). The somatic cell therefore contains 46 chromosomes (22 pairs of autosomes, and one pair of sex chromosomes; XX in females, and XY in males). The male gametes contain 23 chromosomes; 22 autosomes and one X or Y sex chromosome while the female gametes contain 22 autosomes and one X sex chromosome.

The chromosomes are classified according to their length and position of their centromere (constriction) into 7 major groups (A,B,C,D,E,F. & G).

CHROMOSOMAL ABERRATIONS

Chromosomal aberrations can be separated into 2 categories :

1) Abnormal chromosomal number — this usually results from lag or non-disjunction during meiosis or early mitosis. This will result in a cell having a single chromosome instead of a particular pair (*monosomy*), and another cell having 3 chromosomes (*trisomy*).

The presence of an extra autosome alters genetic balance and distorts development, while absence of an autosome is lethal. An extra X or Y also distort development, but only lack of any X at all is lethal.

2) Abnormal breakage and fusion — here, there is a normal chromosomal

number, but a certain chromosome has an extra piece (*translocation*), or lacks a certain part (*deletion*). Examples :

Monosomy	45 chromosomes	22 pairs + X	Turner's
Trisomy	47 chromosomes	23 pairs + 1	Mongol
	47 chromosomes	due to XXY	Klinefelter's

NUCLEAR SEX

The presence of an XX chromosomal pattern in females and an XY chromosomal pattern in males was a puzzle, in view of the fact that the X chromosome contains more genetic material than the Y. However, it was found out that one of the XX chromosomes in the somatic female cell is inactive, and can be seen condensed as the «sex chromatin» or «Barr's Body» throughout the post-natal life.

Subsequent studies of individuals with abnormal numbers of the X chromosome revealed that the number of Barr's Bodies is equal to the number of the X chromosomes minus one. This is the basis of the buccal smear test. In a normal female, most of the cells will be chromatin positive, i.e. there will be one Barr's Body in the cell. In females with Turner's syndrome (XO) there will be no Barr's Body, and they will be termed chromatin negative. In males with Klinefelter's syndrome (XXY), there will be one Barr's Body, while in females with (XXX) pattern two Barr's Bodies are found.

PATTERNS OF INHERITANCE

There are 3 main hereditary patterns, these are : autosomal dominant, autosomal recessive, and sex or X-linked traits. In a strict sense, a dominant trait is one whose effects are the same whether the related gene is homozygous or heterozygous. A recessive trait is one which does not express itself unless the related genes are homozygous. The combination of a pair of similar genes is called homozygous, while the combination of dissimilar genes is heterozygous.

Autosomal Dominant Traits : In general, it is convenient to speak of a dominant trait as that which can manifest itself in a heterozygous state. Individuals who are homozygous for a dominant trait are so infrequently encountered in nature that the possibility of their existence can be neglected, and all matings of affected and normal can be assumed to be of the Aa X aa type (A = autosomal dominant gene). Figure -2- is a hypothetical pedigree illustrating the possibilities for the offsprings of such a mating.

The characteristics of autosomal dominant inheritance are :

- The trait is transmitted directly from affected person to affected person.
- The 2 sexes are affected in equal number.

- Children of an affected individual have a 50% chance of being similarly affected.
- Absence of affected children from normal parents.

However, skipping of one or more generation may rarely occur and a normal appearing offspring of a person with the trait will produce an affected offspring. Again, an affected person may develop the trait as a result of mutation of the gametes of one of his normal parents.

Examples of autosomal dominant traits in man are found in chondrodystrophic dwarfs, neurofibromatosis, tuberous sclerosis and Huntington's chorea.

Autosomal Recessive Traits : Here, the clinical manifestations of the trait show themselves only in the homozygous state. Both parents of the affected individual are usually heterozygous for the trait in question. The mutant gene could be transmitted undetected from heterozygote to heterozygote for many generations. Fig. -2- is a diagrammatic representation of recessive inheritance.

The characteristics of autosomal recessive traits are : —

- Both parents and more remote ancestors of an affected individual are usually asymptomatic.
- The chances of having homozygous (AA), to heterozygous (Aa), to normal (aa) are 1 : 2 : 1.

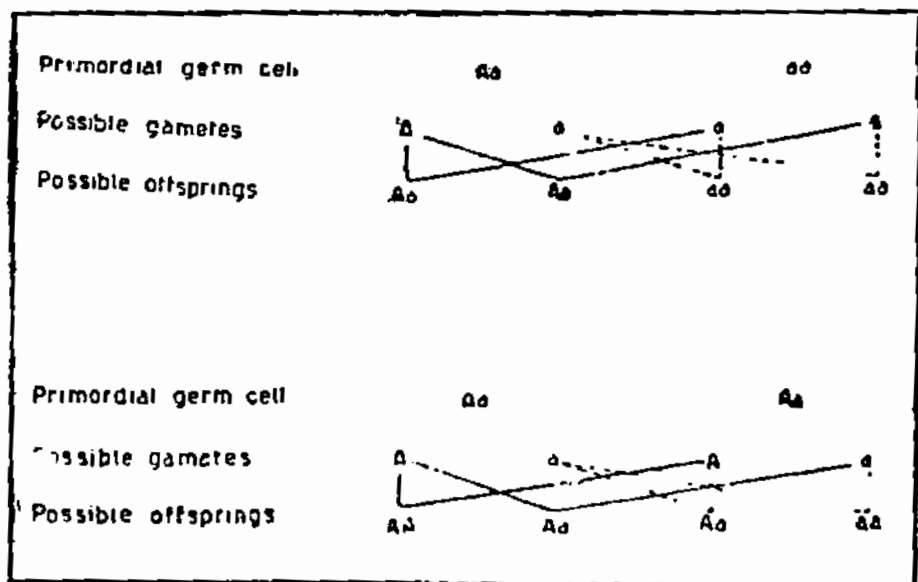


Fig. 2 : (Above) Autosomal dominant trait
(Below) Autosomal recessive trait.

-- Both sexes are equally affected.

— High incidence of consanguinity among parents of affected individuals.

Examples of autosomal recessive traits in man are found in phenylketonuria, galactosemia, maple syrup urine disease and many other metabolic diseases.

X-Linked Inheritance : The large X chromosome carries genes not present in the small Y chromosome; genes which apparently have actions other than those of sex determination. The female with her two X chromosomes is diploid with respect to all genes of the X chromosome, while the male with one X is always haploid to these genes. Accordingly, the features of dominant and recessive X-linked inheritance differ from those of autosomal inheritance.

Dominant X-linked inheritance is characterized by :--

— The trait is transmitted from affected person to affected person.

— Affected males will transmit the trait to their daughters, but not to their sons.

— Affected females transmit the disease to both sons and daughters equally.

Recessive X-linked inheritance is characterized by :

-- The trait shows distinct discontinuities in its descent from generation to generation.

-- Affected males will not produce affected children.

-- Affected males are offsprings of normal females who tend to produce as many affected as non-affected males.

At least 40 X-linked pathologic traits are known in man. The majority of these traits are recessive, and they include hemophilia, colour blindness, ichthyosis and anhidrotic ectodermal dysplasia.

The Effect of Environment on the Developing Embryo

It is well understood now that environmental agents, as well as genes, can be of great influential effect on the development of the organism.

The zygote carries the potential for the mature adult. The only defects that are liable to start in the early stages of cleavage are those known to be associated with gross chromosomal aberrations like non-disjunction, translocation or abnormality of the structure of individual chromosomes. Until now, the only documented factor in man known to produce such accidents of cell division is maternal aging.

Teratogenic environmental factors are mostly effective during the early phases of organ morphogenesis, when the process of cell proliferation and tissue differentiation is highly active. Later in development, after differentiation

has taken place and the fetal membranes have formed, a noxious agent does the most damage to those cells which are growing fastest.

Since morphogenesis of various organs occurs at different developmental times, it follows that different organs are affected at different stages of development. The specificity of the agent, dosage and genetic variations among individuals are as important as the time factor.

The effect of a teratogenic factor may be inhibition of growth and development, hypertrophy, atrophy, splitting or fusion of tissues in abnormal ways.

Factors which are known to affect adversely the course of development in the embryo are :

1. *Physical Agents* -- X-ray irradiation, hypothermia, hypoxia and elevated carbon dioxide level, have all been found deleterious in animals. In man, therapeutic and diagnostic x-ray procedures within the first two months of pregnancy are accompanied by a considerable proportion of abortions and a high incidence of malformed children. The reported abnormalities in such cases include microcephaly, microphthalmia, skeletal or genital abnormalities, spasticity and mental retardation.

2. *Maternal Infections* — Some infections which are trivial and inconsequential in the mother, can be disastrous to the developing embryo. Other conditions which produce profound illness in the mother appear to cause little damage to the fetus. German measles acquired a great current interest. A high incidence of abortions and stillbirths is reported among mothers who develop the disease before the twelfth week of gestation. The chief defects in affected live born babies are cardiac abnormalities, cataracts, deafness, microphthalmia and mental retardation.

Intrauterine infection with the virus of Cytomegalic Inclusion Disease can lead to microcephaly, hydrocephaly, spasticity, optic atrophy and chorioretinitis.

Other viruses which are highly suspicious of having similar teratogenic effects include mumps, herpes zoster, vaccinia, influenza, serum hepatitis and equine encephalitis.

Toxoplasmosis, caused by a protozoan parasite, can pass the placental barrier causing hydrocephaly, microphthalmia and chorioretinitis in affected babies.

Congenital syphilis is held responsible for mental retardation and nerve deafness.

3. *Drugs* — Within recent years, the effect of drugs administered to the mother has received increased attention. The mechanisms by which the drugs act may be as variable as their biochemical activities. Only few drugs have documented teratogenic effects. Thalidomide, a tranquilizer, is probably the most famous. Affected infants showed phocomelia, gastrointestinal, cardiac and urinary system abnormalities.

Antimetabolites as aminopterin and amethopterin were reported to produce similar defects. Ingestion of progestins, androgens and estrogens cause masculinization of female newborns. Few cases of hare-lip and cleft palate were reported after massive corticosteroid therapy.

Since the list of drugs with undocumented untoward effects on the fetus is constantly growing, the safest rule is to use as few drugs as possible in pregnancy, and to avoid all drugs unless their need is essential.

SALAH HAMMAD

Chapter IV

GROWTH AND DEVELOPMENT

The chief feature which sets infants and children apart from the adult is the dynamic character of growth and development. An understanding of these processes is necessary to be sure that the infant is growing normally, to diagnose any deviations early and to advise and guide parents regarding them.

The term *growth* has commonly been used to indicate natural increase in size, i.e. weight and length as well as the size of different organs; this is achieved by cell multiplications and by increase in the intercellular substance.

The term *development* signifies maturation of organs and systems, gaining of skills, ability of adaptation and ability to assume responsibilities.

In years from conception to maturity, the child goes into various stages which are : embryo, fetus, perinatal, neonatal period (first 4 weeks), infancy (first 2 years), the preschool age (2nd to 6th year), school age (6th to 12th year) and the adolescent period.

The main problems of various age periods are :-

Intrauterine period :

1. *Genetic disturbances* resulting in inborn errors of metabolism and other congenital anomalies (chapter III).
2. *Chromosomal aberrations* including trisomies, translocation and mosaicism.
3. *Environmental disturbances* as trauma, undernutrition, irradiation, infections, toxic drugs, diabetes mellitus. etc., to which the pregnant mother is subjected to, might injure the embryo or fetus.

Perinatal period : This period extends from the start of labour till the end of the first 24 hours after birth. Many thousands of infants

die or suffer from :-

- *Birth injuries* due to prematurity, precipitate labour, improper use of forceps... etc. that may ultimately lead to crippling.
- *Poisoning* due to sedation or anesthesia of the mother may lead to respiratory failure in the baby. This needs immediate and adequate clearing of the air passages and may be resuscitation also.
- *Hypothermia* should be given enough care especially in prematures, otherwise sclerema develops and may be fatal.

- *Infections* acquired at this time as gonorrheal ophthalmia, oral moniliasis, salmonellosis, listeriosis, herpes simplex or bacterial pneumonia could be fatal.

Neonatal period : This period of transition from intra-uterine to well established independent extra-uterine life is the most critical period in the whole life of the individual. The physiologic changes or adjustments of respiration, circulation... etc., may pass peacefully or they may become pathologic leading to particular diseases of the newborn. These together with prematurity, congenital malformations, birth injuries and cross infections are the main causes of the high mortality rate during the neonatal period.

Infancy period : This is the period of most rapid extrauterine physical and mental development. During this period the baby is dependent on others for maintenance and he is more susceptible to infections and nutritional disorders. He has some degree of passive immunity during the first 4 - 6 months of life for measles, poliomyelitis, diphtheria and scarlatina if the mother has had them, but not for other common contagious diseases or for pneumococcal, staphylococcal, or influenzal infections. Primary immunizations are carried out during this period (chapter I).

Preschool age period : (Toddler age) This is a safer period than that of infancy. A guiding hand is needed for such a baby who is exploring his world. The parents must not prohibit the child from developing his own natural pattern. Adequate nutrition, boosting of immunization against the preventable diseases and care to avoid the non-preventable ones, —especially the accidents are of importance during this period (chapter I).

The goal is a physically sound, mentally alert and socially adjusted candidate for entrance to school.

School age period : Infections, cardiac disturbances, accidents and malignant diseases are the main causes of death in this period.

Confidence and love must be given continuously to prevent emotional troubles.

With a well planned school health program, together with the co-operation of parents, the goal of physically sound, mentally alert and socially adjusted pre-adolescent child could be reached (chapter I).

Adolescent age period : In this age of the young adult there are tremendous physical and psychological problems. The understanding of the problems is very essential to avoid serious complications and to adapt the adolescent in the society.

Factors affecting growth and development :

There is an inherited capacity of the skeletal system and other tissues to grow and to respond to the appropriate hormonal stimuli in the presence of good nutritional supply, and health environment. The inherent growth potentiality of various tissues interacts with the following factors : —

1. *Heredo-constitutional factors* : These are responsible for the characteristics of the individual pattern of growth, for certain anomalies, for some familial diseases and certain types of short stature. Difference in sex and race are amongst the most important heredo-constitutional factors.

2. *Congenital defects* : These may be due to heredo-constitutional factors or to abnormal environment during the embryonic period. They can interfere with fetal or postnatal growth in a variety of ways.

3. *Endocrine factors* : These can produce normal variations and they account for many of the growth deviations.

4. *Environmental factors* : The nutritional state of the pregnant mother, infectious diseases and pathological conditions that affect her have got a marked effect on the growth and development of the embryo. During infancy and childhood, the socioeconomic condition of the family has got an effect on the growth and development.

5. *Nutritional factors* : Growth of the baby depends on adequate consumption and proper utilization of suitable types of food. Specific deficiencies cause sometimes characteristic deviations from normal growth as in rickets.

6. *Activities* : Normal growth and development depend upon normal activity. A bed-ridden child would not grow as much as an active one.

7. *Injuries and illnesses* : during birth or later on can cause permanent damage to vital organs.

ASSESSMENT OF GROWTH

A number of methods have been proposed to assist the physician to evaluate that growth progresses in a regular and orderly sequence. Tables, charts and grids are available to facilitate the physician's evaluation of physical growth. In addition to the observation over a period of time, the periodic assessment of infants and children permits the early detection of growth deficiencies and pathologic processes, both organic and psychologic.

Mean And Percentiles For Weight According to Age
(Males)

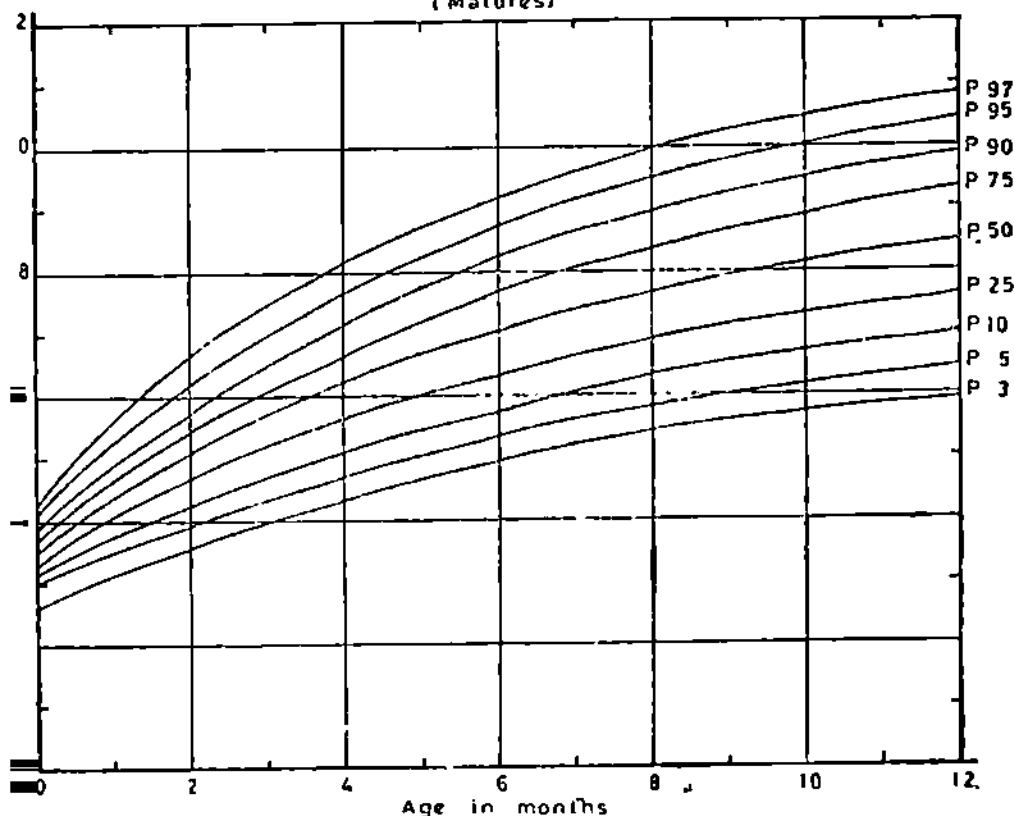


Fig. 3 Gain in weight of Egyptian infants during the first year of life.

(ABBASSY *et al.*, 1972)

In practice, a few selected measurements should be routinely obtained. In infants these may include the weight, the head circumference, chest circumference and total length. In the presence of an obvious growth aberration, a more detailed assessment may be performed. Anthropometric charts provide a means of comparing measurements of physical growth with those of other children of similar age and sex. These charts demonstrate the wide range of normality among children of the same chronologic age. These differences are described according to percentile rankings, that is if a particular child's weight falls in the twenty-fifth percentile, he weighs more than 25 per cent of other children of his age but less than the other 75 per cent. Comparison of the percentile rankings of a child with those of previous examinations should be made in order to detect any significant acceleration or deceleration in his rate of growth, i.e. the child

may be compared with others of the same age, but much better with himself (Fig. 3).

Not all physical measurements of a child necessarily fall into the same percentile channel, but each measurement with healthy growth, tends to follow its own channel.

Growth during the intranuterine period :

The period of intrauterine life may be divided into two principal phases : the embryonic phase and the fetal phase. The dividing line between these phases is not sharp.

The embryonic period : This is considered to be the first 12 weeks during which the fertilized ovum differentiates rapidly into an organism with the gross-anatomic features of the human subject

The fetal period : The period after the 12th week of gestation and through the 40th week, is distinguished by rapid growth and elaboration of function.

Before the 28th week the fetus is considered as pre-viable and from 28th week until term as viable. During the early weeks the fetal rate of gain in length is greater than the rate of gain in weight. By the end of the first trimester of pregnancy the sex of the fetus can be distinguished.

During the second trimester of pregnancy there is rapid growth especially linear and in acquisition of new functions. By the end of the 28th week the fetus weighs 1200 Gm and is about 35 cm. in length.

In the third trimester the further increase in size involves mainly the muscles—and subcutaneous tissues. The following table shows the average fetal growth—in length and weight.

Table 2 : Average fetal growth in length and weight.

Intrauterine age in weeks.	Weight in Grams.	Length in centimeters.
12	14	9
16	110	16
20	300	25
24	600	30
28	1200	35
32	1700	40
36	2500	45
40	3300	50

Growth during the postnatal period :

The patterns of growth vary at different ages. At birth the proportion of the weight of organs in relation to the total body weight is not as that of the adult, e.g. the proportion of the muscle mass is less than its proportion in the adult being 25 % of the total body weight in infancy and 43 % in adulthood. The proportion of the skeleton, lungs and the stomach is the same as in the adult, while the rest of the organs have greater proportion than in the adult e.g. the liver is 5% in infancy and 2% in childhood. Thus the different organs follow in their growth various patterns.

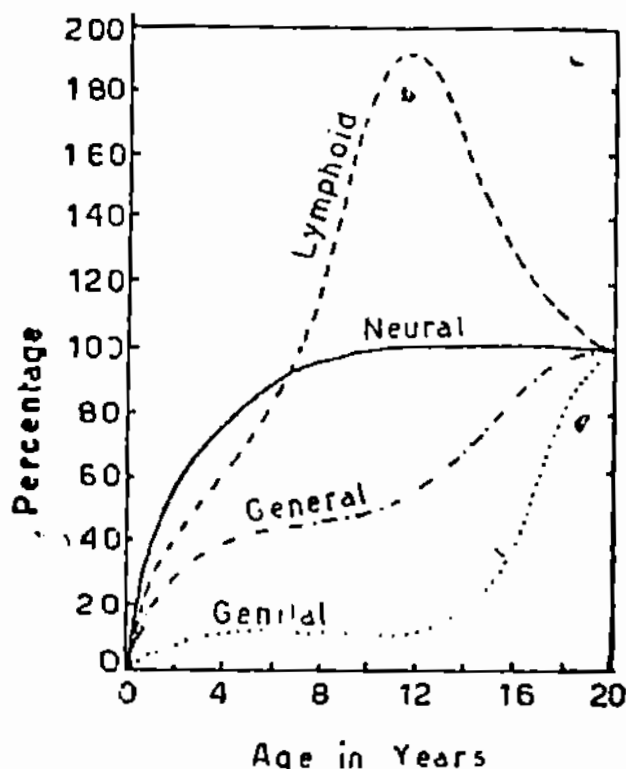


Fig. 4 : Main types of postnatal growth of the various parts and organs of the body (After Scammon).

There are 4 characteristic growth patterns, the lymphoid (includes the lymphoid tissues and the tonsils), the neural (the brain), the genital (includes the external and internal genitalia) and the general (includes the rest of the organs mainly the skeleton, the muscle, the liver, etc.) (Fig. 4).

There is a number of deviations from these growth curves e.g. the uterus is relatively large at birth with subsequent involution. Also the heart is initially

large compared to body size, then it follows the general growth curve, and the thymus follows the general pattern during the first years and then remains steady till the adolescent age then diminishes. The subcutaneous tissues increase up to the 9th month, then diminish up to the 6th year, lastly they increase again up to puberty.

Growth of the head: Six fontanels are usually present at birth, the anterior and posterior are the most important ones. The posterior closes by the 2nd month and sometimes at birth while the anterior closes between the 4th and 26th months of age (10 - 14 average).

The maxillary and ethmoid sinuses are present at birth and get aerated at the 6th month, the sphenoid sinus is usually pneumatized at the third year while the frontal sinus is usually pneumatized at the sixth to ninth year.

Growth of the brain can be followed by following the normal increase in the head circumference. At birth the circumference of the skull is 13.8 inches (35 cm), at the end of the first year it is 18.3 inches (45 cm), at the second year 19.4 (48 cm), at the third year 19.6 (49 cm), fifth year 20 (50 cm), seventh year 21 (52 cm) and the adult head circumference will be 22 inches (55 cm). The cranial sutures ossify completely in late childhood or early adult life.

Growth in chest and abdomen: The chest and abdominal circumferences are equal in the first 4 years. The abdomen tends to be prominent in infants and young children.

Growth in length: The neck and extremities are relatively short and the head is relatively large at birth and the ratio of the upper to the lower segment of the body is 1.7 : 1, then the legs will grow more rapidly than the trunk and the ratio becomes 1 : 1 at the twelfth year of age.

During the first year of life the infant gains in length roughly 2 cm/month during the first 6 months and 1.5 cm/month during the second 6 months. A formula can be used after the first year of life to estimate roughly the length of the child before puberty :

$$(\text{Age in years} \times 5) + 80 = \text{Length in centimeters.}$$

Gain in weight: There is an initial phase of loss of weight after birth and most full terms regain their birth weight by the age of ten days. Then the weight gain averages approximately 20 - 25 gm./day. Roughly the newborn gains $\frac{3}{4}$ kg/month during the first four months of life, $\frac{1}{2}$ kg/month during the second four months and $\frac{1}{4}$ kg/month during the last four months of the first

year. Thus the average birth weight (3.25 kg) is doubled between the 4th-5th month and trippled by the end of the first year. A formula can be used after that to calculate the weight :

$$(\text{Age in years} \times 2) + 8 = \text{Weight in kg.}$$

Teething : Eruption of the teeth follows a special pattern and retardation of the dental development may indicate retardation in osseous development.

A. Eruption of the milk teeth : They erupt in the Egyptian infants in the following order (Abbassy et al. 1972) :—

Lower central incisors	.	.	.	.	.	7 - 8 months
Upper central incisors	.	.	.	.	.	8 - 9 »
Upper lateral incisors	.	.	.	.	.	10 - 11 »
Lower lateral incisors	.	.	.	.	.	11 - 12 »
First deciduous molars	.	.	.	.	.	13 - 14 »
Canines	.	.	.	.	.	17 - 19 »
Second deciduous molars	.	.	.	.	.	19 - 25 »

B. Eruption of the permanent teeth :

First molar	.	.	.	.	.	6 - 7 years
Central incisors	.	.	.	.	.	6 - 8 »
Lateral incisors	.	.	.	.	.	7 - 9 »
Canines	.	.	.	.	.	9 - 11 »
First premolar	.	.	.	.	.	10 - 12 »
Second premolar	.	.	.	.	.	11 - 13 »
Second molar	.	.	.	.	.	12 - 13 »
Third molar (wisdom tooth)	.	.	.	.	.	17 - 22 »

The osseous maturation : There is no better index of general growth than bone age as determined from X-ray films by the following data :—

- 1 The number and size of epiphyseal centers.
- 2 The size, shape, density and sharpness of outline of the ends of bones.

3. The distance separating epiphysis and metaphysis or the degree of fusion between these two elements

The hand and wrist are useful at all ages of childhood, and useful information can also be derived from the lower limb especially in early infancy

The ossification centers usually present at birth in full term infants are those of the distal end of the femur, proximal end of the tibia, the head of the humerus, the calcaneus, the talus and the cuboid. Usually the carpal centers are not present at birth, but appear about two months of age. Two carpal centers are present at one year of age, and in general, one additional carpal center appears each year, so that seven are present at six years of age. During the third year of life, the metacarpal and phalangeal epiphyseal centers are demonstrable radiologically. The distal radial epiphysis is usually present by the first year, and the distal ulnar epiphysis appears in most girls between the ages of six and eight years, and in the majority of boys between seven and ten years.

In general, the ossification centers appear in a definite sequence. As in other aspects of growth and development one must allow for a range of individual variation, less in infants and greater in adolescents. Skeletal development in girls is advanced over that of boys, slightly so at birth, but as much as two years at puberty. In girls, a sesamoid bone appears at the distal end of the first metacarpal, one or two years before the menarche.

ASSESSMENT OF DEVELOPMENT

Development is a continuous process from conception to maturity.

The sequence of development is the same in all children, but its rate varies from child to child and the progress in one field does not necessarily run parallel with that in another field. The direction of development is cephalocaudal, i.e. the infant controls his head before he can sit, and crawls before he can walk.

The developmental process is intimately related to the maturation of the nervous system, i.e. the brain must be ready before the child can perform any new ability. At birth, the cerebral cortex is not completely myelinated. So, the newborn is not capable of initiating any volitional activities, i.e. all his behaviour is reflex in nature, and as maturation proceeds the generalized mass activity is replaced by specific individual responses e.g. the young infant when excited moves his trunk, arms and legs but the older child expresses his excitation only with his face. The primitive reflexes such as the grasp reflex and the stepping reflex have to be lost before the corresponding voluntary movement is acquired.

The normal developmental faculties are usually classified into four major fields of behaviour which are : -

Motor behaviour : The motor capacity of the infant constitutes the natural starting point for estimating his maturity. Thus we have to consider head balance, sitting, standing, creeping, walking, approach to objects etc... i.e., the milestones (tables 3, 4, & 5).

Sensory-motor behaviour or Adaptive behaviour : It deals with the finer sensory motor adjustments to objects and situations e.g. co-ordination of eyes and of hands in reaching objects and in manipulations etc. . (tables 3, 4, & 5).

Language behaviour : Broadly it includes all visible and audible forms of communication whether by facial expression, movements, and/or vocalization. It gives a clue to the organisation of the infant's central nervous system (tables 3, & 4, 5).

Personal-social behaviour : This comprises the child's personal reactions to the social culture in which he lives. Therefore it will be variable. Bladder and bowel control, feeding abilities, self dependence, cooperation and response to training are examples. The following tables help to give a sound idea about development from birth to three years.

Table 3 : Development in the infant 1 — 34 weeks.

AGE ZONE	MOTOR	ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
4 Weeks	Lacks head control	Brief eye following	Impassive face	Stares at surroundings
	Asymmetric in supine position	Drops toy immediately	Small throaty sounds	Listens to sounds
16 Weeks	Head erect, slight babbling	Incipient approach to rattle	Coos	Spontaneous social smile
	Symmetric supine position	Regards rattle in his hands	Laughs aloud	Hand play
28 Weeks	Sits, leaning forwards	Reaches & grasps toy	Squeals	Feet to mouth
		Transfers toy	M - M sounds	

Table 4 : Development in the infant 35 weeks to 15 months.

AGE ZONE	MOTOR	ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
40 Weeks	Sits well, creeps	Combines 2 toys	Dada-mama	Nursery tricks
	Pulls to feet at rail	Picks pellet, thumb & index	One other word	Feeds self cracker
52 Weeks	Walks, one hand held	Cube into cup	Two other words	Co-operates in dressing
		Tries tower cubes	Responds «give it to me»	
1 $\frac{3}{12}$ Years	Walks alone, toddles	Tower 2 cubes	4 - 6 words	Points & vocalizes wants
		Six cubes into cup		Casts toys

Table 5 : Development from 15 months to 3 years.

AGE ZONE	MOTOR	ADAPTIVE	LANGUAGE	PERSONAL-SOCIAL
6 $\frac{1}{12}$ Years	Walks well alone	Towers 3 - 4 cubes	10 Words	Toilet regulated by day
	Seats self in a small chair	Imitates a stroke (1)	Jargon	Carries, hangs dolls
2 Years	Runs	Towers 6 - 7 cubes	Joins 2 - 3 words	Asks for toilet by day
	Up-down stairs alone	Imitates circular scribble	Names 2 - 5 pictures	Puts doll to bed etc
3 Years	Rides tricycle	Imitates house of cubes	Sentences	Feeds self well
	Stands on one foot momentarily	Imitates cross (+)	Gives full name & sex	Puts on socks, unbuttons

However, for a rapid bed-side evaluation of the state of physical and mental development, a battery formed from some of the 4 fields of development provides a sound diagnosis. The following is an example :-

First day	vigorous sucking.
3rd week	fixes bright light (squints).
1 month	raises chin when prone. smiles.
2 month	raises head when prone. coos.
3 »	holds head erect. co-ordinated eye movements.
4 »	voluntary grasping. laughs.
5 »	rolls from back to stomach. recognizes his mother.
6 »	remains sitting when put so. turns head to voice.
7 »	sits alone. transfers toy from hand to hand.
8 »	holds object between thumb and fingers. creeps to purpose.
9 »	stands supported. starts to speak.
10 »	walks supported. responds when called by name.
11 »	stands unsupported. uses pencil and paper.
12 »	attempts to walk alone. uses cup to drink.
18 »	walks alone. sphincters controlled by day.
24 »	runs. sphincters controlled by day and night.

M. M. ZEITOUN

Chapter V

THE NORMAL NEWBORN BIRTH INJURIES DISEASES OF THE NEWBORN

The "newborn" period is generally considered to be the first month of life.

The initial examination of the newborn is essential to detect any abnormalities and to establish a base line for subsequent examinations.

General appearance : The normal newborn declares his arrival to the world by crying and body movements.

Physical activity may be absent in the relaxation of normal sleep or depressed by central disturbances. The infant may be lying with motionless extremities in cases of respiratory distress, or he may be vigorously crying with accompanying activity of arms and legs. Coarse, tremulous movements with ankle or jaw clonus are common in normal newborn infants. Nutritional status is evidenced by the weight and the length and by wrinkling or smoothness of the body surfaces. Edema may be present specially in the premature infant.

Skin : It is usually red in colour, mottled, bluish red over the extremities, due to vasomotor instability and sluggish peripheral circulation. It may be dry, peeling and covered by lanugo over the face, shoulders and back.

The vernix caseosa (whitish or clay-coloured, cheesy, greasy material) may cover most of the body. Milia of face (distended sebaceous glands producing tiny pin-point papules) are frequently present and disappear within 2-3 weeks. Well demarcated areas of blue pigmentation known as Mongolian spots are common over buttocks and back. Transient capillary hemangiomas are common on the eye-lids and neck. Icterus of physiological nature may be present after the first few days. Pallor may indicate anoxia, anemia or shock.

The head : It is large in relation to the rest of the body and may exhibit considerable moulding with overriding of the cranial bones. The face may be asymmetric from persistent abnormal fetal posture. The eyes remain closed most of the time in early days and often open spontaneously if the infant is held up and moved gently forward and backward. Subconjunctival and retinal hemorrhage may occur.

In the mouth, labial tubercles are found on the upper lip, they disappear when the suckling period is over. On the hard palate on either side of the mid-line, there may be transient accumulation of epithelial cells (Epstein's pearls), which disappear later on.

Retention cysts may be seen on the gums. Precocious dentition is very rare. The throat is hard to visualize because of the steep arch of the palate. There is no active salivation. The cheeks are full due to the presence of the suckling pads.

During birth, the newly born is subjected to much compression, stretching and bending, specially if the labour is difficult or instruments have been employed to deliver the baby. It is therefore expected that injuries to the baby take place, these might affect the soft tissues or bones.

Caput succedaneum : This is a diffuse, edematous swelling of the soft tissues of the scalp involving the portion presenting during delivery. It disappears within the first few days of life.

Cephalhematoma : This is a subperiosteal hemorrhage. Unlike caput succedaneum it is limited by the borders of one or more cranial bones. Other points of distinction from caput succedaneum are: (a) There is no discoloration of the overlying scalp due to subcutaneous hemorrhage as in caput succedaneum, (b) The swelling is not usually present for several hours after birth. Subperiosteal bleeding is a slow process.

In approximately 25% of cephalhematomas there is an underlying skull fracture. It is rarely of the depressed type, although a sensation of central depression is usually encountered on palpation of the organized rim of the cephalhematoma.

A meningocle is differentiated by the presence of pulsations, increased pressure on crying and the X-ray evidence of bony defect.

Cephalhematomas begin to calcify by the end of the second week. Most are resorbed during the first six weeks of life. A few remain as bony protuberances for years. They require no treatment. Puncture should not be done to avoid the introduction of infection.

Injury to the sternocleidomastoid muscle : A firm mass 1 to 2 cm. in diameter is occasionally noted in the mid position of the sternocleidomastoid muscle about the second week of life. It is believed by most to be a small hematoma caused by overstretching the muscle after the shoulder has been born in breech presentation, while others believe it to be a fibromatous malformation of the muscle.

The majority of these tumours resolve spontaneously within the first year of life, and any accompanying torticollis disappears. In the presence of torticollis and as a prophylactic measure, the mother can be taught to overextend the affected muscle twenty times on two or three occasions daily. If torticollis persists beyond one to two years, surgical correction may be undertaken.

NERVOUS SYSTEM

The cerebral cortex participates very little in the function of the central nervous system during the neonatal period.

The developmental process is intimately related to maturation and myelination of the nervous system (chapter IV).

The most constant evidence of neurologic abnormality in newborn and young infants is failure of development of reflex patterns appropriate to age. Persistence, reappearance or exaggeration of some of these reflexes may also indicate an abnormal nervous system. The following reflexes are present in the normal newborn infant :—

Normal Reflexes :

The Moro reflex : is generalized extension of trunk and extension and abduction of limbs, followed by flexion and adduction. It can be elicited by a hand clap or slap on the mattress, while the infant is supine and quiet. It is a good index of normal reflex irritability. Consistent absence of the reflex bilaterally suggests brain damage. Unilateral absence of the reflex indicates brain damage, fracture or obstetrical palsy. The reflex normally disappears in the first few weeks of life.

The tonic neck reflex : with the infant supine, turn the head sharply to one side, the arm and leg on the side to which the jaw is turned extend, the limbs of the opposite side flex. In normal newborn infants this reflex may be incomplete, often more definite in lower than in upper limbs. It tends to disappear during the first year, but partial responses may persist until the second or third year. Persistent asymmetry or complete and easy excitation of the full response suggests a cerebral lesion.

Placing and Stepping reflexes : Examples of these reflexes are :

The prone newborn tries to make crawling movements. When held erect with soles flat on the table, head and trunk inclined forwards, he takes regularly alternating steps. If the dorsum of the foot is drawn against the under edge of the table top, the foot is lifted and placed on top of the table.

Suckling reflex : stroking the lips produces suckling.

Rooting reflex : stimulation of the side of the cheek or the upper or lower lip causes the infant to turn his mouth to the stimulus.

Grasp reflex : stroking the palmar surface of the metacarpophalangeal joints towards the fingers bring out a sudden grasp reflex followed by maintained contraction, if the stimulus is continued. The reflex is normally present in infants under four months of age; if it persists to later ages it suggests frontal lobe lesions.

Abdominal reflexes : are generally present but sluggish.

Planter response : is usually extensor.

Chvostek's sign : can often be elicited in healthy newborns.

Blinking and pupillary light reflexes, sneezing, coughing and withdrawal with painful stimuli are present in the newborn.

Intracranial hemorrhage : Intracranial hemorrhage results usually from trauma or anoxia to the brain and rarely from primary hemorrhagic disturbances or congenital vascular anomalies. Traumatic hemorrhage occurs in breech, precipitate deliveries or when there is mechanical interference in delivery. Intracranial hemorrhages may occur in infants, especially prematures delivered spontaneously without apparent trauma. The hemorrhage may be subarachnoid, intracerebral or intraventricular.

Clinical manifestations : Signs of intracranial hemorrhage may be present at birth or may not appear for a variable time after delivery. The commonest signs to appear soon after birth are general failure to move normally, diminished or absent Moro reflex and lethargy. Marked irregularity of respiration in the absence of other signs of respiratory distress is often a sign of severe hemorrhage.

Pallor, cyanosis, cyanotic attacks, failure to suck well, forcible vomiting, anxiety and restlessness, a high-pitched shrill cry, muscular twitching, convulsions or paralyzes may be the first indication that an intracranial hemorrhage is present. The fontanel may be tense and bulging. Retinal hemorrhages, ocular palsies, irregularity in the size of the pupils, and their failure to react to light or nystagmus may be observed.

Diagnosis: This is based chiefly on the history of delivery, the clinical manifestations and the course. Lumbar puncture is indicated in the presence of signs of increased intracranial pressure to identify gross subarachnoid hemorrhage, to rule out the possibility of bacterial meningitis and possibly to relieve pressure

on vital centers. Since a small amount of bleeding often occurs in the course of normal deliveries, small numbers of red blood cells or slight xanthochromia in the subarachnoid fluid is not necessarily indicative of significant intracranial hemorrhage. Conversely, the subarachnoid fluid may be absolutely clear with severe subdural or intracerebral hemorrhage.

Prognosis : Fatalities usually occur within the first three days and result from respiratory failure. If an infant survives, recovery often may be complete, or there may be permanent residuals e.g. mental retardation or cerebral palsy. Subdural effusions may follow. Prevention is through better obstetric management.

Treatment : The infant should be handled as little and as gently as possible. A small dose of vitamin K (0.5-1 mg.) should be administered. Oxygen is administered for cyanosis and sodium phenobarbital to control convulsions. A small transfusion of fresh blood (10 ml. per kilogram) is indicated in the presence of hemorrhagic disease of the newborn. Spinal punctures may be done for the relief of increased intracranial pressure and to remove gross blood in order to reduce its irritant effect on the cerebral cortex and to prevent possible interference with the normal absorptive mechanisms for cerebrospinal fluid.

Injuries of the spine and spinal cord : Such injuries are most likely to occur when difficulty is encountered in delivering the shoulders in cephalic presentations and the head in breech presentation. The injury is most commonly at the level of the seventh cervical and the first thoracic vertebrae. Transection of the cord may occur, but hemorrhage and edema may produce similar neurologic signs which are not permanent.

Peripheral nerve injuries :

- (a) *Brachial palsy :* Injury to the brachial plexus may occur when traction is exerted on the head during delivery of the shoulder in a cephalic presentation or on the shoulder during delivery of the head in a breech presentation.

Erb-Duchenne paralysis : the injury is limited to the fifth and sixth cervical nerves. The characteristic position consists in adduction and internal rotation of the arm with pronation of the forearm. The Moro reflex is absent on the affected side. The power in the forearm and the hand grasp are preserved unless the lower part of the plexus is also injured. When the injury includes the phrenic nerve, alternation of the diaphragmatic excursion on the affected side may be observed under the screen.

Klumpke's paralysis : is a rare form of brachial palsy. Injury to the seventh and eighth cervical nerves and the first thoracic nerve produces a paralyzed hand. Ptosis and miosis are present if the sympathetic fibers of the first thoracic root are also injured. Differentiation of both the two types of brachial plexus palsy must be made from cerebral injury, fractures of the clavicle or bones of the upper limb, dislocation and epiphyseal separation of the humerus.

If the paralysis was due to edema and hemorrhage, and the nerve fibers are intact, there should be a return of function within a few months, if due to laceration, permanent damage may result

Treatment consists in relaxation of the paralyzed muscles by preventing the antagonistic pull of the nonparalyzed muscles. While the infant is in his crib, the wrist can be held by a clove-hitch to the head of the bed so that the arm is maintained abducted and rotated externally with the elbow flexed. If the hand is paralyzed, padding should be placed in the fist. Physical therapy is a necessary adjunct to the treatment. If the paralysis persists for two or three months because of laceration of the nerve fibers, neuroplasty offers hope for partial recovery.

- (b) *Phrenic nerve paralysis* : It is usually associated with brachial palsy. In this condition breathing is thoracic and laboured and cyanosis may be present. Breath sounds are diminished on the affected side. Screen examination reveals the elevation of the diaphragm on the paralyzed side, and the scesaw movements of the two sides of the diaphragm during respiration.

There is no specific treatment, the infant should be placed on the involved side. Oxygen therapy may be necessary. Feeding by gavage should be carried out to save the infant's energy. Recovery usually occurs within few weeks. Pulmonary infections are serious complications.

- (c) *Facial nerve palsy* : This occurs as a result of pressure over the facial nerve from bony prominences of the pelvis during labour or from forceps application during delivery. When the infant cries, there is movement on one side only of the face, and the mouth is drawn to that side. On the affected side the eye cannot be closed and the nasolabial fold is absent.

The prognosis depends upon whether the nerve was injured by pressure or whether the nerve fibers were torn. Improvement will occur within a few weeks in the former instance. Care of the exposed eye is essential. Faradic stimulation is probably of no benefit, but neuroplasty may be indicated when the paralysis is persistent.

RESPIRATORY SYSTEM

The sudden dependence at birth upon the respiratory system which remained so far inactive during the intrauterine life, necessitates very rapid readjustment of this system. This involves the presence of an active respiratory center, intact nervous pathways along which stimuli are transmitted to the respiratory muscles, normal respiratory muscles, clear respiratory air ways, healthy alveoli with mature capillary bed, and adequately functioning cardio-vascular system.

Some infants begin breathing after birth as a result of thermal and tactile stimuli, others, whose sensations are dulled by abnormal intrauterine factors, may begin breathing only when chemical changes resulting from the separation of the placenta result in the excitation of the respiratory center.

Respiration in the neonatal period is normally accomplished by the diaphragmatic and abdominal musculature with little thoracic movements. At the start it may be irregular in depth and frequency.

The respiratory rate varies from 30-60/minute depending largely on the physical activity, state of wakefulness or presence of crying.

For the evaluation of the newborn infant's condition, the Apgar score is used most frequently as a guide. A newborn infant is scored in the manner shown in table 6, one minute after complete birth. This correlates well as a prognosticator of neonatal survival. The score at 5 minutes is a better predictor of neurologic damage at 1 year of age.

Table 6 : Apgar Score

Sign	0	1	2
Heart rate	Absent	Slow (below 100)	Over 100
Respiratory effort	Absent	Slow, irregular	Good, crying
Reflex irritability (catheter in nose)	No response	Grimaces	Cough or sneeze
Muscle tone	Limp	Some flexion of extremities	Active motion
Colour	Blue, pale	Body pink, extre- mities blue	Completely pink

A score of	8 - 10	indicates	a normal newborn.
» » »	5 - 7	»	a moderately depressed baby.
» » »	below 4	»	a baby at-risk.

Asphyxia Neonatorum

Anoxia is not a clinical entity but a term applied to indicate lack of oxygen from a number of primary processes, some are known and some are unknown. Anoxia is recognized as the greatest hazard of the newborn and may be caused prenatally, intranatally or postnatally. It may result in perinatal death or permanent damage of the brain with resultant cerebral palsy and mental retardation.

Prenatal Anoxia,: This occurs under the following conditions :

1. Inadequate oxygenation of maternal blood as in cardiac failure and carbon monoxide poisoning to the mother.
2. Low maternal blood pressure as in hypotension complicating spinal anesthesia.
3. Failure of relaxation of uterus with inadequate filling of the 'placenta as in uterine tetany caused by pitocin.
4. Inadequate attachment of the placenta or its premature separation.
5. Inadequate placental capacity as in toxemia of pregnancy and in post-maturity.
6. Inadequate circulation of blood through the umbilical cord due to its compression or knotting.

The duration of Prenatal anoxia influences the prognosis as regards fetal survival and brain damage.

The clinical manifestations of prenatal anoxia : Before delivery, prenatal anoxia is manifested by sudden increase in fetal activity and heart rate followed by diminished activity with slow irregular heart rate.

Immediately at birth, it is evident by yellow, meconium-stained amniotic fluid and vernix caseosa, and low Apgar score.

The respirations may be irregular or they may be rapid and shallow for several days. They may show, increased muscle tone or rigidity and may undergo convulsions. Some may pass from rigidity to flaccidity which usually carries a poor

prognosis. Cyanosis (livid) or pallor (pallid) may accompany the stages of rigidity and flaccidity respectively. Inability to suck is usually present.

Natal and postnatal anoxia : May be caused by : —

1. Anemia severe enough to lower oxygen content of the blood to a critical level as in severe hemorrhage or hemolytic disease.
2. Shock severe enough to interfere with the transport of oxygen to vital cells as in adrenal hemorrhage, ventricular hemorrhage, overwhelming infection or massive blood loss.
3. A deficit in arterial oxygen saturation from failure to breathe adequately postnatally, owing to narcosis or cerebral defect or injury (central origin).
4. Peripheral chest structures leading to inadequate oxygenation of the blood by the lungs caused by conditions such as immaturity of the lungs, aspiration of mucus or amniotic fluid, diaphragmatic hernia, laryngeal obstruction, hyaline membrane with resorption atelectasis, cyanotic heart disease and tracheoesophageal fistula.

The clinical manifestations of peripheral anoxia : In this group, the nervous mechanisms of respiration and respiratory muscles are intact, but the fault is mostly in the lungs. A marked respiratory effort is done by the newborn infant with varying degrees of retraction of the lower part of the thoracic cage and the intercostal spaces. Physical examination of the lungs reveals variable findings of dullness or hyperresonance and an X-ray to the lungs may reveal lung shadows alternating with areas of emphysema.

Prevention and treatment of anoxia :

The following steps should be carried out for the care of the newborn in order to assist the establishment of respiration :

Immediate care at delivery : The infant should be suspended with head downward immediately after delivery until the mouth, pharynx and nose have been cleared of fluid, mucus, blood and amniotic debris by gravity and gentle suction with a soft rubber catheter. The stomach should be aspirated in cases of infants delivered by Cesarean section and in prematures. The newborn should then be placed on his side, head downwards, in a cot tilted at an angle of about 30 degrees to promote drainage from the respiratory tract for four to eight hours. The reverse position is indicated in cases of suspected intracranial hemorrhage.

Resuscitation : Failure to breath spontaneously within one minute of birth is an indication for trying the following methods of resuscitation one after the other :—

- (a) The upper respiratory passages should be cleared repeatedly.
- (b) Gentle physical stimulation should be applied e.g. snapping the soles of the feet.
- (c) Oxygen either steadily or in puffs should be given just to relieve cyanosis.
- (d) Artificial respiration is carried out when necessary by :
 - Gentle pressure on the abdomen by flexed thighs.
 - Intratracheal intubation with suction of the lower respiratory passages and positive pressure ventilation.
 - Mouth to mouth breathing if intubation is not available. This is useful but carries the risk of infection or alveolar rupture. No drug has proved to be of definite value as a stimulant. For narcosis from maternally administered morphine derivatives, nalline in a dose of 0.1 mg. per kg. of body weight in 2 ml. of isotonic saline solution injected into the umbilical vein is indicated. Sodium bicarbonate is given intravenously for cases with severe acidosis.

Pneumonia in the Newborn :

About 10% of neonatal deaths are due to pneumonia.

Etiology : There are two main types of neonatal pneumonias :—

1. *Congenital pneumonia* : occurs during the first few days of life due to aspiration of infected amniotic fluid or vaginal secretion during delivery. It is more common in cases with premature rupture of membranes, prolonged labour, fetal distress and maternal infections.

2 *Acquired pneumonia* : It starts after the first few days of life and it is acquired through contact with adults with respiratory infection.

Aspiration pneumonia may be acquired in the prenatal period from hypoxia which stimulates breathing in utero with aspiration of amniotic fluid containing vernix, epithelial cells and meconium, or it may occur in the postnatal age due to regurgitation of food in cases of improper feeding, esophageal fistula or duodenal obstruction.

The causative organisms are the Coliform bacilli, *Staphylococcus aureus*, *Enterococci*, *Klebsiella*, *Proteus vulgaris*, *Salmonella* or may be viral.

Pathology · Lesions are usually bronchopneumonic in type, occasionally interstitial or lobar lesions are present.

Clinical manifestations · The first signs are non-specific, as loss of appetite, cyanosis, rise or sudden fall in temperature, abdominal distension, sudden loss in weight, then increased respiratory rate up to 80/minute, acting alae nasi, and respiratory distress become manifested.

Physical signs are few; on careful auscultation, fine rales mostly in the perihilar areas posteriorly can be elicited. Also areas of hyperresonance may indicate compensatory emphysema. X-ray, nasopharyngeal, and blood culture are helpful. (Also refer to chapter XII).

Hyaline Membrane disease :

Please consult under the heading "Prematurity".

CIRCULATORY SYSTEM AND BLOOD

The heart : Examination of the heart may reveal transitory murmurs; on the other hand congenital malformations may only produce a murmur later. The pulse rate is characteristically variable. A rate varying from 100-150/minute is normal. The blood pressure by the auscultation method at birth is 80/46 mm. of mercury.

For congenital heart disease see chapter XIII.

The Blood : The hematopoietic system of infants and children differs from that of adults in its relative size, nutritional requirements, and its response to stimuli and noxious agents. As a result, disorders of their blood have qualities and characteristics that set them apart from similar disorders in older persons. (See chapter XIV).

ANEMIA OF THE NEWBORN : At term, blood formation resides almost wholly in bone marrow, with only limited activity in the lymphatic tissues, spleen and liver.

The red cell count at birth is between 5—7 million/cmm. There will be transient increase during the first few hours after birth due to redistribution of plasma, water and electrolytes but there is a rapid fall to a lower level during the first week and a more gradual fall in the next three months. This decrease in hemoglobin and red cell level is referred to as *physiologic anemia of the newborn*.

Other causes of anemia of the newly born according to their time of onset :—

Anemia at birth : This may be due to hemolytic disease of the newborn, tearing or cutting of the umbilical cord during delivery and hemorrhage from the fetal side of the placenta due to incision during cesarean section. It can also be produced by transplacental hemorrhage (from fetal to maternal circulation) and in twin pregnancy from one fetus to another.

Anemia in the first few days : can be produced by hemolytic disease of the newborn; (chapter XIV), hemorrhagic disease of the newborn, bleeding from improperly tied or clamped umbilical cord, a big cephalhematoma, extensive intracranial hemorrhage and subcapsular bleeding from rupture of the liver.

Anemia later in neonatal period : may result from delayed hemolytic disease of the newborn with or without exchange transfusion. Vitamin K in large doses may cause anemia in premature infants due to hemolysis. For other causes of hemolytic anemia refer to chapter XIV.

HEMORRHAGIC DISEASE OF THE NEWBORN : This is characterized by spontaneous and prolonged bleeding between the 2nd and 5th day, due either to deficiency of vitamin K which is formed by the intestinal flora, or to accentuation of multiple coagulation defects resulting from hepatic immaturity normally present in the newborn. There are two forms of the disease :—

1. *Due to vitamin K deficiency* : The possibility of vitamin K deficiency exists until the infant's intestinal flora is established to supply the normal needs of vitamin K or until normal hepatic function is established.

It is characterized by :—

- Prolonged blood coagulation time.
- Low one-stage prothrombin activity.
- Deletion of factor VII and true prothrombin.
- Bleeding time; factor VI, capillary fragility, platelets, and clot retraction are all normal.

The common sites of bleeding are : the nose, gastro-intestinal tract, umbilical stump, birth abrasions and the scalp region.

Treatment : (i) Vitamin K (1 mg.). (ii) Fresh whole blood (10 ml./kg.) should be given if bleeding is excessive or if no response to vitamin K took place, it will give rapid improvement in all the coagulation defects within few hours.

2. *Due to temporary deficiency of coagulation factors* : Occurs chiefly among premature infants and does not respond to vitamin K. It occurs also in infants who have had hypoxia or infection. The most frequent sites of bleeding are lungs and the nervous system. The coagulation defects are less severe than in the previous form, but there is increased capillary fragility and prolongation of bleeding time (chapter XIV).

HEMOLYTIC DISEASE OF THE NEWBORN : See chapter XIV.

DIGESTIVE SYSTEM

The abdomen is relatively large. The abdominal wall is normally weak, and diastasis recti and umbilical hernias are common. The liver is usually palpable, 2 cm below the rib margin. Less commonly the spleen and kidneys may be felt.

The gastric juice changes during early days of life; at birth it is neutral, in the first day it is very acidic and after 1 - 2 weeks it becomes less acidic.

The intestines are characterized by large absorptive surface with immature lacteals and numerous secretory glands. The enzymes are present early with the exception of amylase, and the digestion of the proteins and simple sugars is efficiently performed by both term and premature infants. Starches are less well digested. Fat is easily digested but inefficiently absorbed.

Liver functions are immature, with inadequate development of the enzyme systems.

The muscular coat of the gastro-intestinal tract is thin, lax and favours distension which may be induced by swallowing of large quantities of air leading to colic.

The usual advance of air to the descending colon within the first three hours after birth makes its x-ray demonstration diagnostically useful especially in intestinal obstruction.

Food moves relatively slowly through the upper gastrointestinal tract and portions of a single feed often remain in the stomach as long as eight hours. However, material may traverse the entire large bowel in 2 — 4 hours.

The intestinal tract at birth contains from 60 — 200 grams of greenish-black viscid material known as *meconium* which consists of mucopolysaccharides,

some lipids and residue of digested mucous secretions. Passage of meconium usually occurs within the first 12 hours after birth, but may be delayed until the second day of life in normal newborn.

With the establishment of milk secretion (3rd — 4th day), the meconium stools begin to be replaced by the *transitional stools* which are greenish-brown and contain milk curds. The typical *milk stools* follow after 3 — 4 days. The frequency of stools varies between 4 — 5 stools/day by the end of the first week of life.

Swallowed Blood Syndrome :

Blood or bloody stools may be passed on the second or third day of life. The blood may be swallowed during delivery or from a fissure in the mother's nipple.

This is differentiated from internal hemorrhage, by the fact that the infant's blood contains fetal Hb which is alkali resistant, whereas maternal blood contains adult Hb which is changed to alkaline hematin on the addition of alkali.

Vomiting in The Newborn :

Sometimes infants vomit mucus, often blood streaked, in the first few hours. If this persists after the first few feedings, it is due to irritation of the gastric mucosa by amniotic material swallowed during delivery. If this type of vomiting is protracted, it will need gastric lavage with physiologic saline to relieve it.

Vomiting in the neonatal period : may be caused by regurgitation from over-feeding or due to failure to permit the infant to bring the swallowed air out.

If vomiting occurs shortly after birth and is persistent, it may be due to :

- (a) Increased intracranial pressure (see intracranial hemorrhage).
- (b) Alimentary tract obstruction (chapter VIII) : this might be due to :

Esophageal atresia, Cardiospasm, Chlclasia, Pyloric stenosis or Obstruction of the small intestine.

Physiological Diarrhea:

The newborn infant on the breast may, in 24 hours, have 8 to 12 bright yellow stools, frequently one with each feeding. These loose stools may be

forcibly expelled and alarm the parents, unless they are informed that this is a normal occurrence. The cause is the irritant high pH of the stools of the breast fed infants. It needs no treatment except if the condition is interfering with the average gain in weight when one is justified to give one or two cow's milk feeds in order to turn the stools alkaline.

After the first month, stools usually become less frequent, perhaps occurring once every one or two days, but still soft. Mothers at this time are likely to ask about their infant's constipation.

Loose stools may also occur from overfeeding, underfeeding, high carbohydrate formula, any change of formula or introduction of new food.

Constipation in the Newborn :

More than 90% of newborns pass meconium within the first 12 to 24 hours. The other 10% do so within 36 hours. The possibility of intestinal obstruction should be considered in any infant who does not pass meconium within that time. This can be caused by intestinal atresia or stenosis, congenital aganglionic megacolon, meconium ileus or meconium plugs.

If constipation is not present from birth but appearing during the first month, this might suggest congenital aganglionic megacolon, cretinism or anal stenosis.

Artificially fed babies are usually more liable to constipation than breast fed ones, but even breast fed infants may remain as long as few days without bowel movements and without evidence of discomfort and then pass large but normal stools. Meconium anorectal plugs of low water content may cause intestinal obstruction, ulcerations, perforations or meconium peritonitis.

This is treated by removal of the plug using the examining finger, or irrigation of the rectum by half strength sodium chloride solution.

Dehydration Fever:

If the breast milk is slow in coming, and sufficient fluid is not given especially in hot weather, dehydration fever may develop. The skin loses its elasticity the temperature rises and evident loss of weight may be recorded.

Then as the yield of breast milk increases, the temperature subsides and the weight is recovered. It appears that the temperature is produced by the infant reaction to shortage of fluid by peripheral vasoconstriction and can be prevented by giving the infant adequate amounts of fluid during this critical period.

JAUNDICE IN THE NEWBORN

Bilirubin Metabolism :

1 - Bilirubin Formation :—

The chemical steps by which Hb is converted into bilirubin are not fully understood, but the process is a function of the R.E.S. The normal R.B.Cs circulate for about 120 days. At the end of the life span of R.B.Cs., the normal erythrocyte undergoes intra-vascular fragmentation and disintegration. In the R.E. tissue the Hb splits into 2 fragments : the protein globin which enters the protein metabolic pool and the heme prosthetic group which loses Fe and through chemical changes is degraded to bilirubin (Fig. 5).

2 Bilirubin Transport :—

Newly formed bilirubin is bound to albumin and is carried in the plasma where it gives the indirect bilirubin reaction of Van Den Burgh.

3 - Bilirubin Uptake by the Liver Cell :—

Unconjugated albumin bound bilirubin is delivered to the liver cell membrane, becomes detached from albumin, and transported into the liver cell by the Y and Z soluble proteins.

4 Bilirubin Conjugation :—

In the liver and possibly elsewhere, bilirubin is conjugated with glucuronic acid by the help of glucuronyl transferase enzyme to form water soluble bilirubin glucuronide.

It should be noted that the availability of glucose is of importance in the processes of conjugation and excretion.

5 - Bilirubin Secretion :—

The next step is secretion of the water soluble bilirubin across the normal canalicular membrane into the bile ducts.

6 - Bilirubin Excretion :—

Bilirubin diglucuronide is excreted into the bile and enters the intestinal tract where the bilirubin base is changed to stercobilinogen which appears in feces and it may be partly reabsorbed to be excreted in bile again or in urine as urobilinogen. (Fig. 5).

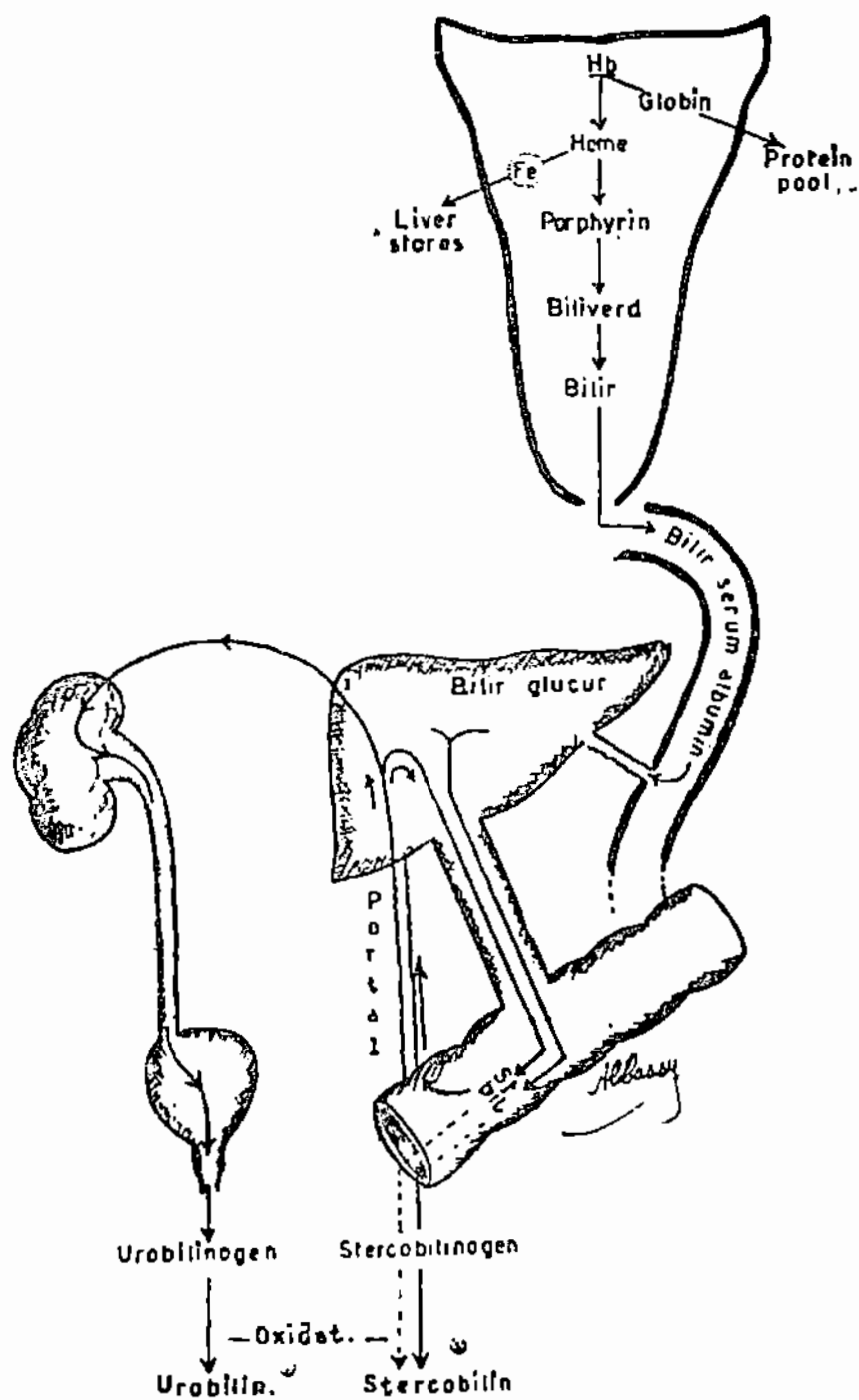


Fig. 5: Metabolism of Bilirubin

Pathogenesis of Jaundice in the Newborn :—

Any malformation, defect or disease of one or more of the forementioned steps of the pathway of bilirubin metabolism will result in jaundice as follows :—

1 — Increased Formation : —

The life span of the R.B.Cs. may be shortened to a few days by such factors as : —

- a) Exposure to hemagglutinins or hemolysins such as in erythroblastosis fetalis, transfusion reaction, acquired hemolytic anemias, etc. (chapter XIV).
- b) Abnormalities of metabolism or of the molecular structure of Hb such as: Hereditary spherocytosis, sickle cell disease, thalassemia, glucose 6 phosphate dehydrogenase deficiency, etc.
- c) Big cephalhematoma.
- d) Sepsis leading to hemolysis.

2 Defective Transport : —

Diminished serum albumin or competition for albumin binding due to administration of vitamin K, caffeine sodium benzoate, sulfonamides or salicylates.

3 Diminished Uptake by the Liver Cells : —

The -Z- protein appears to reach full development during fetal life, whereas the -Y- protein is almost absent at birth, reaching mature levels by the fifth day of life. A defect in their formation leads to elevated indirect bilirubin as in Gilbert's disease, which is a familial nonhemolytic jaundice.

4 Diminished Conjugation : —

- a) Immaturity of conjugation system. "Physiologic Jaundice".
In prematures, physiologic jaundice appears later, is more severe and lasts longer (see prematurity).
- b) Hereditary deficiency of enzyme glucuronyl transferase :
 - i — Crigler - Najjar syndrome.
 - ii — Gilbert's disease (See above also).
- c) Inhibition of enzyme glucuronyl transferase :

- i Breast milk hyperbilirubinemia due to abnormal pregnandiol in milk of mother. Upon discontinuance of breast feeding, the serum bilirubin values return to normal
 - ii Lucey Driscoll syndrome due to unidentified factor in serum of baby and mother.
- d) Competition for conjugation mechanism : chloramphenicol, steroids, caffeine, salicylates and sodium benzoate are excreted along the same pathway.

5 *Interference with Liver Cell Function :*

This type of jaundice is associated with error of or damage to the parenchymal cells of the liver by toxic or infective agents. The power to transfer bilirubin from the blood to the biliary canaliculi in consequence diminishes. The cellular degeneration and necrosis permit diffusion into the blood of bilirubin of the direct reacting type helped by the intrahepatic obstructive element caused by swelling of the liver cells.

- a) Hepatitis : viral (chapter VIII). bacterial, parasitic, toxoplasmosis, cytomegalovirus, toxic etc.
- b) Inborn error of metabolism : glucogen storage disease and galactosemia.
- c) Dubin - Johnson and Rotor syndromes (hereditary).
- d) Infants of diabetic mothers.

6 — *Impaired Bilirubin Excretion :*

- a) Biliary atresia : Intrahepatic or extrahepatic (congenital).
- b) Biliary obstruction . Inspissated bile or biliary calculi.
- c) Choledochus cyst.
- d) Fibrocystic disease of the pancreas.

Hyperbilirubinemia during the Neonatal Period.

Jaundice may be present at birth or appear at any time during the neonatal period, depending on the condition responsible for it.

Jaundice present at birth or appearing within the *first 24 hours* of life should be considered due to Rh iso-immunization until proved otherwise.

Jaundice which first appears on the *2nd. or 3rd. day* suggests "physiologic

Jaundice" or the more severe form termed "Hyperbilirubinemia of the Newborn". Familial non-hemolytic Icterus is an infrequent possibility at this age period.

Septicemia is the most likely cause for jaundice between the 3rd and 7th. day of life.

Congenital toxoplasmosis, Cytomegalic inclusion disease and Congenital syphilis may be associated with jaundice during the first week of life.

Delayed neonatal jaundice suggests septicemia, congenital atresia of the bile ducts, homologous serum hepatitis, herpetic hepatitis, idiopathic dilatation of the common bile duct or galactosemia.

Hereditary spherocytic and hereditary non-spherocytic hemolytic anemias (due to glucose 6-phosphate dehydrogenase enzyme deficiency) may be responsible for anemia and jaundice in the neonatal period.

Persistent jaundice during the first month of life suggests inspissated bile syndrome, neonatal hepatitis, cytomegalic inclusion disease, congenital syphilis, toxoplasmosis, familial non-hemolytic icterus, congenital atresia of the bile ducts, galactosemia or idiopathic dilatation of the common bile duct.

Rarely physiologic jaundice may be prolonged for several weeks; when this occurs the possibility of cretinism should also be considered.

THE UMBILICUS

There are 3 types of navels :

Normal Navel : When the skin of the abdominal wall meets the umbilical cord at the level of the abdomen with normal cicatrix.

Amniotic Navel : If the skin does not extend to the base of the cord and the amniotic membrane covers the skin surface adjacent to the base with superficial ulcer that gives granulation and flat scar.

Skin Navel : When the skin extends up the sides of the cord with a protruding stump.

Hemorrhage from the umbilicus may be due to :

— Inadequate ligation of the cord.	— Trauma.
— Failure of normal thrombus formation.	— Septicemia.
— Hemorrhagic disease of the newborn.	— Local infection.

Granuloma of umbilicus : The umbilical cord usually dries and separates within 6-8 days after birth. Mild infection will delay the separation of the cord and result in moist granulating area at the base of the cord with the persistence of exuberant granulation tissue at the base of the umbilicus. The tissue is soft, vascular and granular and may ooze seropurulent secretion.

Treatment is by cauterization with silver nitrate. It should be repeated at intervals of several days until the granuloma is dry.

Umbilical Hernia : This occurs due to imperfect closure or weakness of the umbilical ring. It is often associated with diastasis recti. It is covered by skin and consists of omentum and a portion of small intestine. The size of the defect varies from less than 1 cm. to 5 cms.

Most umbilical hernias disappear before six months. Even large hernias (5 - 6 cms. in diameter) may disappear spontaneously with one year of age.

Strapping can be done, by reducing the hernia by finger pressure and the defect is closed by drawing each side of the adjacent abdominal wall towards the midline and fixing it by means of interlocking straps of broad adhesive plaster.

Indications of surgery are :— If the hernia persists to the age of 3 years, if it causes symptoms, if it becomes strangulated, or if it becomes progressively larger after the age of 1 or 2 years.

URINARY SYSTEM

The general features of the metabolism of the newborn are his large surface area in relation to his body weight and his tendency to metabolic acidosis due to the limited renal functions and the accumulation of chloride ions and acid radicles.

At birth the kidney is relatively large extending to the iliac crest, its surface is lobulated and histologically it has a less lobulated capillary tuft and cuboid capsular epithelium.

Urine is usually present in the bladder at birth, but it is common that the infant does not void until more than 12 hours after birth. The frequency in the first 1 or 2 days may be 2—6 times which increases up to 10—40 times/day in the subsequent period.

A high percentage of nitrogen in the urine of the newborn is excreted in the form of uric acid which may be deposited in the kidney giving uric acid infarct or it may stain the diaper by pink coloration.

The renal function as tested by glomerular filtration rate and tubular excretion is limited, and as a result the newborn will contain more water than in later infancy and the loss of water in the early days will contribute to the physiologic weight loss in which the baby loses 1 ounce or more per day during the first four days. By the tenth day, he should have regained the loss and may be even 1—2 ounces above his birth weight. Some of the early loss can be prevented by giving drinks of boiled water until breast milk comes in.

GENITAL SYSTEM

The prominence of the female genitals, often with mucoid or mucosanguinous secretion from the vagina are transitory manifestations. The scrotum is relatively large, its size may be increased by the trauma of breech delivery and by a transitory hydrocele which has to be distinguished from a hernia.

The testes may be in the scrotum or palpable in the inguinal canals, or may not be felt until spontaneous descent, which may not occur until late in infancy. The prepuce is normally tight and adherent so that it should be dissected if circumcision is done early.

ENDOCRINE SYSTEM

There is lack of reliable information about the secretion of the growth hormone or its transplacental passage during the intrauterine life. Some oxytocic and antidiuretic activity can be obtained from the neurohypophysis of the newborn but to a lesser extent than from the adult gland.

The thyroid gland attains full anatomic and functional development at the end of the third intrauterine month and the pituitary-thyroid axis is operative at the sixth month of fetal life. The maternal thyrotropic hormone does not cross the placenta but the maternal thyroxin crosses it. Goitrogenic substances may cross the placental barrier producing fetal goiter. Thyroid deficiency appears at birth in genetically determined cretinism or in infants of mothers treated with thiouracil. Temporary hyperthyroidism may be seen at birth in infants of mothers with hyperthyroidism or of those who have been on thyroid medication.

The maternal parathyroid hormone crosses the placenta to the fetus and the secretion of the parathyroid gland of the newborn is under transitory depression in the immediate postnatal period.

The fetal demand for calcium is fulfilled on the expense of the maternal stores and the calcium in the cord blood is higher than that of maternal blood. There

is a subsequent rapid fall of serum calcium during the first 24 hours due to the transient functional hypoparathyroidism which may be secondary to the hypercalcemia.

Neonatal tetany : Tetany unrelated to vitamin D deficiency occurs occasionally in newborn infants, usually in the first week of life. The increased neuromuscular irritability is due to diminished serum calcium associated with an increase in serum phosphorus. Serum alkaline phosphatase level is normal. Contributory factors are transient physiologic hypoparathyroidism, diminished ability of the kidney to excrete phosphate and high phosphate load from undiluted cow's milk formulas. (chapter VII).

The diagnosis is established by : (a) Lumbar puncture to exclude meningitis and intracranial hemorrhage. (b) Chemical examination of the blood.

Infants of diabetic mothers : These infants have distinctive physical characteristics, and they have a high incidence of intrauterine death after the 36th week of gestation, and a high neonatal mortality rate also.

Infants of prediabetic women have a lesser but increased neonatal mortality rate. They are large and plump with puffy, plethoric facies resembling that of patients who receive cortisone. Respiratory distress syndrome and cyanotic attacks are common. Convulsions associated with severe hypoglycemia which respond to intravenous administration of glucose may be present. The prenatal mortality may be secondary to maternal ketosis, hydramnios, pre-eclampsia or vascular degeneration of the placenta which are commoner in diabetic women.

Treatment : The baby should be taken care of as if he is a premature baby.

Early feeding of glucose in water or in 0.4% NaCl solution beginning 2 - 3 hours after birth. This is to reduce hypoglycemia.

In presence of convulsion, blood should be drawn for sugar determination and glucose is given I.V. If the blood sugar level and the response to I.V. infusion of glucose confirm the cause as hypoglycemia, I.V. glucose is continued until the baby is feeding well by mouth.

The adrenal glands : The neonatal cortisol production seems to be no less than that of the adult per unit of body surface.

Androgens are formed by the adrenal cortex at birth and their concentrations in plasma and urine decline during the first month of infancy.

Acute adrenal hemorrhage and failure is seen after breech presentation and other traumatic deliveries or with overwhelming infections. Adrenal cortical hyperplasia with clitoral enlargement and signs of salt losing syndrome (vomiting, diarrhea, dehydration, convulsions or shock) may occur. Hypoplasia of adrenal glands gives signs of adrenal insufficiency during the first few weeks of life.

The sex hormones : Most infants of both sexes have hypertrophy of the breasts during the first week of life and may have some secretion of the so called witch's milk. This may be due to 2 types of hormones :

1. Estrogens from placenta and ovaries.
2. Prolactin from anterior pituitary of infant or mother.

The estrogenic hormones may produce also in the female newborn enlargement of the vulvar tissue, vaginal discharge and desquamation, or uterine bleeding.

Anomalies of the gonads, as gonadal dysgenesis (Turner's syndrome) may be encountered in the newborn.

BONES AND JOINTS

Osseous maturation is the best index of general growth (chapter IV).

Osseous development is retarded in the presence of hypopituitarism, cretinism, malnutrition, severe illness, male hypogonadism, and delayed adolescence. Osseous development is accelerated in patients with the adrenogenital syndrome or sexual precocity.

■ **Congenital anomalies** of bones and joints are many e.g. meningoencephalocele, spina bifida, cleft palate, talipes equinovarus, dislocation of the hip, etc...

■ **Fractures** : Fractures of the newborn are remarkable for the excess of callus they tend to form and the ease with which they tend to heal. A good alignment no matter how much shortening or displacement of the fragments was originally present.

⇒ *Fractures of the skull* : May occur as a result of pressure from forceps or against the maternal symphysis pubis, sacral promontory or ischial spines. They are sometimes associated with cephalhematoma and/or intracranial hemorrhage. Linear fractures are the most common. They cause no symptoms and require no treatment. Depressed fractures should be

elevated surgically to prevent injury to the cerebral cortex from sustained pressure.

- (b) *Fractures of the clavicle* : This is one of the commonest forms of birth injury. Fracture of the clavicle occurs when there is difficulty in delivery of the shoulders or if they are pressed against the symphysis pubis. The infant fails to move the affected side and the Moro reflex is absent on that side. A remarkable degree of callus develops within a week at the site of the fracture. The fracture may be missed and the detection of the callus may be the first evidence of a fracture.

Treatment, if any, consists in immobilization of the arm and shoulder on the affected side.

- (c) *Fractures of the bones of extremities* : The humerus is the commonest to be fractured. This occurs if there is difficulty in delivering the arm. The femur is the next one in frequency. The bones of the fore-arms and legs are rarely fractured. The epiphysis of the head of the humerus and the upper femoral epiphysis may be sometimes separated in difficult labour e.g. in breech extraction and after version.

Spontaneous movements and Moro reflex are absent on the affected side. The possibility of associated nerve involvement must be considered.

The diagnosis is established radiologically, the prognosis is good although coxa vara frequently results from extensive displacement.

Satisfactory results for a fractured humerus are obtained by strapping the arm to the chest. For fracture of the femur, good results are obtained with Buck's extension splints. These are also effective for treatment of fractures of the forearm or leg.

IMMUNITY AND INFECTIONS OF THE NEWBORN

The main humoral factor available to the newborn in defence against bacterial infection is the immunoglobulin G which can be transmitted transplacentally to the developing fetus, and its concentration in the blood of the newborn is proportional to the gestational age, i.e. those who are born before term have a lower concentration.

The fetus, the premature and the newborn are to some degree capable of producing immunoglobulins. This antibody response is seen exclusively in the immunoglobulin M which contains antibodies against the Gram negative

bacteria. The standard immunization procedures may result in moderate anti-body production if began during the first two months after birth.

Antibodies against diphtheria and tetanus toxins, measles, mumps, poliomyelitis and common cold viruses, usually pass the placenta in sufficient quantities to exert a passive protective effect of some degree for short duration. In pre-matures, less reliance can be placed on the effectiveness of such protection.

Infection during the neonatal period remains a leading cause of morbidity and mortality, despite the extensive use of antibiotics. The newborn infant's reaction to infection differs from that of the older child and adult. Organisms which rarely give rise to significant disease in the older individual cause lethal infection in the newborn.

Most of the bacteria produce hemolysins which increase the rate of hemolysis of R.B.Cs. and result in hyperbilirubinemia. Other bacteria may cause cellular injury.

The newborn infant has a special susceptibility to *E. coli*, staphylococci, streptococci and *H. pertussis*.

Infections of the newborn can be caused by a variety of agents and take place prenatally, during birth or postnatally. Preventive measures can avoid some of them but others are not preventable.

(A) Infections acquired during gestation :

- *Preventable* : syphilis, tuberculosis, rubella, vaccinia, poliomyelitis, pneumonia, and sepsis.
- *Nonpreventable* ; toxoplasmosis, cytomegalic inclusion disease, listeriosis, viral myocarditis, hepatitis and varicella.

■(B) Infections acquired during birth :

- *Preventable* ; gonorrheal ophthalmia, moniliasis, salmonellosis, pneumonia and sepsis.
- *Nonpreventable* : herpes simplex and listeriosis.

—) Infections acquired in the neonatal period :

- *Staphylococcal infections* : carrier state, skin lesions, pneumonia, otitis media, meningitis, osteomyelitis, diarrhea and septicemia.
- *E. coli infections* : septicemia, omphalitis, pneumonia, diarrhea. etc...
- *Salmonella infection* : septicemia, meningitis and osteomyelitis.
- *Streptococcal, pneumococcal and H. influenza infections*: are less frequent pathogenic agents in the newborn than in subsequent months.

- *Enterococci, klebsiella, pseudomonas and proteus* are relatively common bacterial pathogens in the neonatal age
- *Tetanus*.
- *Tuberculosis*.
- *Viral infections* : upper respiratory tract infections, pneumonitis and myocarditis.

The delicate skin of the newborn and the umbilicus serve as easy portals of entry as well as the respiratory tract and the oral route.

The most frequent serious infections of the newborn are pneumonia, septicemia, diarrheas, meningitis and peritonitis. The most frequent causative organisms are *E. coli* and *staphylococcus aureus*. These serious infections are distinguished by their lack of specific signs or symptoms in the early stage. They may be completely difficult to detect, often they are not detected before the infant becomes moribund. Neonatal reactions to infections may be little and vague in the early phases, and often non-specific throughout their whole course. Refusal to feed and failure to thrive may be the only signs. Fever is often absent in the infected newborn. Common non-specific symptoms are cyanosis, pallor, dyspnea, tachypnea, vomiting, diarrhea and jaundice. The same symptoms might be present in non-infectious disease processes. The situation could be clarified by a roentgenogram of the chest, a blood culture and a spinal puncture. These should be performed in infants who «are not doing well» and showing no specific symptoms.

SEPTICEMIA OF THE NEWLY BORN :

Infection may enter the blood stream through the skin, mucus membranes, umbilicus or from an infection of any of the viscera. Staphylococcal septicemia is frequently preceded by skin pustules. The onset is frequently insidious, usually after the third day of life but symptoms may be present at birth. Anorexia, poor weight gain, lethargy or restlessness, vomiting, diarrhea or episodes of cyanosis may be the only findings. The temperature and leukocytic count are usually elevated but may be normal or low throughout the illness. Jaundice, hemorrhage, hepatomegaly and splenomegaly often occur. Localization may occur in any part of the body (meningitis, pneumonia, peritonitis etc ..).

With early treatment the majority of infants recover

PNEUMONIA :

Pneumonia is common and serious in the newborn. Pneumonia in the first two days of life is usually acquired from aspiration of infected amniotic

fluid. Symptoms are tachypnea, retraction of the rib cage and flaring of the alae nasi, besides the other symptoms of neonatal infection. Physical signs in the chest may be completely absent. Empyema, pyopneumothorax and pneumatocele indicate staphylococcal infection.

MENINGITIS :

Meningitis may be present at birth or may occur at any time in the neonatal period as an isolated infection or as a part of septicemia. Signs and symptoms may be typical of meningitis or may be those of septicemia. *E. coli*, staphylococci and meningococci are the common causative organisms.

EPIDEMIC DIARRHEA OF THE NEWBORN :

Anorexia, vomiting and fever may occur early. Weight loss, dehydration, restlessness, acidosis and shock rapidly supervene. The stools are frequent, watery and explosive, and generally do not contain pus or blood. Occasionally the infant goes into shock and dies from water and electrolyte loss in the intestinal lumen before a diarrheal stool is passed. Hyperpnea may be absent in the presence of acidosis. Pneumonia frequently precedes, or follows, diarrhea in the newborn.

The Choice of Antibiotic Against Neonatal Infection :

If the infection is probable and therefore antibiotics are to be given before a definite bacteriological diagnosis is made, such antibiotic should be :

- a) Against both gram negative and gram positive bacteria.
- b) Bactericidal rather than bacteriostatic.
- c) Safe when given in the proper doses.

Kanamycin in dosage of 15 mg./kg./day divided into two equal doses administered intramuscularly is the best drug for *E. coli* systemic infections.

A combination of penicillin (50,000 unit/kg./day) and kanamycin is effective against many strains of staphylococci.

Because of their lower toxicity, possible equal effectiveness and broader range, one of the new antistaphylococcal synthetic penicillins (oxacillin 50mg./kg./day, methicillin 100 mg./kg./day) are probably the treatment of choice in penicillin resistant staph. infection but they are less effective than regular penicillin against streptococcal and pneumococcal infections.

In epidemic diarrhea of the newborn, beside fluid and electrolyte correction, neomycin orally or kanamycin I.M. or both are given for *E. coli*.

Gentamycin may replace kanamycin in the presence of resistant *E. coli* infections.

TETANUS NEONATORUM :

It is an acute infection caused by the anerobic, spore-bearing clostridium tetani which produces a neurotropic exotoxin. Infection occurs by contamination of the umbilicus. The toxin reaches the anterior horn cells either along the motor nerves or through the blood stream. After the toxin has become fixed to the nerve tissue it is not easily neutralized by specific antitoxin.

The incubation period is usually 5—14 days. The onset is usually insidious. Refusal to feed and extreme irritability are followed by increasing degrees of muscle stiffness. Within forty eight hours the disease is well defined and trismus is evident, causing inability to suck. A clonic convulsion is often the first symptom. The spasm is characteristic; the body exhibits boardlike rigidity and opisthotonus, the limbs are stiff and extended and the fists clenched. The spasm of the facial muscles results in a fixed expression «risus sardonicus». The spasms at first are intermittent, later almost continuous. Convulsions may be precipitated by the slightest stimulus. Cyanosis may result from paroxysms affecting the respiratory or laryngeal muscles. Fever is usually low grade except in the terminal stage. The cerebrospinal fluid is normal.

The mortality rate is about 50 per cent. Fatal cases terminate within a week or so. Death is due to prolonged laryngeal or respiratory muscle spasm, laryngeal obstruction by secretions, or pneumonia.

Treatment : The patient should be kept quiet and external stimulation should be avoided. Oral and gastric feeding should be deferred until the dangers of vomiting and aspiration no longer exist. Phenobarbital in individual doses of 15 to 30 mg. by gavage is a satisfactory sedative as is paraldehyde rectally. Oxygen, tracheotomy and the use of respirator may be required. Penicillin should be given every twelve hours for its probable effect on the clostridia tetani and to control secondary infection. Antitoxin is the only specific agent, 50,000 units intramuscularly and 50,000 units intravenously should be given immediately. Thereafter, daily intramuscular injections of 5000 units may be administered.

DIAPER DERMATITIS :

Diaper dermatitis is a cutaneous reaction pattern localized to the area ordinarily covered by the diaper

There are :—

- (a) *Mild form* : Essentially an erythematous or chaffing reaction which occurs where two moist surfaces are in opposition or where normal skin is subjected to the prolonged irritation of a wet diaper, especially if the diaper has not been rinsed thoroughly from soap. The lesion consists of a patch or a diffuse erythematous reaction.
- (b) *Ammoniacal diaper dermatitis* : It is caused by the ammonia formed in the voided urine by the action of urea-splitting bacteria in the diaper or on the skin. It produces papulovesicular lesions which become umbilicated, leaving ulcer-like craters.
- (c) *Infection of diaper dermatitis* : This may occur as folliculitis due to skin and intestinal bacteria, monilial infection or vaccinia of the diaper area.

Prevention : The diapers should be washed with soap, mixed in water, boiled and rinsed thoroughly from traces of soap. Diapers should be changed frequently. Tight-fitting water proof pants should be avoided. The diaper area should be washed when the diaper is changed and should be dried and painted with cotton seed oil or mineral oil.

Treatment : Exposure of the uncovered diaper area to dry heat, as from an electric light, is especially helpful. Application of zinc oxide ointment or 0.5 per cent hydrocortisone ointment is useful. Vioform cream alone or in combination with 0.5 per cent hydrocortisone or with nystatin is used for monilia infection. Bacterial infections should be cleansed with a detergent containing hexachlorophene. Neomycin, bacitracin or polymyxin ointment should be applied.

A. S. ABBASSY
M. M. ZEITOUN

LOW BIRTH WEIGHT

Until recently, the premature infant has been defined as one weighing 2500 gm. (5½ lb) or less at birth, irrespective of the period of gestation. This definition, was statistically convenient for international comparison of records. However, it was not scientifically and clinically accurate as infants of the same weight might have different gestational ages. The term low birth weight infant, is nowadays used to describe any infant whose birth weight measures less than 2500 gm., irrespective of his gestational age. Within this general category are included infants who have grown well but are born early and infants born at or before term who are disproportionately small because they are mal-developed or their growth has been restricted. The recognition of these two groups is of great value as they differ in morbidity and prognosis and require different management. The term premature or preterm infants is often used to describe the first group. While, the second group has been called light for date, small for date, intrauterine dwarfs or dysmature infants. This terminology, however, is not exclusive, since some premature infants will also be light for date and some preterm infants like those of diabetic mothers weigh more than 2500 gm.

Incidence : Recent estimates of the incidence of low birth weight suggest that approximately 5 to 12 per cent of all live births weigh less than 2500 gm.

Causes : Low birth weight is idiopathic in nearly half the cases. Toxemia of pregnancy and multiple pregnancy are the next two most important factors, followed by accidental hemorrhage, placenta previa, fetal abnormality or disease and various maternal conditions like chronic respiratory diseases, urinary infection, malnutrition, etc.

PREMATURE INFANTS

Clinical Features : The premature infant, besides the low birth weight has low anthropometric measurements. Prematures are often weak, hypoactive, sleepy, cry feebly and infrequently and suck poorly. The head and abdomen appear relatively large compared with the limbs. The skin is thin, red and often appears shiny and translucent. The subcutaneous fat is diminished or absent. Respiration may be rhythmic but is often jerky and irregular and periodic spells of apnoea are frequent. The

cartilage in the ears, subcutaneous fat in the breasts and breast nodule, genital appearance and the creases in the sole of the feet are underdeveloped. These and other physical characteristics are used to estimate gestational age, which can also be assessed by the presence or absence of certain neurological reflexes. The generally underdeveloped and immature body functions and systems predispose the premature child to feeding and respiratory difficulties, jaundice, infections and other handicaps and complications.

THE PHYSIOLOGICAL HANDICAPS OF THE PREMATURE :

There are certain physiological characteristics of the premature which constitute considerable handicaps in comparison to the full term babies.

1. *Respiratory system* : The respiration is rapid, shallow, irregular with periods of apnea and cyanosis due to poorly developed respiratory center, weak respiratory muscles, poor gag and cough reflexes, poorly developed lung alveoli with diminished elastic tissues, diminished formation of surfactin, and immature capillaries of the lungs and respiratory center.

2. *Thermo-regulatory mechanism* : The premature is liable to develop hypothermia or hyperthermia due to an immature thermo-regulatory center, increased surface area of the skin in relation to the body weight and diminished sweating mechanism, low subcutaneous fat and poor muscular activity.

3. *Gastro-intestinal tract* : Regurgitation and vomiting occur more frequently due to weak cardiac sphincter and active pyloric sphincter with low capacity of the stomach. The poorly developed lacteals of the small intestine result in low absorption of fat. The hypotonicity of the muscle coat of the colon leads to increased liability to distention and constipation.

4. *Liver functions* : are impaired with low activity of some enzyme systems and storage capacity resulting in increased incidence of hypoglycemia, hypoproteinemia, hypoprothrombinemia and deeper and more prolonged physiological icterus.

5. *Hemostatic mechanisms* : The premature infant is more susceptible to develop hemorrhage due to increased fragility and vascular permeability of the capillaries, inadequate elastic supporting tissues and impaired clotting mechanism.

6. *Renal functions* : are impaired in the premature with increased tendency to develop edema due to low glomerular filtration rate, low clearance of chloride and urea and inability to concentrate the urine.

7. *The brain* : is less protected due to the soft skull bones. It is poorly developed with increased incidence of cerebral hemorrhage which is one of the commonest causes of death in prematures. Kernicterus which means a yellow staining of the basal nuclei of the brain, due to deposition of bilirubin in the brain cells may result in development of cerebral palsy and mental retardation.

8. *Blood* : Anemia in the premature infant is attributed to a variety of factors, viz. hemolysis, immaturity of the blood forming organs rapid post-natal growth and the poor iron stores. Normochromic anemia occurs by 6-8 weeks secondary to relative erythropoiesis. The condition does not need special management unless the hemoglobin percent is very low, when blood transfusion is indicated. By the third to fourth month, hypochromic anemia secondary to the low available iron develops, and is readily managed by iron administration. In the very small preterm infant, folic acid deficiency may cause megaloblastic anemia which can be corrected by folic acid administration.

9. *Nutritional status* The premature is more liable to get nutritional disturbances due to weak sucking and swallowing reflexes, faulty absorption of fat and fat soluble vitamins, low gastric acidity and low stores of some minerals and vitamins. The premature is more liable to develop rickets due to reduced antenatal storage of calcium, phosphorus and vitamin D, decreased absorption of vitamin D and rapid rate of growth.

COMPLICATIONS :

Anoxia and Atelectasis : Anoxia in the premature child is often attributed to the same factors and conditions that operate in normal term infants. Yet, the poorly developed respiratory center, weak respiratory muscles, feeble gag and cough reflexes, diminished lung elasticity and less lung perfusion augment its risks in the premature infant. Primary atelectasis might follow the failure of the initial lung expansion after birth and Secondary atelectasis might be caused by aspiration of amniotic fluid, meconium, blood or milk after the establishment of respiration. Treatment includes the clearing of the airway, the judicious use of oxygen and in some cases assisted respiration.

Hyaline Membrane Disease : Hyaline membrane disease, is the commonest cause of respiratory distress among premature infants. It occurs predominantly in small preterm infants, infants of diabetic mothers and those delivered by Caesarean section.

Pathology : The genesis of hyaline membrane disease is complex and not yet satisfactorily explained. It is believed, however, to be related to some pre-natal

disturbance in the systems responsible for the control of the pulmonary blood flow and for the synthesis of the alveolar surfactant. Deficiency of the surfactant (a lipoprotein which reduces surface tension within the lung) hinders the lung expansion during inspiration and favours atelectasis during expiration. The high pulmonary resistance in premature infants and the consequent hypoperfusion of the lungs, result in bypassing the blood from the pulmonary artery to the aorta through the ductus arteriosus. This abnormal right to left shunt increases the anoxia and produces more spasm in the pulmonary vascular bed. Other possible etiological factors— for which there is some evidence—is the slow clearance of fluid by the pulmonary lymphatics and the excessive effusion from the pulmonary circulation and the conversion of the fibrinogen in the effusion fluid to fibrin through the thromboplastic activity of the aspirated amniotic fluid.

The affected infants usually have difficulty in establishing respiration at birth. After few hours, they develop rapid laboured breathing with rib retractions, expiratory grunting and cyanosis. The air exchange is diminished and fine rales can be detected on deep inspiration over both lungs. A precordial murmur due to the shunt through the ductus arteriosus is usually heard. The x-ray examination of the chest shows bilateral diffuse reticulo-granular opacity. Laboratory investigations reveal normochromic anaemia, hyponatremia, hypocalcemia, hyperkalemia and respiratory and metabolic acidosis. If the child is not supplied with i.v. fluid, the blood sugar level decreases. The condition may progress to death within few hours. Milder cases reach the peak within 3 days and then regress gradually.

Treatment : includes the administration of oxygen in sufficient concentration to relieve cyanosis, humidification of the atmosphere to 90 to 100 per cent relative humidity, and antibiotics if infection is suspected. Correction of water and electrolyte disturbances and hypoglycemia is mandatory. Digitalization is recommended by some authors. An attempt should be made to maintain the arterial oxygen tension within normal limits, if necessary by the use of mechanical ventilation.

Intraventricular Hemorrhage : Bleeding into one or both of the lateral ventricles is specially common among premature infants. The condition might follow an apparently easy and spontaneous vaginal delivery of a small sized baby. It is more common, however, after breech or high forceps deliveries. Anoxia, immaturity of the vascular system and permeability of capillaries, coupled with softness of the skull bones are the main underlying factor. The affected infants show different clinical features, depending on the rapidity and massiveness of the bleeding. In severe cases, the infant is born asphyxiated and shocked. In milder cases signs of

cerebral irritation and coma develop gradually. Treatment includes vitamin K administration, the management of acidosis and respiratory difficulty as well as the signs of cerebral irritation, maintenance of body temperature and satisfactory feedings. Prognosis is usually grave.

Jaundice of Prematurity : The incidence of jaundice among premature infants without blood group incompatibility is definitely higher than in matures. Many factors contribute to this :

- (a) The-Y-protein is deficient and its maturation takes a longer time.
- (b) Marked deficiency in the enzyme system required for conjugation of bilirubin in the liver due to immaturity.
- (c) The availability of glucose is of importance for formation of uridine-diphosphate glucuronic acid which is necessary for the enzyme glucuronyl transferase. Glucose level is lower in prematures.
- (d) Other factors include hypoxia, hypothermia, septicemia, dehydration, administration of sulfonamides or novobiocin or excessive dosage of vit. «K» analogues either to the infant or to the mother.

The incidence of "Kernicterus" is greatest in severely jaundiced prematures with small birth weight. This is because the fat soluble bilirubin can enter the brain and the subcutaneous adipose tissue; and as the adipose tissue of prematures is very little, the pigment is concentrated in the brain. It usually occurs when the serum level of bilirubin reaches 20 mg. / 100 ml. but sometimes less.

Treatment :

- (a) Exchange transfusion is indicated if the serum bilirubin reaches 20 mgm./100 ml.
- (b) Phenobarbitone therapy induces the synthesis of glucuronyl transferase and other hepatic enzymes. It is given in dose of 8 mgm/Kg./day. I.M. 12 hourly.
- (c) Phototherapy : Whilst phenobarbitone is ineffective once jaundice has appeared, phototherapy is effective in lowering serum bilirubin levels. Blue light (440-475 mu) causes bilirubin to change to other products which do not appear to be neurotoxic.

Cold Injury-Sclerema Neonatorum : Although cold injury might occur in any newborn infant exposed to much cold after delivery, small feeble babies are specially vulnerable. Affected infants fail to suck and appear apathetic, red, cyanosed with cold extremities. Hard edema of the extremities or sclerema soon develops. The sclerematous child dies from respiratory failure, infection and/or intrapulmonary hemorrhage.

The condition is treated by gradual warmth, administration of glucose by gastric tube and antibiotics to avoid intercurrent infection.

Retinopathy of Prematurity : This condition was the main cause of blindness among premature infants before the risks of excessive oxygen administration were recognized. It is particularly common in small premature infants who are nursed continuously at high concentrations of oxygen for a week or more. The retinal blood vessels undergo a proliferative angioblastic change, which is at first reversible. Subsequently an opaque membrane forms behind the lens and vision is lost. The incidence of the disease has been greatly reduced by the nowadays practised extreme caution in oxygen administration.

Infections : The pre-term infant is specially vulnerable to infection because of the low levels of immune-globulins, reduced phagocytic activity, excessive need for special interference like endotracheal intubation and aspiration and probably other factors. Severe infections might develop with only slight clinical manifestations such as failure to suck and grey pallor. The temperature is frequently subnormal. Respiratory infections, septicemia, meningitis and diarrhea are particularly lethal in the premature infant.

Congenital Malformations : The incidence of congenital abnormalities is high among premature infants. The abnormality might be responsible for the early termination of pregnancy or could be, itself, the result of some adverse factor that terminated pregnancy earlier than usual.

Prognosis : About 65% of all mortality among the newborns occur in premature infants. The prognosis depends on the cause of prematurity, the intrauterine age, the nursing care, the occurrence of any complication and the birth weight. With good care, the survival rate was found to be 5% in cases with birth weight less than 1 kg., 35% in cases with weight from 1 — 1.5 kg., 75% from 1.5 — 2.0 kg. and 85% in cases from 2.0 — 2.5 kg.

MANAGEMENT OF PREMATURITY :

Prevention : by the avoidance of the preventable causes.

Special natal care : must be given by avoidance of version, forceps and the unnecessary cesarean sections and giving the mother vitamin K (5—10) mg. 12 hours before delivery and oxygen 100% during labour.

Postnatal care : This consists of : —

- Immediate care.
- Maintenance of the body temperature.

- Oxygen administration.
- Prevention of infections.
- Maintenance of adequate humidity.
- Proper feeding.

The baby is received in a warm sterile towel and is handled gently. The airways and the stomach are cleared from the mucus and the amniotic fluid and the baby is placed in a cot or in an incubator with dependent head position and with minimal interference. Adequate oxygen, warmth and humidity must be maintained. The oxygen concentration should never exceed 35—40%. The humidity is adjusted to be 65% and whether the infant is put in an incubator or wrapped in cotton with water bottles around, his temperature must be between 36—37° C.

In the premature who needs resuscitation, avoid vigorous chest pressings, contrast baths and excessive doses of vitamin K. Strict measures must be taken to prevent infection by reducing atmospheric contamination, the attendants must be free of any infection and should wear sterile masks and gowns, also prophylactic antibiotics may be given in special situations (see nursery care).

Feeding : The feeding schedule should be flexible and not fixed. After a fasting period of 6—12 hours (due to the large content of body water, and to avoid respiratory difficulties and aspiration pneumonia) the initial feedings should be sterile 5% glucose. Then the baby is given one of the suitable formulas (refer to chapter VI).

THE LIGHT FOR DATE, DYSMATURE AND POSTMATURE INFANTS

The light for date, dysmature and postmature infants, have two main features in common, viz. : that body weight is disproportionate with age and that the cause of fetal undernutrition is mainly placental insufficiency with resultant interference with the fetal supplies of essential nutrients and oxygen. Some cases who exhibit low birth weight for gestational age, however, could be the result of an inherent fetal factor rather than a placental abnormality. The case is well illustrated in infants suffering from a chromosomal abnormality or intrauterine infection like congenital syphilis, toxoplasmosis, etc.

The term "*postmature*" is usually reserved for infants who are born after 42 completed weeks of gestation and who show signs of placental insufficiency.

The "*dysmature*" infant is that who shows signs of placental insufficiency but who is born at term or preterm.

The term "*light for date*" includes all those infants whose body weight is small for the calculated period of gestation. It is thus conceivable that the term *light for date* includes all postmature as well as dysmature infants besides some abnormally small but not preterm infants who, generally, do not show the signs of placental insufficiency and appear more neurologically competent compared to premature infants of similar weight (Fig. 6).

THE SMALL FOR DATE BABY

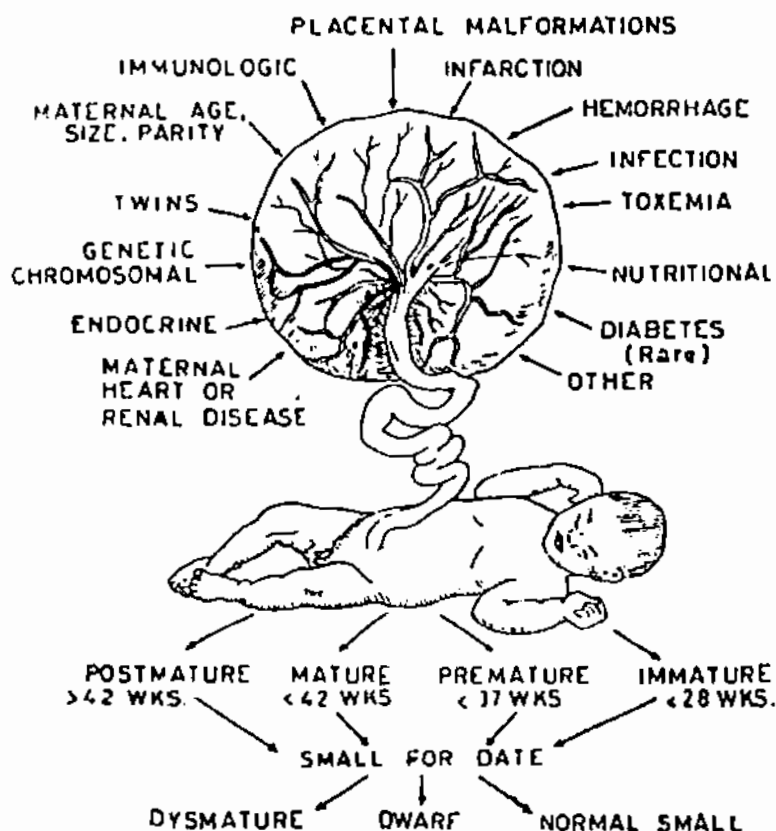


Fig. 6 : Causes of the light-for-date baby.

The external appearance of the infants in the three groups vary-though frequently overlaps-according to the severity of the placental insufficiency, its duration and the time of pregnancy at which the placental insufficiency was operating.

The postmature infant looks thin and wasted, though the head size is normal and the body length is equal to that of a term infant. The skin is usually

dry and desquamating, and the nails, skin and cord are frequently meconium stained.

In the dysmature baby who sustained a longer period of placental insufficiency both the head circumference and body length are reduced, but to a lesser extent than the body weight. There are skin, cord and nail discolouration similar to those of the postmature child. There is commonly a fully wakeful look that is characteristic for these children.

COMPLICATIONS :

Infants suffering from placental insufficiency in general are liable to certain complications.

Meconium Aspiration Syndrome : Meconium aspiration is the commonest cause for respiratory distress among postmature and dysmature infants. Such infants often suffer from hypoxia during delivery that results in passage of meconium. The asphyxiated infant gasps and aspirates the contaminated amniotic fluid which results in intensive irritation of the bronchiolar epithelium. Clinically the condition simulates closely that of the hyaline membrane disease. X-ray examination shows coarse streaking with varying degrees of aeration and emphysema. Treatment is like that of the hyaline membrane disease.

Transient Symptomatic Hypoglycemia of the Newborn : The condition is specially liable to occur in the male dysmature infant delivered to a pre-eclamptic mother. However, it occurs with less frequency among other infants with advanced dysmaturity. The low glycogen storage and the less available glucose for the relatively large infant brain predisposes these infants to permanent brain damage unless they receive active and early treatment. The infant appears well for the first hours or days after birth, then develops jitteriness, twitchings, attacks of apnea, cyanosis, pallor, apathy and convulsions. Diagnosis is confirmed by the finding of a low blood sugar level (below 20 mg. per 100 ml). Treatment includes intravenous glucose solution administration and ACTH i.m. injection for maintenance correction of the low blood sugar level.

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Chapter VI

NUTRITION AND FEEDING OF INFANTS FUNDAMENTAL PRINCIPLES OF NUTRITION

I. Calories : In the first year of life the infant needs 100 ± 10 calories per kg. per day. One calorie is supplied by 1.5 ml. of human milk, humanized milk or cow's milk; therefore the daily requirement is 150 ml. of milk per kg. body weight :

- 50% of calories for basal metabolic processes,
- 30% of calories for growth and specific dynamic action,
- 10% of calories for muscular activity of the infant and,
- 10% of calories lost in excreta.

In the second year the needs are 70 calories/kg./day (an adult requires about 44 calories/kg./day). After puberty the requirements are 10% more than the adult.

II. Water : The normal infant requires daily 150 ml. water/kg. body weight, i.e. $1/6$ his body weight per day in the first six months, $1/7$ in the second six months and $1/5$ of his body weight if premature or underweight.

When more than one liter of milk is required, solid foods should supply the extra calories, in order to avoid overloading of the stomach.

III. Food stuffs :

Protein : (1 gm. = 4 calories). Dietary protein is necessary for replacement of body tissue, construction of new tissue as well as for its maturation (which requires more nitrogen), for the supply of amino acids which are required for metabolic functions and to cover inevitable fecal losses.

The nutritional value of proteins depends on :

1. Content of essential aminoacids in relation to total aminoacids.
2. Their presence in the best ratio to each other, and to be eaten together within a reasonable time.

Animal protein, fulfils the above, 50% of it is in the form of essential amino acids, it is superior to vegetable protein which usually contains only about 30% with some essential acids either deficient or poorly represented. If more than one vegetable protein is present in a mixture, the ratio may be improved and if properly chosen, the protein quality may reach that of animal protein; on condition that the proteins of the mixture should be eaten together or within a short interval of 1 or 2 hours at most. The child needs daily 2 gm./kg. body weight of a protein of high biological value.

Fats : (1 gm. = 9 calories), Fats help in resisting infection, they are a concentrated source of energy and a vehicle for vitamins A and D.

Saturated fatty acids and oleic acid can be formed from the acetate resulting from the breakdown of carbohydrates or proteins. Poly-unsaturated (essential) fatty acids cannot be formed. Their absence may result in skin diseases. Human milk fat contains 7% linoleic acid which is absent in cow's milk.

Carbohydrates : (1 g = 4 calories). They are mainly used to supply energy and can be readily synthesized from fat or protein. Excess carbohydrates in the diet favours fermentative flora to flourish with the result of developing vomiting and/or diarrhea. The absence of carbohydrate from the diet may help ketosis to develop if fat is used in excess.

A carbohydrate supplement is usually needed as an addition to animal milk, the most practical forms are dextrimaltose and cane sugar. Lactose has no special advantage. Dextrimaltose is non-fermentable, slowly absorbed and maintains the blood sugar more or less constant which helps protein metabolism.

Best ratio of calories for nutritional requirements is obtained when 50% are from fat, 40% from carbohydrate and 10% from protein of high biological value (by weight : 50% carbohydrate, 35% fat and 15% proteins).

IV. Vitamins : Vitamins are essential to maintain good health; a good number of them function as co-enzymes. Those which are usually added to infant feeding are vitamin A, B₁, B₂, B₆, C and D.

With the exception of the need for vitamin D to prevent rickets (400 units daily) there is usually no need to supplement a natural well-balanced diet.

V. Minerals : These are as important as vitamins, they are indispensable to the structure and function of tissues and they should be present in proper balance. Because of growth, infants need relatively more minerals than older children or adults.

The chief minerals of the extracellular compartment are sodium and chlorides whereas potassium, magnesium and phosphorus are the chief minerals of the intracellular compartment and calcium and phosphorus are the chief minerals of the skeleton. With the exception of iron, in a balanced diet, there is no need to worry about mineral disturbances. Other minerals are needed in minimal amounts (trace elements). These include copper, manganese, zinc, cobalt, molybdenum, iodine and fluorine.

THE FEEDING OF INFANTS

BREAST FEEDING

Advantages of breast feeding :

1. To the baby :

- (a) Natural food.
- (b) Self-regulated.
- (c) Perfectly balanced biologically, chemically and physiologically, therefore there is no error in calculating the formula.
- (d) Contains the proper amounts of carbohydrate, protein and fat.
- (e) Infant on breast milk thrives well, gains weight steadily and sleeps well.
- (f) Sterile (thus intestinal infections are less common in the breast fed than in the artificially fed infants where infection and allergy are more liable to occur, and consequently mortality and morbidity are higher).
- (g) Specific growth factor has been identified in human milk which helps the flourishing of bacillus bifidus which may be responsible for the better health and growth of the breast fed infants.
- (h) Rickets is less liable to occur in breast fed infants.
- (i) Breast milk is albumin milk containing little casein and so, it is easily digested. Some say that it contains antibodies but this is of no practical value (except for diphtheria antibodies which are not destroyed by the stomach secretion). It is possible that it has an inhibitory effect on Polio virus.
- (j) Human milk contains lipase which helps to digest fat.
- (k) The mother takes better care of her infant kept constantly in her company.

2. **To the mother :** Easy (needs no preparation), cheap, helps uterine contraction and emotional satisfaction for mother and infant

For all these advantages : «always advise the mother to breast feed her infant but never oblige her».

Common Problems in Breast Feeding :

I. Contraindications of breast feeding :

1. Causes in the mother :

- a) *Active pulmonary tuberculosis* is an absolute contraindication.
- b) *Acute infections* e.g. typhoid, pneumonia are only temporary contraindications. Antibiotics shorten the course of diseases therefore empty the breast repeatedly, so that the mother can resume breast feeding after recovery.
- c) *In chronic illness* such as chronic nephritis, cancer and heart failure, it is unwise to allow breast feeding. The infant can be fed by his diabetic mother when properly controlled. Syphilitic infants should be fed by their mothers, as they may infect a wet nurse. Insane and epileptic mothers can nurse their babies under supervision.
- d) Although neither *menstruation* nor *pregnancy* contraindicates breast feeding, yet in the interest of the mother and fetus, breast feeding should be discontinued after four months of pregnancy.

2. Causes in the infant :

- a) *Allergy* to the human milk is extremely rare.
- b) *Metabolic disorders* and enzymatic deficiencies such as phenylketonuria, galactosaemia, hypercalcaemia.

II. Difficulties met with in Breast Feeding :

A — Defects in the breast:

- Poorly developed breast (hypogalactia) : Resort to mixed feeding.
- Retracted nipples : Antenatal care and breast pump may be helpful.
- Sore or cracked nipple : Prevention by avoiding engorgement of breast, daily application of lanoline, wash before and after feeding.

Treatment : Paint with Tr. Benzoini Co, 1% silver nitrate or 2% gentian violet. The baby is not allowed more than 10 minutes on one breast every 12 hours. The rest will be of animal milk,

i.e. - At 6 a.m. : Give right breast for 10 minutes.

At 9 a.m. : Give left breast for 10 minutes.

- At 12 o'clock and 3 p.m.: Give artificial feeding.

- At 6 p.m. : Give right breast for 10 minutes.

At 9 p.m. : Give left breast for 10 minutes.

- Engorgement of the breast : This condition is common and usually occurs on the 3rd - 5th day. The main cause is blockage of ducts by epithelial secretions and debris. Other causes are excess of milk or weak suckling baby. It can be prevented by squeezing the breast once or twice during the last two months of pregnancy, and applying a firm binder (Fig. 7). This condition is an important cause of failure of lactation. The best way to overcome it is to evacuate the breast completely after each feed by squeezing.



Fig. 7 : Binder for breast engorgement.

Mastitis and breast abscess : Surgeons like to stop breast feeding but this is not always right. Usually the infant can be fed on the healthy breast (with complementary feeding) until the affected breast resumes its function.

B - Causes in the infant

- Malformations such as harelip, cleft palate and dysplasia of mandible : using a long teat is helpful.
- Nasal obstruction - nasal catarrh : Use 0.5% ephedrine in saline nose drops - (in purulent discharge use proper antibiotic) - In congenital syphilis we get serosanguinous type of discharge called nasal-syphilitic snuffles, it usually occurs between the first and second month. Treatment of congenital syphilis is two million units of penicillin divided on ten days.
- Stomatitis such as thrush stomatitis : Treated by painting the mouth with 1-2% of gentian violet in water.
- Weak sucklers as in prematures, intracranial haemorrhage, congenital heart, mental deficiency, shy child, nervous or irritable child or it may be simple physiological delay of suckling reflex for the first few days. For weak sucklers, express the breast milk and give it by spoon or Breck feeder (not practical), if the baby cannot suck, spoon or even tube feeding is necessary.

Establishment of lactation : The infant should not be fed during the first day, but if he cries, decoctions sweetened with little glucose or sugar are offered and should be continued until milk secretion is established (third day after labour) in order to avoid dehydration fever and uric acid colics. On the second day the infant is put to his mother's breast. This will help the practice of suckling and allow the baby to get the benefit of the early milk known as colostrum.

HOW TO FEED :

1. **Nursing position :** The mother should sit well-supported and comfortable and the baby placed in semi-upright position on her arm with his head supported, the other hand is used to support the breast, guide the nipple and control the excessive flow of milk. The infant should be warm and not wet. The mother should train her infant to grasp the areolar tissue around the nipple in his mouth and not only the nipple (Fig. 8 & 9). The infant should not be allowed to sleep on the breast by repeatedly pulling the nipple out. At the end of lactation, the mother should massage the breast by the thumb to supply the last drops, which are rich in fat. After



Fig. 8 : Wrong breast feeding



Fig. 9 : Correct breast feeding

nursing, the infant is kept in an upright position with few taps over his back, to allow for eructation, otherwise vomiting and colic may occur.

2. **Times of feeding** : Two methods : the self-demand and the o'clock schedule. During the first two weeks, up to the first month, the breast is given two hourly or on self-demand. Once lactation is established, the infant should be fed every three hours for the first three months and later every four hours. The time-table should not be rigidly adhered to, half an hour before or after is a reasonable allowance. Whether to give a night feed or not is dependent on the child, but usually it is not necessary after the first month or two.

3. **One breast or both** : The answer depends upon the quantity of milk that could be supplied by one breast.

In Egypt, it is advisable to give both breasts each feed because the amount of milk from one breast is usually insufficient. In other countries, if the supply of one breast is enough, it is advisable to give one breast at a time to prevent soreness of the nipple.

4. Duration of the feed : Seven to eight minutes on each breast is enough. Never allow more than 20 minutes on both. The infant usually evacuates the breast in five minutes, but give two to three minutes more to allow complete emptying. The side given first should be alternated in the next feed.

HOW MUCH IS NEEDED :

150 ml./kg./day is the average amount needed in breast feeding. The best guide is a steady gain in weight. The infant should add 100 - 120 gm. every four days in the first four months. Test weighing for 1 - 3 days can tell if he is getting enough milk or not (never start before the tenth day as the infant loses weight in the first days, and the mother's milk is still not fully established).

The *criteria of adequacy of feeding* is a calm infant, who sleeps well and gains weight (a weight chart should be done).

WHAT TO FEED :

Besides breast milk; by the end of the first month, start vitamin A and D (drops of cod liver oil) and vitamin C (orange or lemon juice). Iron should be administered by the end of the second month.

HUMAN MILK

Mechanism of production : Formation of milk constituents is an active process that takes place in the secretory epithelial cells of the breast as regards fat, protein and carbohydrate, while the vitamins and minerals reach the milk by passive filtration from the blood.

Composition : Colostrum is the secretion produced by the breast in the first few days. It is a thin, yellowish fluid, high in protein content (3-5% mainly globulins), rich in vitamin A and in minerals (0.35%) especially potassium and sodium chloride. The fat content is 3% and lactose 4.5%. In other words colostrum is a transition from plasma to milk (weaning from the placenta). On microscopic examination, large endothelial cells called colostrum cells are observed. It is said that colostrum contains digestive enzymes as well as antibodies, but their value is doubtful. It has a laxative effect, possibly through stimulating the gastro - colic reflex. Colostrum is followed by transitional milk. This is intermediate in composition between colostrum and mature milk, which is established after about 20 days. It has a specific gravity of 1030 and a pH of 6.5. Human milk contains less buffer su-

stances, thus it needs less HCl acid than cow's milk. Human milk supplies 20 calories/30 ml. Its fat (about 4%) is highly emulsified and so easily digested. It contains less than animal milk of volatile short chain fatty acids which are irritating to the gastrointestinal tract. It contains as well, linoleic acid which is absent in cow's milk. The protein is 1.2% of which casein is 0.4% while lactalbumin and lactoglobulin are 0.8%. The casein curd of human milk is fine and readily crumbles, whereas that of cow's milk is large, tough and fills the whole stomach. Emptying time of the stomach with human milk is more rapid than with animal milk. As regards carbohydrate, human milk is sweeter than cow's milk and contains 6-8% lactose. This favours a certain type of intestinal flora, *B-bifidus* which is acid producing organism associated with a growth factor for the bacillus. Human milk contains usually 3000 units of vitamin A and 10 units of vitamin D per 100 ml. However, the amount of these as well as of other vitamins depends on the nutritional status of the mother. The content of minerals is $1/3-1/4$ that of cow's milk. The only exception is iron which is three times more than cow's milk. These minerals are well absorbed and sufficient for the first 3-4 months. After that, iron should be added as such, or by administration of vegetable soup to supply it together with other minerals.

Bacteriology : Unless breast infection exists, human milk is considered sterile. T.B. bacillus is not secreted in it, unless the breast is tuberculous.

Variations in quantity and quality : A 24 hours specimen is almost constant. Under famine conditions, the breast milk may be halved, while high protein diet increases the quantity. The total amount per day depends on the breast capacity and force of suckling, as well as the degree of completeness of emptying of the breast. However, the amount of milk in one feed varies according to the time of the day; the morning feed may be double that of the afternoon. Overwork, fatigue, anxiety and sleeplessness diminish the amount.

— The first part of the milk is low in fat, whereas at the end of the feed it is richer. Although the quality of milk may vary slightly under particular conditions, yet under ordinary circumstances the composition is efficient whatever the quantity.

Excretion of Drugs in milk :

1. Those which are secreted in sufficient amounts are bromides and laxatives such as cascara and phenolphthalein. They may produce effects on the infant.

- 2 Those which are secreted in small amounts are penicillin, sulfa, iodides, salicylates, quinine, atropine and morphine.
3. Moderate amounts of tea, coffee, alcohol and smoking (up to four cigarettes a day) are not harmful. Nicotine is secreted in small amounts in milk.

UNDERFEEDING IN INFANTS ON BREAST MILK :

This means that the infant receives insufficient amount of milk.

Symptoms :

1. Excessive crying and sleeplessness due to hunger.
2. Infant gains weight slowly and irregularly. Later the weight may become stationary. This is followed by loss of weight.
3. Constipation, but if the infant is very underfed, stools become frequent, small in amount and green in colour (hunger stools).
4. Vomiting due to excessive swallowing of air from an empty breast, this distends the stomach and the vomiting may be forcible but never projectile. (commonest cause of vomiting in infants is swallowing of air during breast or bottle feeding).
5. Colic : air may reach the intestine and the infant suffers from colics (commonest cause of colic in breast or bottle fed baby is sucking of air).

These symptoms may be mistaken for overfeeding and as a consequence, the feeds of the infant may be diminished and the condition gets aggravated.

Diagnosis :

1. Test weighing : weigh the infant at regular intervals at a fixed time with the same clothes, under the same circumstances (e.g. before giving the breast at 9 o'clock), and repeat weighing the infant every four days. An infant, in the first four months, should add 25-30 gm./day on the average weight chart, and if not do the next test.
2. Test feeds : baby is weighed before being put on the breast and immediately after the feed without changing the clothes; the difference shows the amount of milk taken. One test feed is useless, and the complete output of the mother in the day should be ascertained (3 - 4 tests/day should be done for 2-3 days). If he receives the proper amount but does not add the proper weight then the fault is in the child himself (celiac disease, congenital heart disease, enzymatic disease etc ...).

Treatment : Try to increase the milk supply and meanwhile give either complementary or supplementary feeding .

In *complementary feeding*, one gives a feed after the breast (to complete the feed), while in *supplementary feeding* we replace a breast feed by animal milk. It is not easy to complete each time by artificial feeding, the best way is to give each breast five minutes and then, give a small bottle-feed of about fifty grams to the infant who will take what he needs from it. Complementary feeding is particularly needed in the mid-day feeds (12 noon, 3 p.m., and 6 p.m.). The bottle must be given after the breast and never before, this ensures that the breasts are completely emptied and hence can be refilled again.

Complementary feeding should never be too sweet otherwise the infant will refuse the breast. If breast feeding does not supply 50% of the calories required, better stop and give animal milk.

Methods of increasing or maintaining milk supply :

1. Avoid engorgement of the breast.
2. Make certain that the baby empties the breast at each feed otherwise evacuate it completely by manual squeezing.
3. Mother should receive proper adequate diet and enough fluid (about 1.5 liter a day, in the form of water and beverages or milk. She should have enough rest and sleep, and should be relieved from domestic worries and psychological problems.
4. The mother should be encouraged to breast feed her baby and she must be convinced of the advantages of breast feeding.

OVERFEEDING IN BREAST-FED BABIES :

This may occur in hot countries where children need more fluids and will take it in the form of breast milk. As a consequence of this overfeeding, the baby is usually plumpy and overweight (weight chart). Sometimes the excess fat in the diet is a factor whereas excess carbohydrate leads to fermentative diarrhea and loss of weight; thus he may lose weight because of the occurrence of both vomiting and diarrhea. Colics may also occur as a result of overfeeding.

Diagnosis : Test feeds per 24 hours for 2-3 days.

Management : After ascertaining the diagnosis, the intervals between

the feeds are lengthened, or only one breast is nursed per feed. It may help to give the baby fluids between the feeds or just before feeding time. On the other hand, one should not be too strict as regards the increase in body weight, particularly if the child looks healthy and in good humour.

ARTIFICIAL FEEDING

The aim is to supply as a substitute for breast milk a modified animal milk, which as far as possible, promotes health and normal growth of the baby which should be as near as possible to a normal infant put on breast milk regardless of its chemical composition.

The main difficulty in feeding animal milk is the hard curd formation of caseinogen. This could be modified by boiling for about five minutes, by evaporation as in making evaporated milk, by dilution with water or better by boiling with cereal water, by acidification (addition of lactic or hydrochloric acid or acid producing organisms such as lactic acid bacillus or *B. acidophilus*), by adding citrate 0.3% or by the process of preparing dried milk by homogenization through pressing the milk through very small holes that break casein and fat into tiny particles.

Indications of artificial feeding

1. Contra-indications of breast feeding.
2. Death of the mother.
3. Diminution of breast milk (less than 50% of the required).
4. Twins.
5. Institutes.
6. In particular diseases such as allergy, fat intolerance, metabolic disorder etc...

Comparison of milk of various animals with human milk :

Casein and lactose are not found in nature except in milk. Casein in cow's milk constitutes 70% of its protein and is responsible for the hard big curds formed in the stomach, which interfere with digestion unless the milk is modified.

The fat emulsion in cow's milk is less complete than in human milk and the fat globules are bigger. When milk is left to stand they rise up to the top of the container and about 80% of the fat can be skimmed, but with the centrifugation

most of the fat (up to 98%) may be removed together with some casein. Cow's milk fat, like that of breast milk, consists mostly of triglycerides but the fatty acid composition is different; it contains more of the lower fatty acids (butyric, caproic, caprylic and capric) which may cause diarrhea, and smaller amounts of poly-unsaturated fatty acids which have proved to be essential constituents of the diet. Linoleic acid is almost absent from cow's milk but forms 7% of the fatty acids in human milk fat.

Table 7 : Constitution of human and various animal milks

Per 100 ml. milk		Human	Cow	Buffalo	Goat	Ass
Water	Gm.	87.65	87.25	83.2	86.3	89.9
Ash	Gm	0.2	0.7	0.9	0.8	0.5
iron	mg.	0.15	0.05			
Protein (total)	Gm.	1.2	3.5	4.1	3.7	2.0
lactalbumin	Gm.	0.4	0.4	0.6	0.4	
lactoglobulin	Gm.	0.4	0.4	0.4	0.3	1.4
casein	Gm.	0.4	2.7	3.1	3.0	0.6
Total lipids	Gm.	3.8	3.7	7.3	4.8	1.6
Essential fatty acids	Gm.	0.35	0.10			
Lactose	Gm.	7.0	4.8	4.5	4.4	6.0
Calories / 100 ml.		67.0	66.5	100	75.5	46.5
% from protein		7.5	21.0	16.5	19.5	17.0
% from fat		51.0	50.5	65.5	57.0	31.0
% from carbohydrate		41.0	28.5	18.0	23.5	52.0

The ash in animal milk (3-4 times that of breast milk), is a burden to the kidney of the newborn, which is not yet fully developed. The difference in iron content is an important consideration in infant feeding.

Forms of animal milk and artificial foods :

Liquid forms :

A) *Fresh milks* : These may be tuberculin tested milk (from tubercle-free cows), which may be pasteurized as well. Certified milk (animal is under medical supervision). Pasteurized milk (milk heated to 65°C for 20

minutes then cooled rapidly to 10°C). Here casein is slightly modified but the microorganisms are not all killed and therefore although older children may drink it, pasteurized milk for infants should always be boiled.

B) Evaporated milks : 1. Unsweetened full cream : Milk is concentrated to half its quantity by heating to 110° C and vitamins are reduced to 50%. When diluted 1 part to 2 parts of water, and sugar added, a good humanized animal milk is obtained. However, vitamins should be supplemented, and once the tin is opened it must be used on the same day. The casein is softer and lactalbumin gets less allergenic. This milk is homogenized, sterile, cheap and easy to administer.

2 Sweetened full cream : It contains much carbohydrate, little fat and protein and so is not suitable as such for feeding of infants.

II. Dried milks : They are manufactured either by :

- a) *Roller process :* milk runs on a hot roller where its solid constituents remain as a fine film on the surface, which is scraped off and the powder tinned
- b) *Spray process :* by forcing milk through fine hot jets, the fluid portion evaporates and the dry powder falls to the bottom.

Liquid milk is reconstituted by suspending the powder in water 1:6 by volume, or 1 : 8 by weight.

Advantages of dried milk :

1. Sterile and highly soluble.
2. Composition is constant.
3. Keeps for a long time.
4. Effect of heat on protein renders it more easily digestible (size of clot is reduced).
5. Available on travelling in the tropics and where fresh milk is not present.
6. Can be modified according to different children and different localities.
7. Prepared in different forms to fulfill requirements in health and disease.
8. Compared with fresh milk, the dried form is not expensive.

Types of dried milks :

- a) As regards fat content : full cream (3.5% fat), half cream (2.5% fat), _____
skimmed (0.5% fat). High fat content is not desired in fat intolerance. _____

convalescence from gastroenteritis, malnutrition and for prematures, otherwise any normal child can thrive well on it.

- b) As regards pH : Milks can be acidified by fermentation of lactose with *Lactobacillus acidophilus* (biological acidification) or addition of lactic acid in different concentrations varying between 0.3 - 0.7% to the above mentioned milks. So we get acidified full cream, half cream or skimmed milk. The main advantages of acidified milks are easy digestion, modified curd and less favourable for bacterial growth. Indicated in prematures, malnutrition and convalescence from gastroenteritis.
- c) Protein milks : rich formula with protein 2½-3%, very useful in premature and debilitated infants.
- d) Humanized milks . trials have been made by different firms in different ways to get a milk whose composition is not only identical with human milk as regards amount of protein, fat, sugars and minerals, but as well as regards the quantitative details of its constituents such as unsaturated fatty acids, lactose and amino acid contents so much so that chemical identity with human milk is obtained. However, giving such milks to infants, have proved less efficient than the breast milk on the growth curve "weight chart" of the infant, This has been overcome by increasing the protein content to 2% and minerals to 0.3-0.4% and by modifying the fat by mixing the animal fat with vegetable oil.
- e) Modified forms : Many firms have their own modifications for example:
 - reducing the lactose content and adding cane sugar and dextrimaltose which is less fermentable than lactose :
 - albumin and globulin removed for cases of allergy.
 - phenylalanine low milk for phenylketonuria.
 - lactose free milk for galactosemia and in cases of lactase diminution such as after gastroenteritis, malnutrition, lactose intolerance.
 - low calcium milk for hypercalcemia.

III. Non-complete proprietary foods which can be given only as additions :

- a) Starchy food such as corn flour, cereals, etc. to supply extra calories.
- b) Protein food mainly casein (Casec and Caseylan) may be used in cases of fermentative diarrhea.

IV. Animal milk substitutes : vegetable milks e.g. soya milk or vegetable mixture milk in milk allergy and the latter for poor socioeconomic states.

EXAMPLES FOR DIFFERENT FORMS OF DRIED MILKS

- Modified milks :** Nestogen full cream (Nestlé, Switzerland).
 - Bebelac Z18 (Lijempf, Holland).
 Lactogen (Nestlé) : modified full cream milk.
- Full cream cow's milk:** Nido (Nestlé).
 - La friziana (Lijempf, Holland).
- Half cream milks :** - Nestogen half cream (Nestlé).
 - Bebelac Z12 (Lijempf, Holland).
- Humanized milks :** - Nan (Nestlé).
 - Bebelac humanized (Lijempf, Holland).
 - S.M.A. (Wyeth, U.S.A.).
 S 26 (Wyeth, U.S.A.).
 - Similac (Abbott, U.S.A.).
 - Similac with Iron (Abbott, U.S.A.).
- Acidified milks :** Felargon (Nestlé) : full cream, biologically acidified.
 - Bebelac Z18 acidified (Lijempf) : full cream acidified.
 - Prodicton (Nestlé) : half cream biologically acidified.
 - Eledon (Nestlé) : partly skimmed, biologically acidified.

N.B. : The terms Butter milk and Protein milk are not used now.

**SPECIAL FOODS USED FOR ALLERGIC, METABOLIC &
ENZYMATIC DISORDERS.**

DISEASE	TYPE OF FOOD
— Galactosemia, lactase deficiency and lactose intolerance.	— Lactose free milk (al 110, Nestlé).
— Sucrase-isomaltase deficiency.	-- Disaccharide free milk (al 110, Nestlé).
— Congenital glucose-galactose malabsorption.	— CHO free formula base to which fructose is added.
— Phenylketonuria.	— Phenyl alanine low milk, rich in tyrosine (Phenelolac).
— Histidinemia.	— Histidine low milk.
— Other metabolic disorders of amino acids	— Appropriate milks are given.
— Allergy to milk.	— Soya milk : Isomil (Abbott), Sobee (Mead).
-- Allergy to cow's milk.	- Goat's milk or Soya milk.
— Hypercalcemia.	- Decalcified milk (Locasol).
— Congestive heart failure.	— Low sodium milk.
— Cystic fibrosis of pancreas.	— Formulas in which medium-chain or long-chain triglycerides are substituted for milk fat.

NON-COMPLETE PROPRIETARY FOODS.

1 — Mainly starchy foods :

— Rice powder	- Starch.	Corn flour
— Corn flakes.	— Quacker oats	

2 — Mainly protein foods :

- Casilan (Glaxo) : contains 90% protein.
- Casec (Mead)

3 — Starchy foods enriched with milk :

- Cerelac (Nestlé).
- Milo (Nestlé).
- Bebelac creme vanilla and creme cocoa (Lijempf, Holland)
- Home made milk pudding (Mehalabia).

4 — Vegetable mixtures rich in protein :

- Supramine (the Nile co.) : vegetable mixture + skimmed milk.
- Home made mixture consisting of : 3 parts of peanuts, 2 parts of chickpea and one part of sesame-dreg (Tehina) by weight.

Methods of Artificial Feeding

I. What to feed? (Quality) : This depends mainly on the infant himself. Infant's food must be easily digested, free of harmful bacteria, and must contain sufficient protein, fat, carbohydrate, minerals, vitamins and water. It must be satisfactory as regards calories. The following points are of importance :

- a) If the baby does not thrive on a diet which is balanced in quantity and quality the fault is in the child (infections, organic disease, metabolic, etc . . .).
- b) Individual babies vary in their food requirements although they may be of the same age and weight. Some infants are active and cry excessi-

vely so they require more food (particularly food which is rich in fat), others are calm and so require less food.

- c) In warm weather the infant requires less food but needs more water.
- d) Under ordinary circumstances, the foods of choice are either humanized fresh cow's or buffalo's milk or half cream dried milk.
- e) Acid milks are indicated in cases of fermentative diarrhoea as they are rich in proteins, poor in carbohydrates and so they prevent fermentation and diarrhoea.
- f) High protein in milk or skimmed or half cream lactic acid milk are helpful in treating wasting.
- g) Whenever you want to change from one formula to another, do so gradually e.g. replace 1/4 at a time and allow 2-3 days interval before the next move.

Humanization of fresh milk : This is the process by which animal milk is modified so that it becomes as far as possible similar to human milk in composition. For this purpose, equal parts of cow's milk and water are mixed and sugar and cream are added to the mixture to bring these constituents to their level in breast milk. Since buffalos milk is the one mostly used in Egypt, its humanization does not involve addition of cream but only 5% sugar is added to the mixture of milk and water in equal parts. It is then boiled for sterilization and modification of the casein. The composition of the modified buffalo's milk becomes; protein 2%, fat 3.6%, carbohydrate 7.2% and minerals 0.45%. It supplies 70 calories per 100 ml. equivalent to 70 calories per ounce (30 ml.) distributed as follows : 12% from protein, 47% from fat and 41% from carbohydrate.

It is advisable to prepare the whole 24 hours formula and sterilize it by using the Soxhlette apparatus (it is a pan with a valve in its cover to allow for the steam and regulate the pressure). Inside, there is a metal holder for seven bottles, so there is an extra bottle. After preparing the formula the bottles are filled and covered and the apparatus with the bottles is heated till boiling. They are then cooled and kept in the refrigerator until the time of feeding when a bottle is warmed and given to the baby.

II. How much to feed ? (Quantity) : 150 ml./kg./day. Range 150-180 ml./kg./day in the first four months and later according to age, the quantity per kilogram diminishes gradually.

Choice of a particular type of dried milk : Though we get different formulas and their indications are given on the tin, yet the real answer as to which type

should be administered is given by the infant himself. There are infants who thrive on high fat, others do not grow well on low protein or develop diarrhea and fermentation on using a milk containing 7% lactose. The best rule is to start with half cream milk and modify it later, according to the response of the infant. Some pediatricians prefer to start with one of the dried humanized formulae and react accordingly by enforcing it by one or other forms of dried milks.

III. How to feed ? (Method of administration) : The formula is given with a bottle, spoon or special feeder.

i — *The bottle* : should be plain with no angles, graduated and with a capacity of about 250 ml. There are two varieties :

- a) Boat-shaped bottle : It may break easily being unsteady because of its shape. Its advantage is that it can be easily cleaned and that suckling from it is easy (Fig 10).

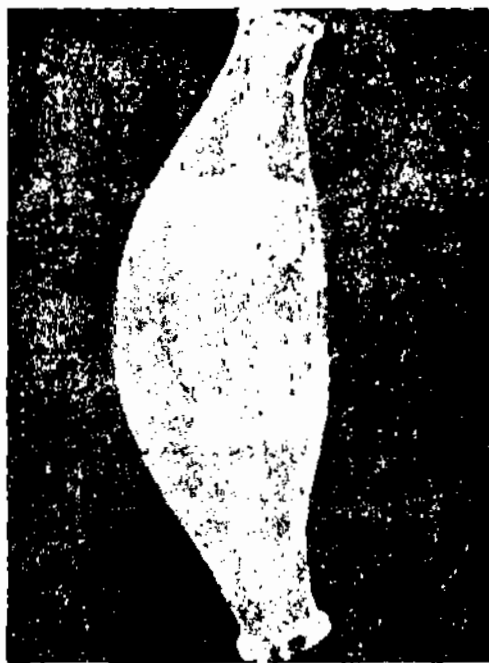


Fig. 10 : Boat-shaped bottle

- b) Upright bottle : The best type is made from pyrex glass and should be rounded with no edges so that it can be easily cleaned, capacity 250 ml.



Fig. 11 Upright feeding bottle

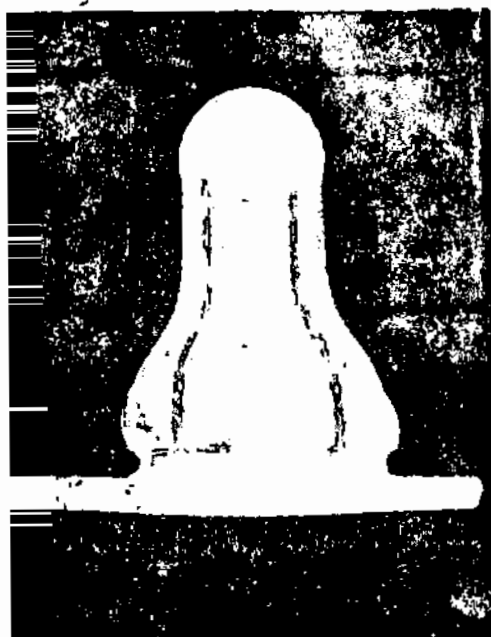


Fig. 12 Good teat



Fig. 13 Correct method of artificial feeding

and is graduated. It can be easily transferred, kept covered, and the teat can be inverted inside until needed (Fig. 11).

ii — *The teat* . It should be of moderate size, elastic and of a small bulb. Particular attention should be paid in choosing the teat for weak sucklers and for cleft palate (Fig. 12).

iii — *Preparation of the feed* : The quantity of milk should be measured and added to previously boiled warm water, mixed well and administered at 38°C (Fig. 13).

FEEDING OF THE PREMATURE

What to feed ? Once he is aware, in few hours start by sweetened water because of the fear of the liability of aspiration. On the third day the child is put on the breast if he can suckle.

If not, squeeze the breast and give the milk by dropper or spoon.

In absence of breast milk a humanized milk formula may be resorted to.

Vitamin D is particularly needed after the second week and the true indication for it, is when the infant starts to gain weight. You may start by 100 units daily and increase daily by 100 units to reach the proper dose (800 units daily)

How to feed ? (Methods of feeding) : If the infant is above two kilograms, he usually can suck the breast or bottle, only a smaller teat is needed. If he is a weak suckler, a dropper protected by rubber tube, or less practically Breck-feeder may be used (Fig 14). The mother's milk can be expressed and is given by dropper or spoon because the premature



Fig. 14 : Breck-feeder

is usually a weak suckler. If the infant cannot suck or swallow, tube feeding is essential; a small catheter is passed through the nose to reach half an inch above the stomach (± 15 cm. in length), it is connected to a funnel which is fixed about 50 cm. above the head of the baby to allow the fluid to flow by gravity. (Pinch the catheter before removal to prevent aspiration of fluid into the larynx). As the feeding is to be repeatedly administered, a polythene catheter may be used; it is passed through the nose where it is fixed and left for three to four days so that the infant will not be disturbed. A premature infant below 2 kg. should be fed two hourly, then 2.5 hourly and lastly three hourly.

How much to feed : At first, small amounts are given in each feed and gradually increased. Within 2-3 weeks the baby should receive the amount calculated according to his weight, i.e. 150 calories, or 200-250 ml. milk/kg /day or roughly about $1/5$ his body weight in the form of human milk or an equivalent.

FEEDING OF TWINS

Twins are usually born under-weight. If below two kilograms, they should be treated in the same way as the premature infant. When they exceed two kilograms at birth or later on, the management will then be :

1. If the mother has sufficient milk, she can breast feed both. First feed one baby on right breast then put the other on the left. For the next feed, give the first baby the left breast, and the second the right.
2. If milk supply is inadequate for both infants (and usually it is so, especially after the first month or two), complementary or supplementary feeding may be given.
 - a) Supplementary feeding : One baby is fed on both breasts while the other is given a bottle, on the next feed the twins are reversed. Giving the bottle may make the infant suck less from his mother, so it is advisable if possible to replace the bottle by spoon feeding.
 - b) Complementary feeding : Each baby is given one breast alternatively and enforced by a bottle or spoon afterwards. This method takes a longer time and one baby has to wait a considerable time unless a helper is present. Another method to feed the twins is to put one baby on the breast and the other on the bottle according to the circumstances of the family and the babies.

WEANING

"Weaning" is to accustom the child to food material other than milk. There are indications for sudden weaning such as acute illness of the mother or grave disease, e.g. T.B. and other debilitating conditions. Weaning is also advised in pregnancy (at the 5th month). Generally, weaning should be gradual. The aim of mixed feeding is :

1. Child cannot tolerate more than one liter of fluid/day, and so, more solid foods should be added gradually to cover his extra needs.
2. With growth, the baby requires more food which cannot all be supplied by the breast.
3. To train the gastro-intestinal tract to digest starch, as well as more solid food.
4. Supply sufficient nutrients in which milk is particularly deficient (Iron, Vit.B₁ and Vit.D).
5. To educate the child independence by using spoon or cup.

By the end of the third month, start starchy food such as rice pudding with milk (Mehalabia).

End of the fourth month start vegetable soup.

First three months give six feeds/day.

Second three months give five feeds/day.

From 6-12 months give four feeds/day.

These are subject to variations according to the growth curve and the response of the child.

Scheme of feeding of infants :

At 6 months : 6 a.m. give breast or bottle (200 ml. formula), 10 a.m. give milk pudding (150 ml. of buffalo milk + 50 ml. water + two teaspoonfuls sugar + 2 teaspoonfuls starch, corn flour or powdered rice), 2 p.m. give breast or bottle + little vegetable soup, 6 p.m. give breast or bottle, 10 p.m. give breast or bottle. Add vit. D (At noon give orange juice about 30 ml.).

At 7 months; Either continue 4 hourly feeds or change to 4 feeds/day.

If four hourly, the schedule will be exactly like that of six months but the 6 p.m. feed should consist of milk pudding, banana, orange

juice or yoghurt with a piece of apple scraped or beaten up. The latter schedule is preferable in summer.

7 a.m. breast or bottle. 11 a.m. milk pudding + $\frac{1}{2}$ egg yolk (but not the white to avoid allergy). 3 p.m. vegetable soup or chicken soup. 7 p.m. breast or bottle.

At 8 months : Introduce a piece of chicken, liver, fish or meat, boiled and made into paste, later pounded and finally can be given minced.

Bread can be given half toasted with little butter and salt. This will please the child, educate mastication and help teething.

You can increase the amount of egg yolk gradually. Whole egg is taken at one year of age (yolk and egg white), and you can alternate it with cheese or meat.

At 9 months : The scheme will be : 7 a.m. breast or bottle. 11 a.m. milk pudding. 3 p.m. vegetable soup + chicken or a piece of lean meat with butter and alternate with special dishes e.g. yoghurt, minced meat with macaroni, etc. 7 p.m. breast milk or milk + banana.

N.B. Additions and change of diet should be very cautious or arrested altogether in summer months.

Between 1-2 years :

- a) The amount of milk is reduced to half a liter/day.
- b) In summer the diet must be light and overfeeding avoided.
- c) No ices or spices
- d) Educate the child good manners, order and ethics of feeding, e.g. food should be administered well arranged in dishes, etc

Full Menu of a child one year old

The breakfast (7-8 a.m. : May be served in three dishes, on a tray and a napkin.

- a) First dish is half a cup of milk + one or two plain biscuits. You can change the taste of milk by tea, coffee, cocoa or you can add quacker—oats or some of the market preparations (Cerelac, Nestum, etc.)

- b) The second dish should be one of three foods to be changed daily, e.g. one day an egg half boiled, second day a piece of cheese about 1-1 ½ tea-spoonfuls and third day boiled mashed beans with little butter or oil.
- c) The third dish will be a dessert, the type of which depends on the season and the appetite of the child, e.g. banana, one teaspoonful of jam or honey or some jelly.

Lunch at noon (12 O'clock) : Same tray with three dishes, free of spices

- a) First dish is starchy (2 tablespoonfuls of rice or macaroni and a piece of butter) or a paste.
- b) Second dish will be boiled vegetables with butter (sauté) and a tablespoonful of minced meat (the meat may be chicken, calf's meat, rabbit, brain, fish or liver).
- c) The third dish is the dessert according to likes and dislikes, season of the year, appetite, etc. e.g. starch or rice pudding with milk, jelly, fruits such as a banana or an orange.

The 3 p.m. feeding : Must be very light and may consist of half a cup of milk + tea and biscuits, milk pudding or yoghurt beaten up with half an apple or one banana.

Dinner (7 p.m.) : Must be rich, but easily digestible to allow the infant to sleep well. It offers many possibilities according to the habit of the family. If they have dinner similar to lunch, you can habituate the child so that he gets the same diet as given in lunch (but no need to give meat). If the family is accustomed to a light meal, give a big dish of milk pudding or quaker oats (250 ml. milk in little or no water + one or two tablespoonfuls of rice, starch, or quaker and 1-2 tablespoonfuls of sugar).

Menu after the second year : At this age, the child can eat the usual diet of the adult. He learns to use spoon, knife and fork and sits at the family table to learn good habits. Spicy foods are to be avoided and one must be careful as regards fish bones and also nuts because of fear of aspiration.

M. M. HANAFY

Chapter VII

NUTRITIONAL DISORDERS

Malnutrition is one of the gravest medical and social problems in our country as well as in many other countries.

This condition is caused by a combination of a number of factors which are social, economic, sanitary, educational problems of food production and transportation and the rapid growth of population.

These disorders may be due to : —

- I — Specific deficiencies of vitamins or minerals e.g., vitamin D deficiency or iron deficiency. In this group, the clinical picture is clear cut and the deficient etiological factor should be the title, i.e. vitamin D deficiency rickets, and iron deficiency anemia . . . etc.
- II — Food deficiencies : P.E.M. — P.C.M.
 - a) Caloric deficiency only where the diet is balanced but the quantity is not adequate e.g. insufficient amount of milk. This results in pure nutritional wasting or marasmus.
 - b) Protein-calorie deficiency (P.C.M.) or protein energy malnutrition (P.E.M.) where the diet is inadequate and unbalanced also. The protein fraction is the fraction which is mainly diminished and carbohydrates are administered in excess. The term kwashiorkor is usually given to this type of combined deficiency. Specific deficiencies may and usually are present in this group of cases and they add additional features to the clinical picture.

SPECIFIC DEFICIENCIES

VITAMIN A

Functions :

- 1 — It combines with a protein to form "the protein pigment" retinine or visual purple which is responsible for light adaptation.
- 2 — It maintains the integrity of the epithelial structure.

- 3 - It participates in the formation of mucopolysaccharides in the matrix of bone and teeth.

Deficiency of vitamin A leads to :

- 1 — Night blindness, xerophthalmia (dryness of conjunctiva), and keratomalacia (softening of the cornea).
- 2 - The columnar epithelial cells change into stratified form which invites infection, so we get recurrent attacks of bronchitis, gastro-enteritis or pyelitis.
- 3 - Faulty epiphyseal bone formation.

Diagnosis of vitamin A deficiency :

- 1 — Blood level below 45 units in infants (13 mg.) or below 75 units in older children (22 mg.) indicates vitamin A deficiency .
- 2 - Demonstration of keratinized epithelium of the conjunctival or corneal smear. Occasionally fleshy masses may be present over the conjunctiva (Bitôt spots).
- 3 Presence of poor adaptation to light or night blindness that responds to vitamin A administration.

Treatment - Vitamin A 30,000 to 60,000 units should be administered daily for two weeks. Response may start in hours but it may need 2 to 4 weeks to attain complete recovery.

Overdosage : Administration of huge doses in a short period leads to acute poisoning manifested by drowsiness, diplopia, papilledema, bulging anterior fontanel and vomiting.

The chronic form is manifested by anorexia, irritability, bulging anterior fontanel, subperiosteal thickening due to new bone formation, enlarged liver and spleen, dermal and hair changes as pruritis, alopecia . . . etc.

Excess of carotene pigment in the diet (pro-vitamin A) may lead to golden yellowish pigmentation of the skin and hypercarotinemia; a condition called "Xanthosis cutis". a condition which when diagnosed has no pathological significance.

VITAMIN B COMPLEX

Vitamin B₁ :

Functions : Vitamin B₁, thiamine, antiberiberi : is present in an enzyme form which is concerned with oxidative pathway of the glucose in the Kreb's cycle, its deficiency leads to excess of pyruvic acid in the serum.

Thiamin deficiency : If chronic it leads to demyelination of peripheral nerves as well as central nervous system.

Pathogenesis : Inadequate intake of vitamin B₁, e.g. in rice eating areas.

Diet containing the enzyme thiaminase commonly present in some of the sea foods. Sometimes an intestinal micro-organism may produce this enzyme.

Clinical picture :

1 — Dry Beri Beri :

- Anorexia, vomiting, constipation and failure to gain weight.
- Peripheral neuritis, motor and sensory, hyperesthesia and areflexia.
- Later, the cranial nerves and the inferior recurrent laryngeal nerve may be affected.
- Convulsion and coma in severe cases.

2 — Wet Beri Beri :

- Heart failure and cardiac involvement manifested by tachycardia and cardiac enlargement.
- Edema, usually localized, may occur.
- Therapy with vitamin B₁ (50 mg. daily together with B-complex) improves immediately the anorexia, the neurosis and the edema. Neuritis and cardiac involvement may need 2 to 3 weeks for complete recovery.

D i g n o s i s :

- 1 — History of clinical picture.
- 2 — Excess pyruvic acid in the blood, also thiamine deficiency (difficult procedure).
- 3 — Load test, this is important to differentiate between deficient intake and deficient utilization of vitamin B₁.

Vit. B₂ : Riboflavin :

Function : It is the prosthetic group of a number of respiratory enzymes.

Deficiency : Is characterized by thinness, maceration, fissuring and may be ulceration of the skin at the angles of the mouth, i.e. cheilosis. The tongue becomes smooth and red, i.e. glossitis. Fissures and seborrheic dermatitis at the naso-labial fold occur as well as vascularization of the cornea and may be keratitis with itching, photophobia and tearing.

Diagnosis : None of the symptoms are pathognomonic, so laboratory diagnosis by the load test or diminished concentration of the vitamin in the plasma, or better in the red cells and white cells of the blood are important.

Vitamin B₆ :

Pyridoxin deficiency is rare and is usually a result of administration of boiled food for a long time.

Clinical picture of deficiency : Convulsions, peripheral neuritis, microcytic anemia with hyperferremia and scaly dermatitis. The symptoms may occur as a result of deficiency or as a lack of response to normal amounts "Pyridoxin dependency". Isonicotinic acid increases the requirement of vitamin B₆. All the symptoms mentioned respond promptly to administration of vitamin B₆.

Diagnosis :

- 1 — Therapeutic test.
- 2 -- Vitamin B₆ is necessary for the breakdown of kynurinine (a metabolite of tryptophan) to nicotinic acid. In B₆ deficiency kynurinine accumulates and is excreted in the form of xanthurenic acid. Therefore the appearance of xanthurenic acid in the urine after oral administration of tryptophan is diagnostic.
- 3 — Failure of tryptophan load to cause an increased excretion of N-methyl nicotinamide in the urine.
- 4 — Diminished pyridoxin in the blood (difficult to estimate).

Treatment : Administration of vitamin B₆ in 2 mg. daily dose and then 1 mg. is required, in pyridoxin dependency 2 mg. daily are needed as a maintenance dose.

Vitamin B₃ (Niacin) :

Functions : Nicotinic acid is the basis of the enzymes that deal with oxidation and reduction reactions in the body.

Deficiency : Its deficiency leads to pellagra which is usually common among people living on corn, mainly due to tryptophan and niacin deficiency.

Clinical picture : Pellagra is characterized by rough skin, mainly on the exposed surfaces to sun as well as under pressure points. Gastrointestinal disturbances in the form of vomiting and diarrhea commonly occur. Mental disturbances are not uncommon, increased reflexes and even an extensor plantar may occur. Pellagra is often complicated by other deficiencies such as Vitamin A deficiency.

Diagnosis : Clinical picture. Excretion of N-methyl nicotinamide in the urine.

Treatment : Administer niacin in a dose of 50 mg. together with vitamin B-complex and balanced diet.

VITAMIN C (ASCORBIC ACID)**Functions :**

- It has a role in the metabolism of the aromatic amino acids.
- It converts folic acid into folinic acid which is essential in the blood cell maturation.
- It is concerned in the synthesis of the steroids.
- It is essential for the formation of collagen tissues, cartilage and matrix of bones as well as cement substance of the blood vessels.

Deficiency : Leads to scurvy, the manifestations of which result mainly from hemorrhagic reactions into the skin, gums and subperiosteal areas. These cause marked irritability and severe pain, tenderness, edema and pseudoparalysis with the frog position of the involved extremity.

The chest cage will manifest angular deformity at the costochondral junctions with depression of the sternum. The skin shows keratotic changes with delayed healing of wounds. There may be cardiac ischemia with E.C.G. changes.

The X-ray of the long bones will manifest loss of the normal trabecular pattern of the medulla giving the ground glass appearance, thinning of the cortex and subperiosteal thickening due to hemorrhage giving the dumb-bell-shaped appearance.

Blood level of vitamin C and its concentration in the white blood cells will be below the normal level. The saturation of the tissues with vitamin C can be estimated from the amount of urinary excretion of vitamin C after a test dose of ascorbic acid; children with vitamin C deficiency excrete less "Load test".

VITAMIN D

Functions : Vitamin D is essential for the absorption of calcium from the gut and this consequently increases the absorption of phosphates. It mobilizes the calcium from fully calcified bone making it available for the formation of new bone, and so maintain serum calcium level. Vitamin D helps to govern the equilibrium between blood and bone calcium. This action is a direct one; it is not mediated through the parathyroid gland.

The action of vitamin D on the kidney is to facilitate tubular reabsorption of the phosphate in the proximal convoluted tubules. If vitamin D is deficient in the diet, the urinary excretion of calcium almost ceases, whereas phosphate excretion increases, while vitamin D in large doses increases urinary excretion of calcium as well as phosphates. In that way it resembles the action of the parathyroid hormone.

Vit. D Metabolism (Fig. 15) :

— Vit. D occurs in two forms, Vit. D₃ formed from 7 dehydrocholesterol in the skin by the action of ultraviolet rays and vit. D₂ formed by the action of U.V.R. on ergosterol in plants.

— Vit. D₃ & D₂ are biologically inactive and are hydroxylated in the liver to form a more active metabolite, 25 hydroxy vit. D which is further hydroxylated in the kidney to form very active metabolite 1, 25 Dihydroxy vit. D.

Deficiency of vitamin D leads to :

- 1 — Rickets (Infantile).
- 2 — Osteomalacia of pregnancy and hunger osteomalacia.
- 3 — Infantile tetany.

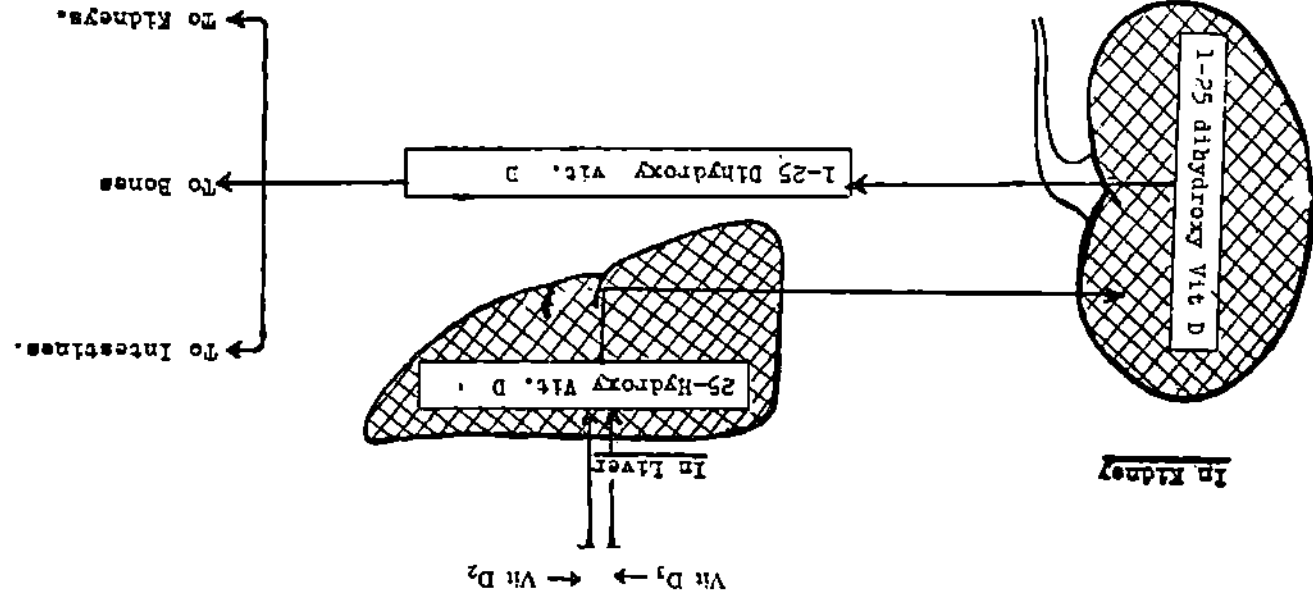


Fig. 15 : Metabolism of Vitamin D.

- 4 Dental decay, in rachitic children the teeth tend to erupt late and decay early; the late eruption appears to be a direct effect of too little vitamin D. Increasing vitamin D will reduce the development of caries and even the teeth which started caries tend to have the disease arrested.

Diagnosis of deficiency of vitamin D (look for vitamin D deficiency rickets).

Hypervitaminosis D : A daily dose of 2000 units per kg. body weight is dangerous. Individuals vary in their susceptibility, some can tolerate 400,000 units daily while others are poisoned with 50,000 units daily. The symptoms can be explained by the rise in the plasma calcium, the patient feels weak, thirsty, anorexic and loses weight. Nausea, vomiting and polyuria with albuminuria and casts are common and there may be even stones and dehydration. Renal failure from nephrocalcinosis is an important complication. Constipation is usual and it is to be expected with hypercalcemia. Diarrhea and abdominal cramps may complicate the picture. Usually there is hyperchromic anemia which is often unexplained. In X-ray, density of bones is increased at their growing ends, but often associated with diminution in density of the shaft, there may be dense metaphyseal lines which resemble that of lead poisoning. A rare finding is a deposition of calcium in the soft tissues, around the joints and also in the walls of the blood vessels. In the arteries, large doses of vitamin D lead to degenerative changes particularly in the aorta. Metastatic calcification may occur in the heart, stomach, lungs, thyroid and pancreas as well as in the kidney and arteries

Chemical changes : Plasma calcium rises to a very high level, plasma phosphorus is normal but may rise if there is renal failure. Urinary calcium is increased and inspite of increased absorption of calcium from the gut and its retention in the metastatic deposits, the calcium is withdrawn from the bones.

Treatment : Stop administration of vitamin D and give a diet poor in calcium. Dehydration must be corrected, electrolyte losses must be looked after. Hypercalcemia may produce polyuria with low specific gravity inspite of the dehydration. Cortisone is an effective antidote of poisoning with vitamin D, it should be given until the plasma calcium has fallen to 12 mg. per 100 ml., then it should be stopped.

RICKETS

Rickets is a general disorder of metabolism affecting chiefly the bone forming minerals, calcium and phosphorus.

Pathology : The essential changes in the bones are :

- 1 — Decalcification of the normal bones already present.
- 2 — Formation of imperfectly calcified new bone resulting in widening and enlargement of the epiphyseal end of the bone (rachitic metaphysis).

Etiological Classification :

- I — Disturbances of vitamin D metabolism (deficient intake, absorption or utilization).
- II — Error in the filtering or absorptive capacity of the kidney (Glomerulotubular dysfunction of the kidney), where the glomerular tufts or the tubular system are affected. In this group, the kidney disturbances play the primary role in producing the rachitic changes.
- III — Other rare metabolic disturbances related to formation of bone, such as, hypophosphatasia, oculocerebrorenal dystrophy and hyperparathyroidism.

I — Disturbances of Vitamin D Metabolism :

1) *Deficient intake :*

- a) *Infantile form*, extremely rare in well developed countries whereas it is the most common type in the under-developed ones including Egypt. (A full description is given later).
- b) *Late rickets*, where food supply is insufficient under adverse conditions, it occurs between six to fifteen years. Besides the usual manifestations of rickets, the child is weak and anemic.
- c) *Atrophic rickets* characterized by osteoporosis. It occurs in cases of arrest of growth such as in marasmus and kwashiorkor. Vitamin D as well as protein deficiency may play a role (It is comparable with osteomalacia in adult women).

2) *Malabsorption Syndromes* such as the celiac syndrome, biliary obstruction, cystic fibrosis of the pancreas; here either we get osteoporosis alone or the

whole clinical picture of rickets may occur particularly in younger children.

3) *Vitamin D refractory or resistant rickets*: Here the clinical picture, chemical changes and X-ray appearance are identical with those of vitamin D deficiency rickets. This condition is due to failure to respond to what would be adequate vitamin D intake in ordinary cases of Vitamin D deficiency. The fault is mainly in the absorption capacity of calcium from the intestine resulting in secondary hyperparathyroidism leading to hyperphosphaturia and hypophosphatemia. It responds to administration of high doses of vitamin D, sometimes one million units daily may be required (Vit. D dependency).

II — Glomerulo-tubular dysfunction :

1 — *FAULT IN THE GLOMERULAR SYSTEM*: (renal osteodystrophy)
In this group there is renal insufficiency which occurs as a result of congenital malformation of the kidney (dysplasia or hypoplasia), urinary infection, destruction of renal tissue from chronic glomerulonephritis, chronic pyelonephritis, hydronephrosis . . . etc. There is marked retardation of growth and the lesion is similar to that of ordinary rickets, blood chemistry shows high serum non-protein nitrogen, high inorganic phosphorus and normal or low serum calcium level. The cause is failure of deposition of calcium phosphate in the bones due to disturbance of calcium phosphorus ratio in the serum (calcium X phosphorus may reach hundred).

2 — *DEFECTIVE RENAL TUBULES* : There is a fault in one or more of the functions of the renal tubule represented by one or more of the following conditions :

A) *Renal tubular acidosis* : A condition characterized by the presence of metabolic acidosis as a consequence of failure of the kidney to form ammonia and hence sodium and potassium are lost in the urine, chloride is retained in the blood, so we get hyperchloremia, hypokalemia, hypercalcuria and an increase of the bicarbonate in the urine. If it occurs in infants, it is usually fatal, but in childhood it may give rise to rickets. Calcium may be deposited in the kidney which may ultimately fail.

B) *Defective renal tubular reabsorption* which may manifest itself as :

- a) Hyperphosphaturia with hypophosphatemia (one form of vitamin D resistant rickets).
- b) Glycosuria.

- c) Aminoaciduria, either with general increase in the amino acids or selective increase such as hyperglycinuria or hypercystinosis.
- d) Any combination of the above may occur namely hyperphosphaturia and/or glycosuria and/or aminoaciduria. To this group "De Toni-Fanconi-Debré syndrome" may be given.

III — Other Metabolic Disorders :

1 — *Hypophosphatasemia* where you get severe bone defect shortly after birth; serum calcium and phosphorus are not diminished whereas the alkaline phosphatase in the blood is markedly reduced.

2 — *Hyperphosphatasemia* which is characterised by cortical thickening of the bones with diminished density in the center; alkaline phosphatase is very high. It responds to cortisone therapy.

3 — *Oculocerebrorenal dystrophy* (Lowe's syndrome) . In addition to the clinical picture of rickets there is mental retardation, glaucoma, organic aciduria, aminoaciduria, diminished production of ammonia and cataract.

4 — *Hyperparathyroidism* : There is local osteolytic activity leading to cyst formation of the bones. The serum shows hypophosphatemia and hypocalcemia. This clinical condition may simulate rickets associated with chronic nephritis but it can be easily differentiated by absence of kidney trouble as well as the presence of hypophosphatemia.

INFANTILE RICKETS

Etiology : Vitamin D deficiency : This may occur if vitamin D intake is inadequate and the skin is not exposed to ultraviolet rays which activate its 7 dehydrocholesterol into natural vitamin D₃. Calciferol or vitamin D₂ is produced by irradiation of ergosterol present mostly in yeast. Cod liver oil is rich in both vitamin D₂ and vitamin D₃. The antirachitic rays of the sun are the more vertical and so they are more effective in prevention of rickets at noon and in summer. The effect of antirachitic rays of the sun is minimal when they are oblique or pass through clouds, dust, smoke or dark skin. Ultraviolet rays do not penetrate window glasses or clothes.

Contributory factors : In border line cases of supply of vitamin D the following factors may affect the development of rickets.

- 1 — Rapidity of bone growth, the more rapid the growth the more severe is the development of rickets.

- 2 — Ratio of calcium and phosphorus in the diet. The best ratio to guard against rickets is 1.5 calcium : 1 phosphorus.
- 3 — Citrates tend to protect against rickets by increasing the solubility and absorption of the calcium from the intestine.
- 4 — Increased acidity helps absorption of calcium and phosphorus.
- 5 — Infection promotes development of rickets.

Incidence : The frequency of rickets in Egypt is very high (20% of the out-patient cases), in spite of the knowledge of its etiology and its response to the treatment.

Age : It is rarely seen below 3 months unless the mother is osteomalacic, the maximal incidence is between 3 and 18 months; after the second year it gets less frequent because the child receives a mixed diet, enough sunshine and he is growing slowly. Prematures and twins, because of their rapid growth, develop rickets easily.

Diet : It is more common in artificial feeding because of infections and because they usually get excess of carbohydrates and so less fat and less vitamin D.

Season : Rickets occurs more commonly during the winter season due to the lack of effective ultraviolet rays.

Geographical Distribution : Depends upon the diet given, and the climatic condition, e.g. in polar regions enough cod liver oil is supplied while in the tropics excess of ultraviolet rays exist and so rickets is less frequent in these two regions whereas in subtropical regions there is neither enough vitamin D in the diet nor enough ultraviolet rays and consequently rickets is more common.

Pathology: There is excessive preparation for formation of bone without it being well mineralized. In other words it is failure of lime to deposit in maturing cartilage at the epiphysis and freshly forming bones. At the shaft of the bones we get demineralization and a new layer is laid on the outside, formed mainly of osteoid tissue, and so we can easily get green stick fractures

In normal bone, at the cartilage shaft junction, usually we get definite zones in the following order (Fig. 16).

- 1 — An area of resting cartilage which is formed of one layer of cells (R.C.)
- 2 — Zone of proliferation of cartilage formed of six or seven rows (P.C.).
- 3 — A very thin area of dead cartilage that passes through different processes

simultaneously; namely calcification followed by decalcification (osteoclasts) and finally ossification (osteoblasts) (L.P.C.). In other words osteoid tissue does not exist in the normal bone.

In active rickets (Fig. 17), we find that the zone of maturation of the cartilage is very irregular, it is massive in amount, calcification is very irregular, ossification is very irregular, there is excess of osteoid tissue formed into tongues (I.A.C.). In other words, in rickets you get disorder whereas in the normal bone you get order.

In healing rickets (Fig. 18), a new line of calcification similar to that of the normal appears in the middle of the metaphysis (L.P.C.) and absorption of the rest of the metaphysis takes place (healed rickets).

Chemical changes : In the normal bone the ratio of the inorganic to the organic material equals 2 : 1, in rickets it is the reverse being 1 : 2. Inorganic phosphate diminishes; in the normal it is 4-6 mg. per 100 ml. of serum as phosphorus, in rickets it may fall down to 2 mg. or less. Calcium is unaffected in noncomplicated rickets, normally it is 9 - 11 mg. per 100 ml. of serum. In the premature you may get the normal calcium and the normal phosphorus and in spite of that rickets develops. This is due to excessive rate of growth demanding more vitamin D. Alkaline phosphatase is increased in active rickets, (the normal is 5-15 Bodansky units). Urinary diastase is also increased and both return to normal when healing is complete. Vitamin D level in the blood is reduced

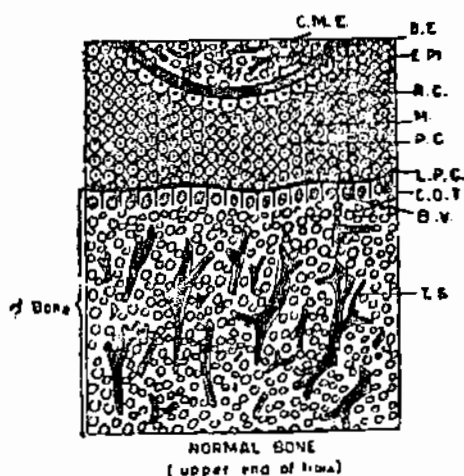


Fig. 16



Fig. 17

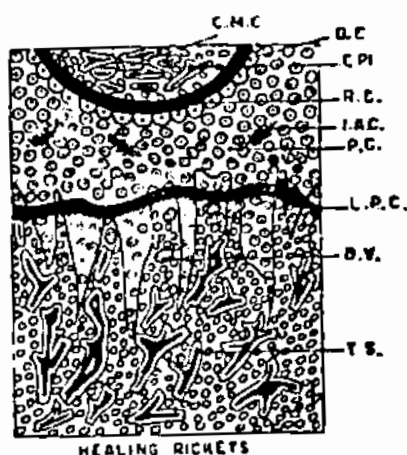


Fig. 18

- C.M.E., = Cavity of marrow of epiphysis,
 E.P.I. = Epiphysis,
 R.C. = Resting cartilage,
 M, = Matrix,
 P.C. = Proliferating cartilage,
 L.P.C. = Line of preparatory calcification,
 C.O.T. = Chondro-ossous trabeculae,
 D.V. = Blood vessel,
 I.A.C. = Irregular areas of calcification,
 T.S. = Trabeculae of the shaft.

Clinical Picture :

Symptoms : Head sweating, irritability by day and sleeplessness by night are the earliest symptoms that appear from the third to the sixth month. Delayed sitting, standing and walking are late symptoms.

Signs : I — Bony changes : Changes in the skeleton are greatest at the sites where growth is most rapid and the deformities are the result of gravity and traction of muscles on the affected bones.

A — Head : (i) Craniotabes is the earliest bony change to be observed.

Its greater incidence is from 3 to 6 months of age. It is best elicited by holding the infant's head between the palms of the hands, the thumbs over the forehead and the fingers fanned out over the occiput. When gentle pressure is exerted over the occipital region, the skull yields under the fingers like a ping-pong ball or egg shell crackling sign.

Rachitic craniotabes must be differentiated from craniotabes that results

from other causes viz., prematurity, osteogenesis imperfecta and hydrocephalus. The finding of vertex softening along the sutures or generalized softening of the skull stands against the diagnosis of rachitic craniotabes, whereas its presence in localized areas away from the suture stand in its favour.

(ii) Anterior fontanel is wider and its closure is delayed than normal

(iii) Frontal and parietal bossings are due to deposits of osteoid tissue which is situated mainly around the centers of ossification of these bones.

(iv) Size : The head often looks larger than normal and shows no signs of increased intracranial tension.

(v) Shape : The vault and occiput are flattened. This together with frontal and parietal bossings and the grooves between the bosses result in caput quadratum (the skull is square) or hot cross bun skull.

(vi) Teeth eruption is usually delayed and deciduous teeth may show enamel defect or decay. Enamel defect in permanent teeth may occur as evidence of previous rickets.

B-Thorax : (i) Beading of the ribs at the costochondral junctions is another early sign and is seen as a row of nodules about the size of cherries extending down and backwards along the line of costochondral junction and are referred to as "rachitic rosary"

(ii) Harrison's sulcus is a horizontal groove corresponding to the line of attachment of the diaphragm with flaring of the costal margins below. It is more seen in the right side.

C — Extremities : (i) Epiphyseal enlargement is common and is best felt at the wrists and ankles.

(ii) Marfan's sign is a transverse groove that is felt over the tibia and fibula just proximal to the ankle joint and its presence is related to the disorderly deposit of osteoid tissue in the centers of ossification of the malleolus and the end of the tibia or fibula.

(iii) Deformities : Tibia and fibula often become curved after the rachitic child has started to walk resulting in genu valgum (or genu varum) deformities. The humerus and the bones of the forearms may be bent as the infant crawls.

(iv) Fractures of the green stick variety are often seen.

D — Pelvis may be permanently deformed, the anteroposterior diameter being shortened and the outlet narrowed.

II — Muscles and Ligaments : Hypotonia and laxity of ligaments may be extreme (acrostatic rickets), genu valgum and genu varum deformities are in part related to hypotonia. The pot belly results from hypotonicity of the muscles of the abdominal wall and of the muscles of the intestines and is accentuated by carbohydrate fermentation and downward displacement of the liver and spleen by the deformed thorax and lax ligaments.

The spinal muscles share in the general muscular hypotonicity resulting in delayed ability to sit up alone. When the infant does sit up alone there is often apparent smooth curvure (kyphosis) that disappears as the infant is suspended from the shoulders. Scoliosis may at times be present.

Radiological Findings : (a) Broadening and cupping of the epiphyseal ends of long bones. (b) Increased distance between the calcified ends of the bones of the forearm and the carpals or metacarpals. (c) Fraying of the epiphyseal ends of long bones. (d) Epiphyseal line is indistinct (e) Diminution of bone density. (f) Fractures. (g) Periosteal elevation, (Fig. 20).

Diagnosis and differential diagnosis of rickets : It is important to diagnose first the rachitic state usually by the clinical, radiological and chemical evidences. The next important point is to diagnose the type of rickets



Fig. 19 Healed rickets Normal



Fig. 20 : Active infantile rickets



Fig. 21 : Healing rickets.

which can be determined easily if the following points are taken into consideration:

- 1 — The dietary and genetic aspects .
 - 2 — Physical examination of the child including weight, height, proportions of the body, condition of the internal organs.. etc.
 - 3 — Corneal examination by the slit lamp for cystine crystals.
 - 4 — Urine analysis for albumin, phosphates, cystine crystals, other microscopic deposits as well as for amino aciduria and phosphoethanolamine in the urine.
 - 5 — Blood examination especially the chemical aspect for total serum calcium, inorganic phosphorus, alkaline phosphatase, blood urea, serum electrolytes, base combined bicarbonates and pH.
 - 6 — Radiology is important especially an anteroposterior view of the wrist and knees; exposure settings should be done for future references.
- Photographs of the child should be taken for future comparison.

Prevention : Infantile rickets can be prevented by exposure to ultraviolet rays or by a daily oral dose of 400 I.U. of vitamin D in the form of cod liver oil (1 teaspoonful per day) or one of the concentrates preferably in water

miscible vehicle. The daily prophylactic dose of vitamin D recommended for premature infants and twins is 1000 units. Vitamin D should be given to the pregnant or lactating mother.

Treatment of infantile rickets : A daily administration of 1500 units will produce healing in 2 to 4 weeks demonstrable in X-ray. In some cases of vitamin D deficiency rickets, massive therapy consisting of 600,000 units (15 mg. once monthly); one, two or three injections may be needed.

Treatment of refractory rickets : The basis of treatment is administration of large doses of vitamin D, the amount varies in different patients and even in the individual child, the required dosage varies from 50,000 to 1,000,000 units per day and in general it is higher during the infantile and adolescent period. Hypercalcemia is an indication of reducing the dose of vitamin D. Though with treatment the serum inorganic phosphorus rarely returns to normal levels, yet the rickets heals with adequate therapy. Orthopedic correction of deformities should never be done until the rachitic process becomes inactive.

TETANY

Tetany is hyperirritability of the nervous system due to lack of active calcium ions.

Etiological classification :

- 1 - Hypoparathyroidism; this occurs in tetany of the newly born.
- 2 - Infants fed on cow's milk may get phosphate tetany.
- 3 --- Infantile tetany usually associated with infantile rickets due to diminished active calcium in the blood which is a consequence of hypoparathyroidism (failure of the parathyroid to be activated by diminished calcium ions in the blood due to vitamin D deficiency).
- 4 - Excessive vomiting with loss of hydrochloric acid "Gastric tetany"; the manifestations here are caused by high carbon dioxide combining power "alkalosis".

- 5 Administration of alkalis in excess, e.g. citrates, bicarbonates or phosphates.
- 6 - Over-ventilation of lungs leading to alkalosis, e.g. in acute encephalitis.
- 7 - Post-acidotic tetany, acidosis with sudden shift to alkalosis, e.g. in treating cases of diarrhea.
- 8 — In nephritis we get acidosis, hyperphosphatemia and hypocalcemia which interfere with Vitamin D action in the blood resulting in tetany.

Acute infections may precipitate an attack of tetany.

Clinical Picture :

Manifest tetany :

- 1 — Carpal and pedal spasms, this may occur instantaneously or after an attack of fever.
- 2 — Laryngeal spasm where you get a crowing or whooping sound, its maximal occurrence is between 6 to 15 months.
- 3 -- Generalized convulsions are commonly manifested in infants and older children.

Latent tetany : All the manifestations under this group are due to hyperirritability of the nerves.

- 1 - Chvostek's sign : When you tap the facial nerve in front of the ear the muscles of the face which the nerve supplies will contract.
- 2 - Trousseau's sign : When you apply the cuff of the sphygmomanometer to the arm above the systolic pressure you get carpal spasm "Main d'accoucheur".
- 3 - Erb's sign : When you apply a current less than 5 milliamperes, you find that the muscles contract (normally a more powerful current is needed).
- 4 Peroneal sign : When you tap the peroneal nerve, the muscles it supplies contract, and the foot is everted.

Diagnosis : This depends mainly on the laboratory findings where you get the serum calcium between 6 to 7 mg. per 100 ml., in addition to the classical clinical picture mentioned above. Cases of convulsion as well as laryngeal spasm must be thoroughly investigated before diagnosing tetany as an etiology.

Management .

- 1 - Emergency : administer calcium in an active ionic form either intravenously, intramuscularly or by mouth, where it can be associated with a sedative, acid or acid producing ion. Parenteral sedatives may be needed in cases with convulsions and/or laryngeal stridor before I.V. calcium could be given.
- 2 — Investigate the etiological factor and treat the underlying cause, e.g. administration of vitamin D will relieve infantile rickets but not central tetany.
- 3 — Deal with any associated condition, e.g. acute infections.

FOOD DEFICIENCIES

Malnutrition is a world-wide problem from which, in varying degrees, more than half of the world's population suffers. Poverty and ignorance in addition to other factors, e.g. infections, parasitic infestations, taboos and prejudices are responsible for inadequacy of nutritive elements resulting in malnutrition.

The specific deficiencies such as vitamin or mineral deficiency are not included under the title of malnutrition. Over nutrition too is not included, nor the metabolic disturbances which may be associated with symptoms of malnutrition.

The main nutritional disturbances may result from :

Calorie deficiency : Where the infant is given a well balanced diet in amounts less than those required. An important example is the inadequate breast milk as the only source of feeding, i.e. quantitative deficiency resulting in nutritional wasting (marasmus) in which the infant's body will live on its own tissues to maintain its daily vital processes. Affected infants manifest growth failure, with varying degrees of diminution in fat and muscle bulk.

Protein deficiency : Pure protein deficiency with no diminution in the calories is well illustrated in the sugar baby of Jamaica who displays a normal or increased body weight with edema, muscle wasting and moon-face i.e. "nutritional edema".

Protein-calorie deficiency : This results when calories are supplied in relative abundance through starchy food stuffs in a protein deficient diet. The resulting syndrome in babies given this diet is referred to as protein-calorie malnutrition (kwashiorkor).

Trials to classify malnutrition on a scientific basis are numerous. However, the classification of the International Committee on Infantile malnutrition in 1970 (Fig. 22) is generally accepted, although it is not without defects because of the high percentages of exceptional cases.

Marasmus and kwashiorkor are different manifestations of infantile malnutrition and the difference in the clinical picture is related to the variability of the deficient elements. Table (8) presents some of the characteristics of marasmus and kwashiorkor.

THE CLASSIFICATION OF THE INTERNATIONAL COMMITTEE
ON INFANTILE MALNUTRITION IN JAMAICA-1970

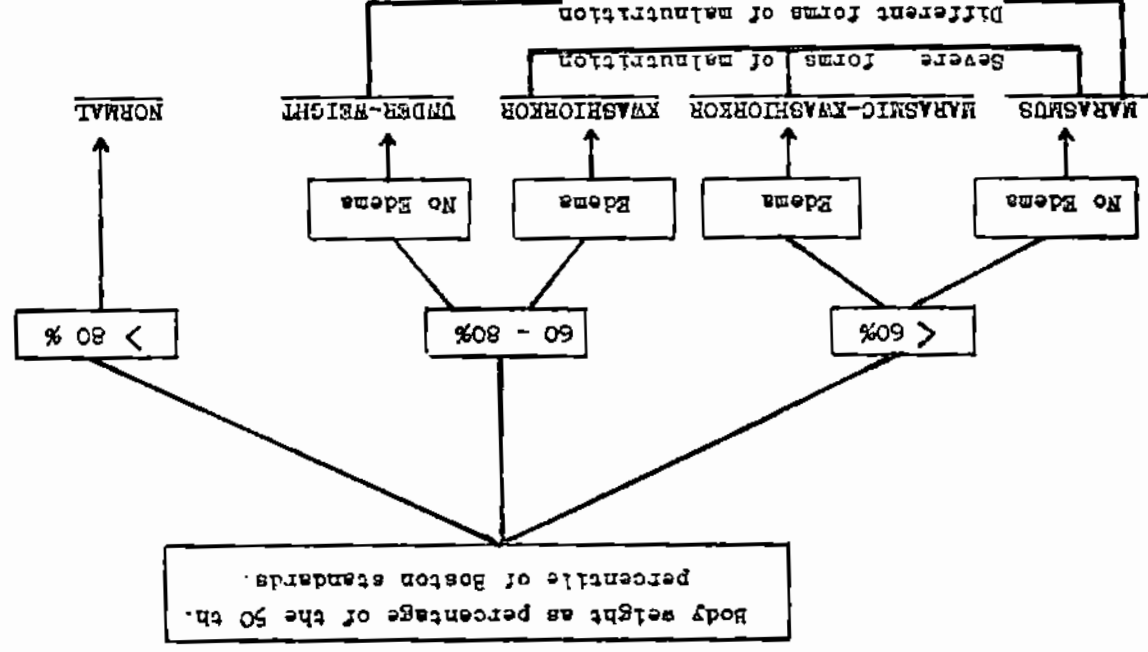


Fig. 22

The commonest form of infantile malnutrition are the intermediate states which stand between marasmus and kwashiorkor and display some but not all of the manifestations of both states. Examples are infants with severe wasting (less than 60% of their expected weight) plus edema. To such conditions, the term marasmic-kwashiorkor is applied. On the other hand infants are seen in whom there is growth failure or wasting and dyspigmentation of the hair but with no edema.

Mehlnahr Schaden (flour feeding injury) described by the Germans half a century ago with its hydremic and anhydremic varieties are comparable with kwashiorkor and marasmus respectively.

Specific deficiencies of vitamins and/or minerals commonly accompany calorie or protein-calorie malnutrition.

Table 8 : Some characteristics of marasmus and kwashiorkor
(Mc Laren)

	Marasmus	Kwashiorkor
General features :		
Occurrence	World-wide	Limited
Usual age	Infancy	Second & third years
Adaptation to stress	Good	Poor.
Response to treatment :		
Immediate	Poor.	Good (occasional sudden death)
Long-term effects :		
Mental	Fair	Good
Physical	Severe	Nil
Liver damage	Severe	Mild
Liver damage	Nil	Nil
Clinical signs :		
Edema	Absent	Present
Dermatosis	Rare	Common
Hair changes	Common	Very common
Hepatomegaly	Common	Very common
Mental changes	Uncommon	Very common
Wasting of fat	Severe	Mild

	Marasmus	Kwashiorkor
Wasting of muscles	Severe	Mild
Anaemia	Common and severe	Mild
Vitamin deficiencies	Uncommon	Common
Laboratory findings :		
General		
Total body water	High	High
Extra-cellular water	Some increase	More increase
Body potassium	Some depletion	Much depletion
Malabsorption	Some	More
Fatty infiltration of liver	Absent	Severe
X-ray bone loss	Mild	Mild
Renal function	Impaired	Impaired
I.V. glucose tolerance	Normal	Impaired
Response to adrenaline	Exaggerated	Lowered
Serum :		
Albumin	Slightly low	Very low
Enzymes (in general)	Normal	Low
Copper, Zinc, sodium	Normal	Low
Non-essential/essential		
amino-acids	Normal	High
Triglycerides	Normal	Normal
Cholesterol	Normal	Low
Non-esterified fatty acids	Normal	High
B-Lipoprotein	High	Low
Insulin	Low	Low
Growth hormone	Low or normal	High
Glucose	Low	Very low
Urine :		
Urea/total N	Above 65 %	Below 50 %
Imidazole acrylic acid	Nil	Present
Hydroxyproline index	Low	Low
Liver :		
Urea cycle enzymes	Low	Low
Amino-acid-synthesizing		
enzymes	High	High

* Mc Laren, D.S. 1972 in "Nutrition and its Disorders. p. 107

CALORIC WASTING OR MARASMUS

Wasting may result as the sequela of chronic debilitating disease (tuberculosis, recurrent gastroenteritis, etc.) but dietary marasmus in developing countries like Egypt, is by far the most common variety.

Infants receiving more or less a balanced diet, the total calories supplied by which are inadequate manifest varying degrees of wasting. According to the deviation of the actual body weight from the expected, three degrees are described. The term wasting, hypotrophy or hypothrepsia are applied to the first and second degrees, while for the third degree marasmus, atrophy or athrepsia are given.

In the first degree, the weight loss ranges between 15 and 30% of the expected weight. The infant is irritable with a characteristic peevish cry and his skin is dry and inelastic. The subcutaneous fat of the abdomen is absent, whereas that of thighs, buttocks and shoulders is reduced as well as the muscle bulk.

In the second degree, the body weight loss is 30 to 50% of the expected one. The subcutaneous fat of the thighs, buttocks and shoulders is absent, while that of the face is diminished. Muscles are more wasted than in the second degree. Consequently, it is of prime importance, when one determines the degree of wasting, to examine the abdominal wall before looking at the face.

In the third degree, the loss of weight is more than 50% of the expected body weight. The subcutaneous fat all over the body except the buccinator pad (probably due to different chemical composition of its fat) is lost. The fat stored in the internal organs is markedly diminished. The face is triangular simulating old man's or ape's face.

Pathology : The main pathological changes are the loss of the stored fat with atrophy of the muscles and internal organs and generalized osteoporosis. Fat is not usually apparent in the liver lobules.

Biochemical changes : The biochemical changes are not so striking in cases of marasmus in spite of the well evident clinical manifestations because the baby is living on his own tissues which supply the essential nutrients in balanced forms. Low serum proteins may be present but not so striking as in cases of kwashiorkor. The fasting blood sugar level is below normal, mainly due to diminished hepatic glycogen. The serum enzymes and minerals are usually within the normal range. The duodenal

enzymes show little or no reduction. In advanced cases the urine may contain excess nitrogen and ketone bodies, possibly due to glycogen depletion that associated starvation.

KWASHIORKOR PROTEIN-CALORIE MALNUTRITION

PROTEIN-ENERGY MALNUTRITION

The word kwashiorkor in the Ga language of the Gold coast literally means "the one before the last" and was used to describe a severe (malignant) form of malnutrition that a child gets when the next baby is born. Protein-calorie malnutrition, as an etiological term, disregards other deficiencies that may be present in addition to that of calories and protein, viz., vitamins, minerals and other trace elements, and it does not show the role played by the excess of the carbohydrate in the diet. Recently, the inter-relationship between protein and energy has been emphasized and the term protein-energy malnutrition (PEM) is preferably used.

As protein malnutrition commonly develops after weaning, when the baby is put on a diet consisting mainly of carbohydrates, it follows that the age incidence of kwashiorkor is related to the duration of breast feeding. In Egypt, kwashiorkor commonly occurs in infants aged 1 to 3 years due to deficient protein intake with relative excess of calories supplied by a high carbohydrate diet, besides the excessive demands of all nutrients, including protein of high biological value, during this period of very rapid growth. Less commonly, however, kwashiorkor may be seen at an earlier age, especially in breast fed infants with early lactation failure where partial replacement by an excess of carbohydrates such as rice water is resorted to.

Pathology : The main pathological lesions in kwashiorkor are in organs with a high protein content and high metabolic activities needed for the utilization of nitrogen especially in the formation of enzymes. The liver with its load of fat resulting from fatty infiltration, is often larger and heavier than normal, and microscopically the cells appear distended. This has tended to obscure the fact that in reality the liver is protein depleted and its cells are atrophic. The secretory cells of the small intestine and the acinar cells of the pancreas undergo atrophic changes, resulting in diminished production of their exocrine secretions. The heart, blood vessels and kidneys are diminished in size. The skin shows hyperkeratosis, atrophy and pigmentary—disturbances.

Clinical features : The fully developed or classic cases of kwashiorkor are not frequently met with. The clinical features result not only from protein malnutrition but also from relative excess of carbohydrate as well as variable degrees of deficiency of the calories. These changes occur independently of the geographic area, specific composition of the protein of the diet or the severity of the syndrome. This however, does not mean that all the features given below must be present before a clinical diagnosis of kwashiorkor can be made, though the first 3 are characteristically present.

1 — *Growth failure and muscle wasting :* In a severe case of kwashiorkor, the weight may be markedly diminished than the expected for age. Muscles are wasted. Subcutaneous fat may be preserved to a variable degree depending upon the amount of the carbohydrate supply. Height and head circumference may also be affected but not to the same extent as the weight. Bone age may be retarded.

2 — *Edema :* Is the most constant clinical manifestation. It starts in the lower limbs then becomes generalized. Ascites is unusual. Though edema is almost invariably associated with hypoproteinemia (total serum proteins being reduced to about 4.5 Gm./100 ml. and albumin concentration to 1.0 or 1.5 Gm./100 ml.), other factors may be responsible, viz metabolic breakdown of cellular tissues associated with potassium depletion and hormonal disturbances manifested by excess of antidiuretic hormone and aldosterone. Sometimes excess sodium chloride in the diet may be an accentuating factor. In some cases ulcers over the feet and in other sites may occur due to disturbed circulation leading to local nutritional deficiency of the area.

3 — *Mental changes :* Babies with kwashiorkor have marked apathy, misery and peevishness. Mental development appears to be below the normal for the age. Possibly a defect in the metabolism of aromatic amino-acids may disturb the functions of the brain.

4 — *Liver enlargement :* Is often present and seems to be more common in some localities of the world than in others and is caused by fatty infiltration that results from relative excess of carbohydrates in the diet, as well as lack of lipotropic factors including amino acids and vitamin B complex (chapter VIII). Occasionally the liver may end in cirrhosis with ascites as a terminal stage or even during clinical recovery.

5 — *Hair changes :* The hair is characteristically sparse, easily pickable, atrophic and often dyspigmented. Normal black hair may become brown or red and is tapered nearer to the scalp like an exclamation mark. When the hair is combed, bands of lighter and darker colour zones appear along the length of the hair resulting in the so-called "Flag Sign". The lighter areas are

taken as evidence of recurrent episodes of malnutrition. The etiology of hair dyspigmentation is obscure. Deficiency of pantothenic acid, sulfur containing amino acids (cystine and methionine) in the hair or a defect in the melanin formation similar to that present in phenylketonuria may be responsible for the colour changes of the hair.

6 — *Skin changes (Dermatosis)* : The characteristic rash when fully developed is most marked on the buttocks, perineum, inguinal regions, back of the thighs and axillae, although any part of the body surface may be involved. Initially the rash is composed of dark hyperpigmented, brownish black areas of skin. These subsequently desquamate as large tissue paper in thin flakes leaving easily damaged atrophic hypopigmented skin or even ulceration beneath. Protein deficiency, diminished essential fatty acids, vitamin A and niacin deficiency as well as suprarenal function disturbances may be responsible factors

7 — *Diarrhea* . The passage of loose stools in babies with kwashiorkor is not uncommon. This may be partly due to infection, whether inside or outside the gastrointestinal tract, and partly due to reduction of the intestinal and pancreatic enzymes as a result of protein deficiency. Low levels of these enzymes including amylase, lipase and trypsin lead to inadequate digestion of food, and the passage of loose stools as a consequence. Deficient intestinal disaccharidases explain the intolerance to carbohydrate resulting in fermentative diarrhea. Marked distension may be present; potassium deficiency as well as lack of absorption of gases from poor circulation may be etiological factors.

8 — *Anemia* . When present is mainly due to multiple factors, viz. deficiency of protein, iron, zinc, copper, folic acid, vitamins A, E, B₁₂, B₂ and/or C, also in severe cases there may be maturation arrest of the bone marrow. The types of anemias encountered may be normocytic or macrocytic (chapter XIII).

9 — Malnourished children have *poor resistance* and are more prone to bacterial and non-bacterial infections which will have more complicated courses.

10 — *Associated deficiencies* . Including vitamins, minerals and trace elements. The most common vitamin deficiencies that accompany infantile malnutrition are those of riboflavin; manifested by excoriations at the angles of the mouth, the nose, the ears, the labiae and the anus and by vascularization of the —cornea from without in. Atrophy of the tongue papillae and its violet coloration may result from niacin deficiency in addition to the ariboflavinosis. Lack of vitamin A may result in dull, dry and lusterless conjunctivae (xerosis). Fleshy masses may be also seen on the conjunctivae (Bitôt spots). The cornea may become dull and soft with subsequent ulceration and infection which may

spread to the interior of the eye (endophthalmitis) or include all its coats (panophthalmitis). Vitamin A deficiency frequently manifests itself, by recurrent infections of the respiratory, urinary and gastrointestinal tracts. This is due to the metaplasia of the epithelium with super-added secondary infection. Hoarseness of voice may result from chronic laryngitis which is due to vitamin A deficiency, or paresis of the vocal cords occurring as a symptom of peripheral neuritis of the inferior recurrent laryngeal nerve resulting from thiamin deficiency (vitamin B₁). Bleeding in different sites which is occasionally present, may be due to deficiencies of vitamin C, K and/or P.

Vitamin D deficiency may be clinically manifest as florid rickets. When wasting is severe, however, osteoporosis is visualized radiologically (atrophic rickets). Blood chemistry is indicative of active rickets in both the florid and atrophic types.

Deficiency of some essential trace elements may complicate the picture of kwashiorkor. Hypocopperemia may contribute to hair and skin pigmentary changes and to the development of hypochromic anemia. Hypozincemia may be a factor in growth retardation. Manganese deficiency may have an effect on mental status resulting in irritability and apathy. Megaloblastic anemia may result from cobalt deficiency. Hypomagnesemia may explain the electrocardiographic changes in severe cases of kwashiorkor.

Biochemical findings

A — Border line cases : (Subclinical varieties).

1 — *Serum protein* : Diminution of the serum albumin is one of the earliest signs. A level of 2.86 Gm./100ml. serum is found in marginal deficiencies. The total serum proteins may be normal.

2 — *Urea nitrogen/creatinine nitrogen ratio* : This can be estimated in a single fasting urine sample. Ratio from 8-12 is found in border line cases; in severe cases the ratio is less while in the normal it is higher.

3 — *Amino acid determinations* : The test is based on determining by paper chromatography the amino acid patterns of the serum. The results are expressed as a ratio of the non-essential to the essential amino acids. Ratio below 2 is found in the normal, from 2-3 in subclinical cases and above 3 in clinical cases.

B — Cases with clinical manifestations of malnutrition :

The most important finding is the deficiency of total protein in the serum characterized by deficiency in the serum albumin, alpha and beta globulin fractions and an increase in gamma-globulin which may be a consequence of

secondary infection superadded to the clinical picture. These protein changes are present whether there is edema or not. The hypoalbuminemia is due to deficiency of intake of proteins. Examination of the extracellular fluid, blood and plasma volumes shows that they are not reduced and even these values are increased if related to actual weight. They are more increased the severer the malnutrition, i.e. the greater the volume of plasma per body weight. Hemodynamics in malnourished children are on the border line of circulatory failure, lowered blood pressure and diminished cardiac output.

Electrolyte studies show that serum calcium is normal, phosphorus, potassium and magnesium are reduced, sodium and chlorides are variable.

Serum enzymes such as amylase, lipase, esterases and alkaline phosphatase are low, but the activities of the liver enzymes which are released to serum as the transaminases and isocitric dehydrogenase are variable according to the extent of liver damage. They tend to increase with more hepatic injury. Pancreatic and duodenal enzymes such as lipase, trypsin and amylase as well as the disaccharidases are diminished. The activity of the liver enzymes D-amino oxidase and xanthurine oxidase is also diminished.

Glucose tolerance test shows marked diminution and is similar to starvation diabetes or "Hoffmeister's diabetes" i.e. a low and prolonged curve. The same also occurs with the fat and we get what is called "Lipemic curve" similar to what happens with starvation.

Prognosis : This depends upon :

The etiology : Whether undernutrition is purely due to dietetic error or whether it is associated with other anomalies such as congenital heart disease, cystic fibrosis of the pancreas or other metabolic disturbances. All these will definitely alter the prognosis.

The degree of malnutrition.

- The presence of other pathological processes such as intercurrent infections, electrolyte disturbances . . . etc.

Management of malnutrition : In the first and second degrees of wasting or malnutrition, the treatment is usually correction of the diet with the addition of the essential elements that may be deficient. This is successful in straight forward cases of pure nutritional deficiency.

In kwashiorkor and in marasmus, hospitalization is necessary where we start by "Emergency treatment", which constitutes the correction of fluid and

electrolyte disturbances using whole blood, plasma or saline and glucose infusions. Anti-shock measures may be needed such as warmth and circulatory stimulants. Treat any infection using the appropriate antibiotics and chemotherapeutic agents. Penicillin and streptomycin may be given for few days on the assumption that hidden infection may exist.

After the infant's condition improves, complete clinical evaluation and investigations must be done to arrive at the proper etiologic factors. Proper nutritional history is essential because underfeeding is the commonest cause of malnutrition in Egypt (accounts for about 95% of cases). Chronic or hidden infections such as tuberculosis, chronic otitis media, chronic pyelonephritis, enteric infections, chronic encysted empyema and deep seated osteomyelitis can be diagnosed by clinical examination and proper investigations, such as urine analysis, blood picture, tuberculin test, examination and X-ray of chest and bone to settle the diagnosis.

Congenital anomalies such as congenital heart disease, congenital renal anomalies, congenital defects of the nervous system, congenital gastro-intestinal lesions such as megacolon, cystic fibrosis of the pancreas and celiac syndrome should be ruled out by their appropriate methods.

Metabolic aberrations involving carbohydrates (e.g. galactosemia), amino acids (e.g. phenylketonuria) and minerals (e.g. hypercalcaemia) may be diagnosed clinically and by proper investigations.

Parasitic infestations such as ankylostoma, malaria and round worms are common associates of malnutrition. The proper management of the possible etiological factors mentioned should be done.

Dietetic management : The diet should, if possible, be of animal origin especially milk or milk products. It must be rich in calories, high in proteins of high biological value and enforced by the essential elements. The dietetic treatment varies according to whether it is given in hospital or institute, where facilities can be offered, or at home. In the hospital, one starts with a diet that is low in fat, high in protein, moderate in carbohydrate and acidified to compensate for the hypo-acidity present in the stomach in malnutrition. The best milk to start with is skimmed lactic acid milk. This should be started in small amounts at frequent intervals within the tolerance and capacity of the gastrointestinal tract, to be gradually increased according to the response of the individual case.

The practical application of the foregoing principles can be illustrated in the following example :

in a malnourished child, one year old, weighing 6 kilograms, one starts by

correcting his fluid and electrolyte disturbances. The fluid requirements of such a child are equal to $1/6$ of his body weight which can be fulfilled by 1 liter of milk (if the weight is more than 6 kilograms and he requires more than one liter of milk, we usually supply him only with that amount and the rest of his caloric requirements is given in the form of solid foods). After that a thorough clinical and investigatory evaluation should be done and managed.

If there is severe anorexia, gavage feeding may be resorted to, using polyethylene tube introduced through the nose to give milk and fluids by the drip method.

The dietetic management starts by giving him powdered skimmed lactic acid milk in very small amounts e.g. one teaspoonful (4 gnu) dissolved in 20 ml. of water to be administered every 1.5 hours for about 12 to 15 feeds a day. The fluid requirements should be calculated and the rest must be given between the feeds in the form of decoction or better in 5% dextri-maltose in water. This scheme should be continued for at least 3 or 4 days without any change. With improvement of the child's tolerance, the amount should be increased gradually making it 1.5 teaspoonfuls in 30 ml. water every 1.5 hours and then increase to 2 teaspoonfuls added to 40 ml. every 2 hours. An interval of 3 to 4 days must always be allowed before any new change. Gradually increase the amount, widen the interval and increase the concentration. So long as the body is adding weight, it is better not to interfere until the weight curve gets flatter, then you start giving more food. With improvement, one should change gradually, from skimmed milk to protein milk ($\frac{1}{2}$ cream acidified) and then half-cream milk. In that way more fat is administered in a gradually increasing dose. For example if 3 teaspoonfuls of milk are given, one starts by adding one teaspoonful of protein milk. Further addition will be in the form of the latter while skimmed milk is withdrawn from the formula. With further improvement in the general condition and tolerance of the child, half-cream milk will gradually replace the protein milk. Following that scheme, even though the child may not add to his body weight for one or two weeks, his general condition improves a lot and he tolerates his food better. In the following five to six weeks, he may only add one kilogram to his body weight and this is usually very satisfactory. At that stage, the usual process of weaning can start by the addition of more solid foods such as custards, boiled beans, minced meat, liver and so on (chapter VI).

For socio-economic conditions, it is usually difficult to treat such children in hospitals, a cheaper and easier way can be achieved by administration of animal milk fermented by *Bacillus Bulgaricus*, a lactic acid producing organism. Such a milk has got the popular name of "Yoghurt", and has the following advantages; it is thick, it can stay a longer time without being spoiled, it can be administered skimmed, half skimmed and full cream. It contains less lactose

and so being high in protein, it is less diarrheic, as well as it contains a proper percentage of lactic acid. This milk should be administered in small amounts at frequent intervals, and inbetween, the fluid requirements could be given as mentioned above.

Vitamins should be given in a water soluble form from the start.

Another cheaper way of dealing with cases of marasmus or kwashiorkor is administration of a mixture of vegetables high in their protein. Though the protein of each vegetable alone is non-adequate, yet mixing known types together can supply a protein formula as adequate as that of an animal protein of high biological value. In our institute it was found that administration of three parts of peanuts, two parts chickpea and one part sesame-dreg (Tehina) by weight produced a successful mixture. The peanut is rich in fats and proteins, the chickpea corrects the deficiency of lysine and the sesame-dreg will prevent tryptophan deficiency. This mixture of lysine and methionine can be administered sweetened with 19% of sugar to the infant, either by the addition of some water to it or eaten as such by older children. This mixture is well tolerated by children, its amino acid pattern corresponds to that of meat, it gives a growth curve similar to that of the normal infant and it cures the clinical manifestations of malnutrition as well.

Associated symptoms and complications must be dealt with. Diarrhea and other infections have to be treated by their proper chemotherapy, dermatosis by painting the skin with a 2% aqueous gentian violet solution and xerophthalmia by vitamin A drops orally and locally in the eye. Antibiotics and atropine ointment may be needed also. When the patient is on the way of recovery, treat parasitic infestations and later give iron and vitamin D.

Signs of success of treatment :

- Definite and steady improvement of appetite.
- Disappearance of edema.
- Progressive increase in body weight.
- Healing of skin lesions.
- Clear evidence of sense of well-being.
- Normalization of serum protein particularly albumin.

Prevention of Malnutrition : The following points will summarize the different ways of prevention :

- 1 — Educate the people to supplement the diet of their infants with :
 - a) Animal protein(milk, fish, meat).

b) Vegetable protein (beans, peas, green vegetables). This should be started early and continued in adequate quantities.

- 2 - Encouraging breast feeding to last more than one year, if possible up to two years; as well as enforcing the diet by cheap elements known by their important value in nutrition. Sweet yellow potato as well as carrots are rich in carotene which is a pro-vitamin A; chickpea is rich in lysine and peanuts are rich in fats and proteins
- 3 — Breaking down taboos and prejudices related to feeding habits.
- 4 — Family planning, by teaching mothers how to practice birth control.
- 5 — Immunization against infectious diseases such as measles, tuberculosis, whooping cough . . . etc.

M. M. HANAFY

Chapter VIII

THE DIGESTIVE SYSTEM

ANOREXIA

Anorexia due to acute illness or fatigue is transitory and the symptom itself usually requires no treatment. Anorexia of psychogenic origin (*anorexia nervosa*) is a severe illness and requires expert psychiatric care. Anorexia in the toddler and preschool child is a daily problem for the parents and the pediatrician (Chapter I).

The child's growth and his appetite are closely related. Since the infant's growth during the first year is rapid, this will be accompanied by eager consumption of food. The weight gain during the second year drops and the child's appetite diminishes to parallel this small gain.

The wrong practice made by some mothers of giving snacks between meals and permitting the use of the bottle in the second or third year will suppress hunger at mealtime. The practice of forcing food to make a child gain weight at a rapid rate, or to compete with a neighbour's child is very common. A spoiled child may dominate the home by his feeding behaviour. The child may be so active and interested in his environment that he does not have time to eat, or eats very little. In addition it should be noted that emotional states as excitement, tension and unhappiness markedly diminish the appetite (chapter I).

Management : A proper handling of feeding is imperative. One must rely on the child's appetite which is a satisfactory guide. The parents should be taught that appetite shows considerable variations; thus the quantity of food eaten at different times is variable. The attempt to standardize a child's intake is the cause of loss of appetite and bribery, or force are useless in such a situation.

DISORDERS OF THE MOUTH

STOMATITIS

Inflammation of the oral mucous membrane may occur as a primary phenomenon or as a feature of systemic disease. In some instances the etiology is well identified, while in others the cause is obscure or unknown.

1. *Catarrhal stomatitis*. Characterized by a mild generalized non-specific inflammation of the oral mucous membrane. It often accompanies the acute specific fevers, notably measles and upper respiratory infections or local factors; chemical, traumatic or thermal.

2. *Herpetic stomatitis* (Aphthous, Ulcerative stomatitis). Symptoms appear suddenly with fever, pain in the mouth, salivation and fetor oris. The initial lesion which is a vesicle, ruptures and an ulcer is formed. The organism usually responsible is the herpes simplex virus.

Treatment : Mouth paint with 1% aqueous solution of gentian violet. Antibiotics may be needed for secondary infection.

3. *Thrush stomatitis* (Moniliasis). This is due to infection of the mucous membrane of the mouth by the fungus *Monilia albicans*. The fungus is conveyed to the mouth by imperfectly cleaned feeding bottles and teats. Undernourished infants are especially susceptible. Antibiotic therapy, by changing the normal flora of the mouth, may enable monilia to flourish. The infection appears as numerous small white flakes on the dorsum of the tongue, inner side of the cheeks and on the palate.

Treatment : Attention should be paid to the cleanliness of the feeding bottle and teats. The infant's mouth is gently painted thrice daily with 1 per cent aqueous solution of gentian violet; this may be combined with nystatin, an antifungal antibiotic, giving 100,000 units by mouth, three or four times daily.

4. *Gangrenous stomatitis* (Noma): A condition met with in severely debilitated children and may complicate the specific fevers, notably measles. It appears on the inner side of the cheek as a large deep ulcer which slowly spreads

by necrosis of the adjacent tissues. There are severe constitutional disturbances, the child appears toxic and death is likely to occur.

Treatment : Careful attention to the hygiene of the mouth, particularly during acute specific fevers, will help to prevent this condition. Antibiotics must be given early and the affected area may require excision.

DISORDERS OF THE ESOPHAGUS

ESOPHAGEAL ATRESIA

The most common anomaly is esophageal atresia with tracheoesophageal fistula. In its most common form, the upper part of the esophagus terminates in a blind pouch and the lower part communicates with the trachea at or near the bifurcation. Over 30% of children with this condition have associated anomalies; the most common of these are congenital heart disease and malformations of other portions of the intestinal tract, chiefly imperforate anus.

Clinical findings :

(A) Symptoms :

- Excessive salivation.
- Coughing and gagging if feedings are attempted.
- Respiratory distress which may lead to cyanosis.

(B) Signs :

- Feeding difficulties.
- Aspiration pneumonia may develop two or three days after feeding is begun.
- Attempts to pass a soft urethral or polyethylene catheter to the stomach will fail.

(C) X-ray findings :

A plain film usually demonstrates the large, air-filled esophageal pouch, the site of atresia and the presence of the fistula. X-rays of the abdomen will help to determine if there is air in the stomach and intestine. The presence of air in association with a blind upper pouch indicates connection between the trachea and lower segment of the esophagus.

Treatment :

1. Fluid therapy : nothing should be given orally. Maintain good hydration

2. Gastrostomy under local anesthesia should be done as soon after admission as possible and the gastrostomy tube should be put on drainage.

3. When the infant's condition permits, the surgical measure taken is usually one-stage procedure with division of the tracheo-esophageal fistula and anastomosis of the esophagus.

4. Postoperative care consists of fluid therapy, feeding through the gastrostomy tube for about one week, then start gradual oral feeding.

ESOPHAGEAL STENOSIS

Congenital stenosis without a fistula can be found at any point but is most common in the lower third.

Symptoms :

Usually appear when the infant starts to eat semisolid or solid food. Symptoms are those of obstruction. Diagnosis is confirmed by esophagoscope and X-ray examination.

Treatment : Esophagoscopy dilatation.

CORROSIVE STRICTURES

The most common type of stricture of the esophagus follows ingestion of some caustic as caustic potash or ammonia, or strong acids as nitric acid.

Clinical manifestations: On ingestion of the caustic material, the child feels intensive burning which inhibits further swallowing. The lips, tongue and pharynx become edematous. Similar changes occur in the esophagus and infrequently in the stomach. Usually the edema subsides and swallowing function returns to normal in 2 — 4 weeks. This symptomless period may be followed by gradual increasing difficulty in swallowing. At first there is difficulty in swallowing solid food, later the difficulty may involve liquids.

Treatment : Immediately after ingestion of the caustic, olive oil is applied to the denuded areas and administered by mouth. Gastric lavage is contraindicated for fear of gastric or esophageal perforation. Feeding may be resorted to intravenously or through a gastrostomy tube.

To prevent stricture, early dilatation by bougies passed daily for 2 weeks, then gradually increasing the intervals between dilatations is done. Corti—

soteroïd therapy for 10 days is given at the same time. Treatment of an established stricture is dilatation using an esophagoscope. In more severe cases resection of the stricture and replacement by a section of the colon or small bowel is carried out.

DISORDERS OF THE STOMACH

CONGENITAL PYLORIC STENOSIS

This is one of the common malformations of the digestive tract. Four-fifths of the cases occur in male infants, and first-born children more commonly affected.

Pathogenesis : The exact pathogenesis is obscure. The abnormality consists of a gross hypertrophy of the circular muscle layer of the pylorus which forms a hard tumour and causes a variable degree of obstruction to the passage of food from the stomach. Some authors believe that it is secondary to spasm of the pylorus, while others suggest that the hypertrophy of the muscle appears first and the spasm is added later on.

Clinical manifestations: The presenting symptom is vomiting, which starts with regurgitation of small amounts of feed, thereafter it rapidly becomes projectile. This symptom does not occur at birth and is seldom observed before the tenth day, being commonest by the third week. The infant rapidly loses weight and becomes dehydrated. He appears restless, anxious and wrinkled. The stools are small and infrequent; sometimes obstinate constipation occurs. The signs which confirm the presence of hypertrophic pyloric stenosis are visible gastric peristalsis and the presence of a palpable tumour. Gastric peristalsis occurs when the stomach begins to fill, hence the infant's abdomen should be carefully observed whilst a feed is given. The abdomen should be palpated to determine the presence of a tumour, which is usually felt at a point right to the umbilicus where the peristalsis was seen to disappear.

To confirm the diagnosis, radiological examination using barium meal may show elongation and narrowing of the pyloric canal with delayed opening and the gastric emptying time is usually prolonged.

Treatment : It is now the general practice to recommend surgery in every fully established case. Dehydration should first be corrected and the stomach washed with physiological saline. The Fredet-Ramstedt operation is the accepted procedure, in which splitting of the circular muscle fibers is carried out along the length of the pylorus. Post-operative feeding with equal parts of glucose and physiological saline can be started 3 hours after the operation. When artificial

feeding is used, e.g. half cream dried milk, a half-strength dilution is used for the first 12 hours and subsequently a full-strength formula. During the first 36 hours after operation, it may be necessary to supplement the fluid intake by parenteral fluids. When the infant is seen for the first time late in the course of the disease, i.e. at 8 or 9 weeks age, medical treatment may be advisable in selected cases, since the duration of the disease is self-limited and spontaneous remission of symptoms may occur at 12 weeks of age. Medical treatment consists of thickening of the feeds with cereal and the administration of eumydrin (atropine methyl nitrate) 2.5 ml. of 1/10,000 solution half an hour before feeds.

VOMITING

The classification of the causes of vomiting is usually made according to the different age periods.

I. *In the newborn :*

1. Physiological vomiting at or soon after birth is a normal process by which swallowed blood and amniotic fluid are removed. It may occur once or twice.

2. Congenital esophageal obstruction, with or without fistula, is manifested by regurgitation, choking and perhaps cyanosis with the first feeds.

3. Congenital pyloric stenosis results in projectile vomiting usually two weeks after birth.

4. Hiatus hernia with a short esophagus may cause dysphagia, vomiting and hematemesis.

5. Intestinal obstruction gives symptoms usually in the first 24 hours after birth. Abdominal distension is generalized, if the obstruction is in or distal to the jejunum. An X-ray of the abdomen in an upright position is of help in diagnosis.

6. Imperforate anus gives symptoms that begin on the first 24 — 36 hours of life, with abdominal distension and vomiting. No meconium is passed.

7. Cerebral birth injuries may cause repeated vomiting following birth. There is usually a history of difficult or precipitate delivery.

II *In infancy :*

1. Feeding difficulties such as failure to «bring up wind», too small a teat or underfeeding may lead to vomiting (The commonest cause).

2. Infections such as otitis media, tonsillitis, pyelitis and pneumonia are possible causes of vomiting at this period.

3. Acute diarrheal disease due to bacterial or viral infection in the intestinal tract may be accompanied by reflex vomiting.

4 Acute abdominal emergencies such as intestinal obstruction and intussusception have to be considered in all infants who present with vomiting

5. Cerebral causes as hydrocephalus, subdural hematoma and meningitis, should be thought of.

III In older children :

1. Acute dietary indiscretions, e.g. ingestion of unripe fruits or contaminated food.

2. Acute infections such as streptococcal pharyngitis, diphtheria, reflex vomiting in pertussis or intestinal infection as food poisoning.

3. Vomiting may be caused by many drugs as digitalis, sulfonamides, broad-spectrum antibiotics and aspirin.

4. Organic nervous disease as meningitis, encephalitis, intracranial hemorrhage and brain tumour.

5. Metabolic disturbances as in advanced renal insufficiency, renal tubular acidosis and diabetic acidosis.

6 Psychogenic vomiting as by forcing a child with poor appetite to eat more than he wants

7. Cyclic vomiting or periodic vomiting is a syndrome characterized by attacks of vomiting which occur at irregular intervals without apparent cause. The condition starts at 2 — 4 years and subsides before puberty. During the attack, the child this condition is unsettled, but food allergy, emotional upsets and infections may play a role.

Treatment : This should be directed towards removal of the cause whenever this is possible.

1. *Diet* : In severe cases food and liquid have to be stopped by mouth, permitting only cracked ice to alleviate dryness of the mouth and resort to parenteral therapy. In milder cases sips of cold drinks or glucose water may be beneficial.

2. *Drug* : Such as atropine and its derivatives are used in the control of pyloric spasm, chlorpromazine in a dose of 1 mg./Kg. body weight, by mouth, per rectum or intramuscularly is beneficial.

3. Take care to correct *electrolyte and acid-base equilibrium* of the body.

DISORDERS OF THE INTESTINE

COLICS

Colic is a frequent symptom of an underlying disease. The clinical picture is that of an unhappy, crying infant with the legs frequently flexed on the abdomen and suddenly stretched out. The hands are frequently clenched tight during the attack. Vomiting and passage of flatus are common. The attacks of colic are frequently intermittent, but with serious underlying cause, an attack may be constant.

Etiology ·

I — *Diseases of the gastrointestinal tract :*

(A) Intestinal obstruction : Pyloric stenosis and stenosis of the gut, intussusception, volvulus, Hirschsprung's disease, fissure in ano and mild anal stenosis.

(B) Gastroenteritis.

II *Disease of the urinary tract :* Infection or obstructive lesions.

III — *Hernias :* Diaphragmatic, inguinal or umbilical.

IV — *Improper feeding:* Underfeeding, overfeeding or improper feeding techniques, resulting in air swallowing.

V — *Allergy :* Milk, orange juice. . . etc.

VI — *Emotional factors :* Hypertonic infant or family tension.

Diagnosis : A careful history is important. Careful physical examination will help to exclude detectable congenital defects of the gastrointestinal tract and other organic causes. Rectal examination to detect anal stenosis and fissure in ano should not be omitted.

Treatment : Treating the underlying cause is mandatory especially if it is serious. The use of drugs is reserved for the most severely disturbed patients. Drugs of benefit are phenobarbital and methyl atropine nitrate (eumydrin).

CONSTIPATION

Constipation may be considered when hard stools are passed at infrequent intervals. We should be careful in considering the complaints of some mothers

that their infants are constipated when normal stools are passed at what they considered to be infrequent intervals.

Causes :

I — In the newborn :

1. Physiological : Normally some meconium is passed within a few hours of birth. Occasionally this is delayed for 24 hours or longer. There is no abnormality and spontaneous defecation occurs.

2. Imperforate anus : The obstruction may be high or low. Inspection of the anus may be misleading as it may appear normal when the obstruction is high in the rectum.

3. Atresia of the gut or intestinal obstruction. No meconium is passed and vomiting is usually associated

4 Hirschsprung's disease

II — In infancy :

1. Underfeeding with insufficient intake of milk and fluid is a frequent cause.

2. Anal fissure causing pain on defecation will lead to constipation.

3. Mental deficiency as cretinism.

4. Atonia.

III — In older children :

1. Dietetic causes from insufficient food intake or the intake of a food leaving little residue after digestion.

2. Faulty training and upset in routine. Regular toilet habits must be established as early as possible.

3. Chronic intestinal obstruction due to organic causes.

4. Neurological diseases which affect reflex mechanisms and the anal sphincter such as meningocele, cerebral palsy, poliomyelitis and various myopathies.

Diagnosis : In the history, the duration of the condition is of importance. A sudden onset of constipation in a previously healthy child accompanied by abdominal pain and vomiting suggests intestinal obstruction. Chronic constipation in a child who is generally well and healthy may suggest a fault in the diet or in the training. Rectal examination is essential. It may reveal an empty rectum in Hirschsprung's disease or a filled rectum as in the functional type of constipation. Anal fissure can be seen by careful inspection.

Treatment : The treatment is that of the primary cause. In cases of habitual or functional constipation in which no cause is found, it is always advisable to increase the fluid intake and to review the diet in order to increase either the fecal or the fluid bulk of the stool. An increase in the amount of orange juice given will sometimes relieve mild constipation. Milk of magnesia may be used as a temporary measure, but should not be given continuously over long periods. The long-continued use of strong purgatives is even more undesirable. The aim should be to establish and maintain regular bowel action by natural means rather than by frequent stimulation of the bowels by purgatives.

E. HASANEIN

DIARRHEAL DISORDERS

Diarrhea is a disturbance of intestinal motility and absorption which, once and by whatever means initiated, may become self-perpetuating as a disease through the production of dehydration and profound cellular disturbances, which in turn favour the continuing passage of liquid stools.

The WHO study Group on Diarrheal Diseases (1959) were of the opinion that "Diarrhea should be held to be present, in children up to 2 years of age if they pass three or more soft or liquid stools within 12 hours, or a single soft or liquid stool containing blood, pus or mucus; and in persons of 3 years or over if they pass two or more soft or liquid stools within 12 hours, or a single soft or liquid stool containing blood, pus or mucus".

Diarrheas are more common during infancy due to the awkward situation of the gastrointestinal tract which, inspite of being immature functionally and to some extent anatomically also, has to work on a fast gear in order to supply the high caloric needs of the growing infant. Added to this is the almost exclusively fluid and therefore very bulky milk diet which can only be given to babies. On the other hand young infants and children have little resistance to enteropathogenic organisms, even in small doses. The younger the child is the higher the rate of mortality.

As why diarrheal disorders are serious during infancy? This is because infants become dehydrated much more quickly than adults due to :-

1. Higher needs for water exchange to meet their high metabolism.
2. Lower power of concentration of urine which results in relative polyuria.
3. Smaller metabolic reserves of water and electrolytes.

Therefore, with limited intake and/or extra losses of fluids during diarrhea, acute dehydration usually occurs and may lead to a state of shock which needs emergency treatment to save the life of the patient. Whereas slow but marked dehydration leads to acidosis, accumulation of metabolites etc... which should be rapidly and specifically treated to correct the volume, electrolytes and pH of blood, interstitial and intracellular fluids which are essential for the body functions. (page 162).

All these factors render the infant particularly liable to diarrhea and / or vomiting which may easily be precipitated by trifling stimuli.

ETIOLOGY :

The means by which diarrheal diseases may be initiated are many and are of heterogeneous etiology. By far the most frequent and important among

them are "enteric infections", but various dietetic and environmental factors may also initiate the disturbance, predispose to it or help its perpetuation.

Dietetic factors :

- Overfeeding (quantitative and / or qualitative).
- Underfeeding (starvation diarrhea).
- Unsuitable formula or article of food for the age.

Environmental and Constitutional factors :

- Rise of atmospheric temperature helps breeding and marked increase of the fly population which is the most important factor influencing the spread of infection.

Hot weather leads also to lowering of resistance, digestive secretions and HCL, and diminution of appetite and gastrointestinal motility, hence the term «Summer diarrhea».

- Humidity (favours fly breeding and lowers resistance).
- Poor sanitation (water, milk, sewage, etc..)
- Bad ventilation (lowers resistance).
- Exposure to cold drafts.
- Bad habits and beliefs.
- Low social and economic status.
- Food allergy.
- Lienteric diarrhea (gastro-colic reflex).
- Physiologic diarrhea of the newborn.
- Disaccharide intolerance due to absence of the splitting enzymes either permanent or transitory after gastroenteritis.
- Premature (real overfeeding).
- Malnourished (relative overfeeding).

Infective factors :

In many developing countries of the tropical and sub-tropical regions, the age and seasonal incidence, suddenness of onset and systemic manifestations, fly population and sanitary conditions; all point to the infective nature of the condition in most cases of summer diarrhea.

In Egypt, gastroenteritis constitutes the leading reported cause of death during infancy and early childhood. It accounts for more than half of all the fatalities during this age period.

A large proportion of infectious diarrhea occurs as a result of infection with relatively few pathogenic bacteria and viruses which tend to recur again and again among the susceptible human population. Table 9 gives a general idea about the inter-relations between the common agents, host and environment involved in producing diarrheal disease and/or dysentery.

Table 9 : Ecology of Diarrheal Disease.

Agent	Age affected	Primary source of infection	Characteristic epidemiologic group
Shigella	Infants & Children	Human	Family infection (adults frequently asymptomatic)
Salmonella (excluding <i>S. typhi</i>).	All ages	Animal (& human convalescent carriers).	Food poisoning outbreaks.
Enteropathogenic <i>E. coli</i>	Infants	Human	Nursery outbreaks
Viruses	Infants & children	Human	Probably infants & children

Thus, *bacteriologically*, infectious diarrhea falls under three known categories, a fourth which is taking shape in the last years, and a fifth one of doubtful pathogens. These groups are : -

1. Shigellosis.
2. Salmonellosis.
3. Pathogenic *E. coli* infection.
- 4 Viral infections of the gastro-intestinal tract.
5. Doubtful pathogens e.g. paracolon, proteus, etc.

Beside these bacterial and viral infections, we may meet cases due to protozoa or fungi, and then we are left with a big *group of unknown etiology* which remains a field for further research.

Shigellosis : Although these pathogens are isolated from house animals, yet the source of infection in infants and children is almost exclusively man himself.

Shigellosis is absent during the neonatal period, rare in infants below six months and is more prevalent in the age group 1 - 3 years.

Shigella affects the small and large intestine i.e. entero-colitis.

Salmonellosis : *Salmonella* may be the cause of severe diarrheal disease in children. The source of infection is usually contaminated food, but healthy domestic pets have been shown to be potential sources also. Clinically the disease simulates *Shigella* infection and therefore laboratory facilities are needed to establish the diagnosis in order to plan the control which is different.

Enteropathogenic E. Coli : The *E. coli* genus includes many saprophytic and some special serotypes of enteropathogenic nature.

Members of the pathogenic group usually attack neonates and infants below one year. The illness usually follows a protracted course with relapses especially among infants. This is because the focus of infection may remain in their bodies and lead to such relapses. Moreover, these babies are often responsible for carrying infections to other homes and institutes.

Viral agents : It is now accepted that certain viruses may be the cause of diarrheal disease that may assume epidemic form in the new-born. The common groups are : -

- (a) Enteroviruses : polio., ECHO, coxsackie and rota virus.
- (b) Respiratory viruses : influenza virus A and B, adenoviruses and reoviruses.

Doubtful Pathogens : These include the *Paracolon*, *Proteus vulgaris* and *morganii*, *Pseudomonas*, *Alkalegines*, *Staph. aureus* and others. These organisms are usually found in the gut as saprophytes, but under certain conditions are suspected to be the cause of diarrheal disease and are then isolated in many colonies or even pure culture.

Protozoa : Diarrhea is known to occur with some parasitic infestations, but need not be caused by them. Of importance is *Giardia lamblia* and *E. histolytica*. These two are known to cause diarrhea either with acute, recurrent or chronic course.

Fungus diarrhea : Some marasmic infants with diarrhea revealed evidence of colonization of candidas in the gut. The chance of this indicating intestinal moniliasis is possible.

Parenteral infection: a relation between diarrhea and extra-intestinal infections such as otitis media, pneumonia and tonsillitis is frequently observed. However, this relationship is uncertain, and may be due to intolerance during the illness.

PATHO-PHYSIOLOGY :

There is a distinct lack of correlation between the anatomic findings in the gut and the severity of the clinical symptoms. This is because the response to infection occurs through one of the following mechanisms:-

- (a) Irritation and / or inflammation of the mucus membrane which becomes slimy, edematous or denuded. There may be pitcheal hemorrhages, ulceration or even altered blood in the gut. The absorptive functions of the intestine is impaired. The classical example is shigellosis, but some cases of *E. coli* and *salmonella* share.
- (b) Enterotoxins adhere to the mucus membrane, without injuring it, and promote the secretory function of intestine out of proportion to the absorptive function, leading to profuse diarrhea as in cholera and in *E. coli*, infection. Fluid and electrolyte disturbances are more common in this type of diarrhea leading to various degrees and different types of dehydration.
- (c) Dehydration.

DEHYDRATION :

This term designates the abnormal states of the body water and electrolytes— in which the volume of extracellular fluid (E.C.F.) is diminished. The intra— cellular fluid (I.C.F.) may suffer as a result of this.

In the normal infant extracellular water constitutes 25 to 30 per cent of body—

weight and intracellular water 45 to 50 per cent of body weight. Extracellular water is further divided into two components; the blood plasma and the interstitial fluid. The differences in the composition of intracellular and extracellular fluids are illustrated in table 10. Only 7% of body sodium is present in the intracellular fluid whereas nearly all body potassium is intracellular.

Table 10 : The differences in composition of intracellular and extracellular fluids.

Intracellular Fluid (mEq./L.)				Extracellular Fluid (mEq./L.)			
Cations		Anions		Cations		Anions	
K	155	Cl	8	K	5	Cl	110
Na	12	HCO ₃	8	Na	145	HCO ₃	27
Mg	15	PO ₄	90	Mg	2	PO ₄	2
Ca	2	Prot.	60	Ca	2	Prot.	15
		Others	18				
184		184		154		154	

Under normal conditions all fluid compartments are in isotonic state. When dehydration takes place, water moves from one compartment to another according to the tonicity i.e. from the hypotonic to the hypertonic one.

In acute dehydration, the initial brunt falls on the circulating plasma volume. This leads to hemoconcentration i.e. rise of hematocrit and hemoglobin levels, and rise of plasma proteins and of osmotic pressure. This upsets the balance between the fluids inside the intravascular and the interstitial compartments. The result is pulling of fluids from the interstitial compartment into the intravascular one trying to restore the circulating blood volume and keeping it more or less constant.

If the fluids lost by dehydration are sudden and enormous so that the interstitial reservoir is incapable of keeping the blood volume, the patient gets a state of shock and may die. If not, therefore with more demand for fluid and depletion of the interstitial compartment, the intracellular fluid starts to move to the interstitial compartment. This exchange involves a more complicated mechanism than that of mere diffusion across the cell membrane.

• The skin reflects very well the state of deficiency of E.C.F., since most of its cells are cornified epithelial cells and the fat cells contain a very small amount of cellular water. Therefore, diminished elasticity and turgor of the skin means diminished E.C.F. volume.

• The tongue reflects the state of fluid inside the cells since it is formed of a huge mass of cells. Therefore, a dry parched tongue means diminished I.C.F. volume and is thus an evidence of cellular dehydration.

• However, the clinical signs of dehydration are not clear cut because they are actually the final result of a mixture of manifestations produced by the degree of reduction of blood volume and interstitial fluid and by changes in cellular hydration as well as changes in the osmolarity of these fluids and the acid base equilibrium. A good understanding of these factors is essential for planning rehydration :

Degree of dehydration :

The following table after the British Medical Research Council (1952) gives a clue to the clinical assessment of the degree of dehydration in early childhood classified into mild, moderate and severe :

Table 11 : Clinical assessment of the degree of dehydration in early childhood.

Signs	Mild	Moderate	Severe
Appearance	Fretful	Restless	Drowsy
Ant. Font.	Normal or depressed	Depressed	Very depressed
Eyes	Normal or sunken	Sunken	Sunken & Staring
Mouth	Dry, red	Very dry	V. dry & cyanosed
Skin temp.	Warm	Cool	Cold
Skin elasticity	Normal or diminished	Diminished	Very diminished
Heart Rate	130 - 140	160 - 180	180 +
Respiration	Normal	Increased	Deep and irregular
Muscle Tone	Normal	Increased	Flaccid
Urine	Normal	Oliguria	Anuria
Loss of Body Wt.	2.5-5 %	5 - 10 %	10 % or more

Type of dehydration :

The loss of water and electrolytes in infants with diarrheal dehydration is not always parallel. This leads to different types of dehydration with different clinical manifestations as shown in table 12.

(1) — *Isotonic dehydration* (70% of cases) : The losses of water and electrolytes are more or less proportional i.e. the amounts are equal. Therefore, serum Na and electrolyte concentration remains within the normal range and there will be no movement of water between the different fluid compartments. The manifestations are the usual signs of dehydration and these vary according to its degree (tables 11 & 12).

(2) — *Hypertonic dehydration* (20% of cases) : When the amount of fluid loss is greater than salt loss, the E.C.F. compartment becomes hypertonic, hence water will move to this compartment from inside the cells leading to "cellular dehydration" (table 12). This condition is especially common in : —

- a) — early infancy and prematures in whom conservation of water by the kidney is limited.
- b) — high fever due to loss of water from the skin.
- c) — cases of severe vomiting and/or diarrhea.
- d) — cases of water restriction.
- e) — administration of solutions of high sodium and electrolyte concentration.

The main manifestations of such hypernatremia are :

- i — very dry tongue (cellular dehydration).
- ii — almost normal skin turgor (little restriction of E.C.F.).

Table 12 · Comparison of features of isotonic, hypertonic and hypotonic dehydration of moderate severity.

	ISOTONIC	HYPERTONIC	HYPOTONIC
E.C.F. volume	Marked decrease	± Decreased	Severely decreased
I.C.F. volume	Maintained	Decreased	Increased
Skin texture	Slight loss of turgor	Doughy, fair	Loss of turgor ++
Fontanello	Depressed	Depressed	Variable
Eyes	Sunken +	± Normal	Sunken ++
Tongue	Normal or dry	Very dry	Moist
Muscle tone	Variable	Increased	Reduced
Mental states	Miserable	Irritable, fits	Lethargic, coma
Circulation	Intermediate	Preserved	Impaired early
Blood pressure	Low	Moderately low	Very low
Plasma Na (mEq/L)	130 - 150	More than 150	Less than 130

(3) — *Hypotonic dehydration* (10% of cases) : In this type the loss of Na and other electrolytes is relatively more than the loss of water; therefore the E.C.F. compartment becomes hypotonic, hence water moves from this hypotonic fluid compartment to inside the cells i.e. to the I.C.F. compartment leading to "Cellular edema" and more reduction in the volume of the E.C.F. (table 12). This may occur with :

- a) — excessive administration of salt-free fluids (dilutional hyponatremia).
- b) — excessive sweating without salt replacement (acute salt depletion).

The main manifestations of hyponatremia are :

- i — marked loss of skin turgor (reduction of interstitial fluid).
- ii — shock (reduction of plasma i.e. intravascular fluid). This is shown clinically by tachycardia, cold ± cyanotic extremities inspite of high fever, collapsed superficial veins, and severe oliguria or anuria.
- iii — The tongue is moist (cellular edema).

Associated acid-base disturbances :

(1) — *Acidosis* in cases of diarrhea is largely due to loss of Na, K and bicarbonate in the stools. The loss of the latter in particular leads to increase of the hydrogen ion concentration i.e. acidosis. Due to impaired, renal function by dehydration (oliguria or anuria) this acidosis is not corrected. Moreover, urea and other acid metabolites may accumulate also (prerenal failure). Starvation, if prolonged, adds a third load to the imbalance since reduction of carbohydrate intake and depletion of glycogen stores lead to production of ketone bodies.

The main physical signs of acidosis are :

- a) — increased rate of respiration (to wash out the acid radicle CO_2).
- b) — increased depth of respiration (to wash out the acid radicle CO_2).

(2) *Alkalosis* in dyspepsia is often a result of excessive vomiting which causes loss of water and HCl from the stomach. The physical signs will be : —

- a) — decreased rate of respiration (to keep the CO_2).
- b) — decreased depth of respiration (to keep the CO_2).
- c) — tetany, either latent or manifest, may occur. It is due to *hypocalcemia* in metabolic alkalosis (diminished ionic calcium).
 - If vomiting is moderate, it compensates the acidosis produced by diarrhea and therefore the pH. of blood remains almost normal.

Associated Potassium disturbances :

(1) — *Hypopotassemia* : Dehydration and acidosis cause changes in cell permeability and the release of intracellular potassium which is excreted by the kidneys. This together with the loss of K in vomitus and stools lead to marked hypokalemia.

Knowing that potassium is responsible for maintaining the tone of all types of muscles, the main physical signs of hypokalemia will be : —

- a) — hypotonia in the plain muscles representing mainly with abdominal distention and ileus.
- b) — hypotonia of the skeletal muscles representing as weakness, flaccidity and hyporeflexia.
- c) — Cardiac irregularities and ECG changes.

(2) *Hyperkalemia* : Potassium intoxication occurs secondary to oliguria or anuria, alkalosis or administration of fluids containing potassium before renal function is restored. Contrary to hypokalemia the signs of hyperkalemia will therefore be : --

a) restlessness.	b) peripheral vascular collapse.
c) bradycardia.	d) abnormal ECG.
e) cardiac arrest.	

CLINICAL MANIFESTATIONS :

Clinically, two major, and a third minor, types of diarrheal disease are observed : —

- a) *Acute diarrheas* which occur in healthy well-nourished infants or children. These are mostly due to infection. They have sudden onset, short duration, and unless they are accompanied with systemic manifestations as marked dehydration, nervous symptoms and/or toxicity, they end in complete recovery in few days. After the third year of age, the condition is often mild or even subclinical.
- b) *Recurrent or persistent diarrhea* which occurs in malnourished babies. This shows variable and complex clinical pattern. Though infection is also frequent here as enteric or parenteric infection, yet other important factors also exist and aggravate or prolong the course of the disease. Reduced tolerance to food, diminished enzymatic activity and digestive juices, impaired absorption and lowered resistance to infections are among these factors. Thus, in malnutrition, diarrhea becomes almost a symptom. Because it lasts long or recurs frequently, it aggravates more and more the original condition of malnutrition and therefore a vicious circle of gastrointestinal disturbances and malnutrition is established which frequently ends fatally unless something is done in due time to break this circle. That this is an important socio-economic problem in Egypt is evident from the greater morbidity and severity, and the higher mortality in the marasmic than the normal weight cases of diarrhea. Evidently, the proper approach to such cases is to prevent or energetically correct the condition of malnutrition—beside dealing with any probable infection.
- c) *Diarrhea of the new-born* is the third clinical entity. It is due to infection by bacteria or viruses and forms a small part of the problem, although it is of importance in nurseries (chapter v).

Onset : Sudden in healthy babies.
 - Preceded by intestinal derangement.
 Terminal in cases of wasting.

Course : - Mild i.e. showing gastro-intestinal manifestations.

Severe i.e. showing gastro-intestinal manifestations + some systemic manifestations.

Fulminating or toxic showing mainly systemic and/or toxic manifestations.

Gastro-Intestinal manifestations :

- Anorexia ; which is severe in cases with infection.
- Vomiting : usually as a reflex at onset (colic or pyrexia) and it disappears after establishment of diarrhea.
- * It may be a reaction against irritant material.
- * Bloody vomitus and motions may occur as a terminal manifestation due to lowered prothrombin level in the blood and changes in capillary permeability by dehydration.
- Colic : intestinal irritation leads to enterospasm. The baby cries and swallows air which causes intestinal distention and more colic and so on.
- Diarrhea : At first the child passes one or two loose but more or less normal stools, and then the motions become watery and frequent due to hypermotility of the intestines and impaired absorption.
- * Green stools denote auto-oxidation of bilirubin in the gut and its transformation to biliverdin which is green.
- * Mucus denotes involvement of colon.
- * Tenesmus denotes involvement of rectum.
- * Blood denotes congestion or ulceration.
- * Pus denotes inflammation.
- * Froth denotes excess of carbohydrates and fermentation.
- * Fat or soap denotes excess of fat and indigestion.
- * Offensive odour denotes excess of protein and putrefaction.
- * Curd denotes excess of soaps and fatty acids.
- * Excoriation of buttocks denotes stools of high acidity.

Beside these valuable data obtained by inspection of stools, we may get also an idea about the causative organism e.g. in shigella infection there is mucus and blood and dysenteric symptoms. In salmonellosis there is fever, severe toxemia and offensive stools which may contain mucus and blood. In *E. coli* affection the stools are profuse and watery if it is caused by an enterotoxinogenic strain.

Systemic manifestations :

- Pallor : (vasomotor disturbance).
- Restlessness : (colic and thirst).

Loss of weight: (the degree depends upon severity, dehydration and duration).

- Pyrexia : denotes infection, marked dehydration and/or toxemia.
- Rapid deep respiration : (acidosis).
- Slow shallow respiration : (alkalosis).
- Irrigular respiration : (cerebral toxemia).
- Dehydration : mild, moderate or severe. Iso-, hyper- or hypotonic etc.
- Shock : due to peripheral circulatory failure.
- Nervous manifestations : prostration, flaccidity and drowsiness. The baby lying helpless on his back with half closed eyes and upward rolling of eyeballs. This may pass to coma. Towards the end, the limbs may become tonic, the neck rigid and convulsions may occur as a terminal manifestation.

COMPLICATIONS :

- Infection : bronchopneumonia, otitis media, pyelitis.
- Circulatory disorders: Thrombosis of cerebral sinuses, subdural effusion or hemorrhage, thrombosis of renal vein or thrombo-phlebitis.

There may be formation of thrombi and fibrin deposits in the circulation especially in lungs and kidneys (Disseminated Intravascular Coagulation). Clinically DIC presents with hemorrhages e.g. melena or hemoptysis, ecchymosis anywhere either spontaneously or on trivial trauma and/or well defined hemorrhagic necrotic areas. Laboratory data show consumption of the coagulation factors i.e. thrombocytopenia, diminished plasma fibrinogen and plasminogen, lowering of clotting factors V and/or VIII and increase of fibrin split products.

- Wasting : prolonged starvation or poor diet.
- Prolapse of rectum : Tenesmus and wasting are the factors.
- Persistent diarrhea : Temporary deficiency of disaccharidase enzymes responsible for hydrolysis of starch, lactose and sucrose. These enzymes are present in the outer brush border of intestinal mucosa which is destroyed by infection or use of neomycin, kanamycin or presence of kwashiorkor or intestinal giardiasis. The responsible mechanism is probably bacterial fermentation of unsplit disaccharides in the intestine leading to explosive frothy diarrhea with acidic stools.

PREVENTION :

Every effort should be made to secure breast feeding. When artificial feeding is necessary, the mother should be properly instructed with regards the choice, preparation, sterilization and storage of formula. Food should be reduced during hot weather and febrile illness. Cases should be isolated and treated as infectious diseases. Improvement of the general hygienic conditions, combating of flies and adulteration of milk etc. . . is the job of governments, social workers and other concerned bodies.

TREATMENT :

There are 3 main principles in the treatment of diarrhea : -

- I -- Correction of dehydration.
- II -- Dietetic management.
- III -- Drugs.

Correction of dehydration : The most important item of treatment is to combat and correct dehydration by restoring and maintaining fluid volume and electrolyte equilibrium.

In this respect three items should be considered : -

- (a) Repair of pre-existing deficit.
- (b) Provision of maintenance requirements.
- (c) Correction of the concurrent losses.

There are certain points to be considered in the history, physical examination and in the laboratory investigations : -

1. *History :* Much of the information needed to assess fluid balance comes from a thorough general history and examination. A history of deficient intake or abnormal loss of electrolytes and water is of importance. The presence of thirst is a distinctive evidence of water depletion but many patients with depletion of sodium or of potassium also complain of thirst.

2. *Physical examination :*

- To assess signs and degree of dehydration, table 11 is helpful.
- To elicit signs of specific electrolyte abnormalities, table 12 is helpful.
- To detect acid - base disturbances.
- To detect signs of hypokalemia, hypocalcemia, etc.

3. *Investigations :*

- Serial records of weight during treatment, and of the amount of urine voided should be done.

- The volume of body fluids through estimation of packed cell volume, serum proteins, non-protein nitrogen and the specific gravity of urine.
- The concentration of specific components of extracellular fluid as Na, K, Cl. & CO_2 .
- The pH of the blood.
- E.C.G.

According to the severity of dehydration, its treatment is started from one of the following three phases : -

Immediate or Emergency treatment to save life in severe cases :

This aims essentially at rapidly restoring the blood volume in order to relieve, combat or prevent shock. Restoration of renal function through initiation of rehydration usually takes place also.

For this purpose, prompt I.V. half strength isotonic Na Cl solution in 5% glucose (15 — 20 ml/Kg) is given over 60 minutes period. If no improvement, repeat again or give an equal volume of plasma or blood over 90 minutes period. Electrolytes are only partially corrected during this phase.

Restoration of Pre-existing deficit and for maintenance : -

This phase follows the previous one in severe cases, or it may be the point of start in moderate cases of dehydration. It is devoted to repair and maintain extracellular fluids. The composition of the fluid given depends upon the kind of dehydration whether it is iso-, hyper- or hypotonic in nature.

- (a) For isotonic dehydration (70% of cases) : isotonic solutions of saline, 5% glucose, $\frac{M}{6}$ Na lactate in the proportions of (2 : 3 : 1) is suggested.
- (b) For hypertonic dehydration (20% of cases), saline, glucose, lactate (2 : 6 : 1).
- (c) For hypotonic dehydration (10% of cases) 3% Na Cl or 5% Na Cl and $\frac{M}{6}$ lactate (2 : 1).

If laboratory data are not available the first mixture of solutions is the recommended one.

Of the chosen solution the amount to be given is roughly as follows : -

- For mild dehydration about 200 ml./Kg/day.
- For moderate dehydration about 240 ml./Kg/day.
- For severe dehydration about 280 ml./Kg/day.

The total amount is divided and given 4 hourly, but in severe cases it should be given by I.V. drip continuously.

With correction of the extracellular fluid and occurrence of diuresis, acidosis—

is usually corrected. If not, alkaline therapy (Na bicarbonate) is to be added after careful calculation.

Potassium level will be controlled by laboratory estimation and should not be corrected except after restoration of urine flow.

Potassium therapy should cover the already present deficiency, replace the continuing loss in stools and provide the body with maintenance requirements. Usually the deficit in a case of diarrhea with severe dehydration and acidosis ranges from 8-12 mEq./Kg. As the maintenance requirements of K. in infants is 2-3 mEq./Kg./day, a total of 5 mEq./Kg./day is given and this corrects the level in a few days. It should be noted that oral administration is safer than parenteral. Potassium therapy is of special importance in cases of diarrhea with protein-calorie malnutrition.

To avoid hypocalcemia 10-30 ml. of 10% Ca. gluconate solution is added to the daily fluids.

Supplies for concurrent losses and for maintenance :

In the next 24 hours and following days 150-200 ml/Kg/day are given parenterally, orally or by both routes according to the condition, presence of vomiting and severity of diarrhea. Thus the oral route alone may be quite sufficient from the beginning in mild cases.

A suitable oral rehydrating mixture may be suggested as follows : -

<i>R_y</i> Pot. chloride	1.50
Sod. bicarb	2.50
Sod. chloride	3.50
Glucose	25.00
Aqua ad	1000.00

Give a tablespoonful of the solution $\pm$ continuously every 10-15 minutes.

- It should be noted that of the pre-existing deficit $1/2$ the amount is given in the first day and the rest in the next 2 days.
- Should infusions continue more than four days, blood to correct anemia may be needed and proteins either by infusion or orally must be supplied.
- During hydration therapy an increase of 8 - 10% of body weight is good, more than 15% means excess of sodium while sharp loss means need for sodium.
- The water soluble vitamins should also be started. Vitamin K and Ca may be needed.

Together with rehydrating measures, the other two major lines of treatment should be started which are the dietetic management and the treatment of the cause of diarrhea

Dietetic management :

Correct any fault in the diet if it is the cause.

Start dietetic management by a short period of starvation (8 - 24 hours) to assure rest to the gastrointestinal tract and to raise its tolerance to food. In the meantime the patient is supplied by fluids, electrolytes, glucose and may be casein hydrolysate also. Do not starve a marasmic or kwashiorkor patient with diarrhea because this intensifies protein deficiency and so aggravates his condition.

This period is followed by one of graduation of feeding. For this purpose either breast, skimmed, protein milk or simple casein is started in small amount (10-20 Calorie/Kg/day) and gradually increased (by same amount) daily to the full requirement. These feeds are given by mouth or by gastric drip, if there is vomiting or lack of appetite.

Lactic acid skimmed milk and protein milk have the advantage of low fat content, modified easily digestible curd and low buffering action.

For older children fruit diet is more palatable e.g. banana, apple or carrots. Finally, gradual shift to more rich milk or food should take place until the diet suitable for the age of the child is given.

In cases of transient disaccharidase enzyme deficiency give lactose-free diet e.g. isomil-similac or nutramigen for a few weeks and then introduce gradually milk, milk products and other carbohydrates.

Treatment of infection :

Antibiotics and chemotherapy are much over-used in the attempted treatment of diarrheal disease of early childhood; usually with little effect, always at considerable expense and sometimes with dangerous side effects. A local policy can only be laid down scientifically with a detailed knowledge of the bacterial and other causes of diarrhea in the community, and the usual antibiotic sensitivity of the organisms found.

Practically speaking this might not be possible and an antibiotic may be used taking into consideration that the offending organisms are usually the shigella, salmonella, and pathogenic E. coli. The antibiotics effective against these organisms are : -

- Ampicillin : 50 - 100 mg. / Kg / day parenterally. It is of special value for E. coli and shigella.
- Chloramphenicol : 50 - 100 mg/Kg/day is effective against certain types of

E. coli but not all. Resistance to it is not infrequent. Relapses following its withdrawal limits its wide usefulness. Its use in the newborns is not without danger.

— Colimycine : 50,000 U/Kg/day orally or 5 - 10 mg./Kg/day I.M.

— Garamycin : 5 — 7 mg / Kg / day I.M., 8 hourly.

Both drugs are of value in *E. Coli.* resistant strains.

— Neomycin : 50 — 100 mg/Kg/day orally. It improves the clinical condition rapidly. It is also effective in carriers.

Being poorly absorbed from the gastrointestinal canal, it can be given in large doses.

— Kanamycin : 10 — 15 mg./Kg/day I.M.

Symptomatic treatment :

Symptomatic measures may be needed to relieve colic, severe vomiting or allergic reactions, help digestion, quieten an irritable patient, stimulate a collapsed one or check undesired prolonged diarrhea.

Complications as lung infections. . . etc. should be discovered early and treated adequately.

In case of DIC, beside correcting dehydration, I.V. heparin 50 - 150 U/Kg. every 4 hours is indicated. Sometimes fresh frozen plasma or platelet infusion or both may be necessary after adequate heparinization. Laboratory data are necessary to guide this treatment.

A.S. ABBASSY

DYSENTERIES

The term «dysentery» denotes a symptom-complex and not a particular disease of distinct etiology. There are many pathological conditions which give rise to a discharge of blood and mucus. The principal forms of dysentery are : —

- I — **Bacterial** : The bacillary dysenteries.
- II — **Protozoal** : Amebic dysentery.
- III — **Helminthic** : Bilharzial dysentery.

BACILLARY DYSENTERY

Bacillary dysentery is a disease caused by a variety of closely related organisms involving chiefly the large bowel and characterized clinically by fever, general toxicity, abdominal pain and frequent loose stools containing mucus, pus and blood.

Etiology : The dysentery bacilli are divided into 4 groups : -

1. *Shigella dysenteriae* (Shiga's bacillus).
2. *S. paradyserteriae* (the various types of Flexner's bacillus and Boyd types).
3. *S. ambigua* (Schmitz's bacillus).
4. *S. Sonne* (Sonne-Duval bacillus).

Pathology : The infection chiefly involves the colon. The mucosa of the intestine is thickened, hyperemic, inflamed and edematous. Shallow ulcers are present which seldom penetrate below the submucosa and perforation is rare.

Clinical findings : In severe and fulminant cases, the onset is sudden with prostration, fever, vomiting, profuse bloody diarrhea, colic and tenesmus. The patient may be in shock very early in the course of the illness. Ringing ears, deep drowsiness, coma or convulsions may occur. Generalized abdominal tenderness is usually present and at times rigidity may be evident. Mild forms of the disease may show only slight fever and a mild watery diarrhea.

Laboratory findings : Pus and blood in a smear of the stools. Leukocytosis and polymorphonuclear increase in the majority of cases. Cultures of the stools are positive

Complications : A chronic, recurrent form of shigellosis may occur. Localization of the disease in a joint, eye, respiratory tract, C.N.S. or urinary tract is rare.

Treatment :

1. Correction of water and electrolyte balance.
2. Drugs : most effective are the sulfonamides as sulfadiazine 0.12 Gm./kg./day. Chloramphenicol and the tetracyclines are also effective.

AMEBIC DYSENTERY

Entameba histolytica is a protozoal parasite which usually lives at the expense of living tissue in the wall of the large intestine. It exists in a free-living vegetative form and as cysts which are highly infective because they can survive outside the body. This cystic form passes unharmed through the stomach and small intestine and changes into the vegetative trophozoite form in the intestine.

Pathology . The characteristic lesions accompanying symptomatic amebiasis are due to tissue destruction from active invasion by the amebae to various depths in the wall of the colon or other hematogenously infected organs. Frequently secondary bacterial invasion produces inflammation and suppuration about the minute openings of the mucosal lesions.

Symptomatology . The great majority of infected individuals are asymptomatic. When symptoms arise, they vary from mild gastro-intestinal upsets to typical chronic ulcerative colitis. The disease may run an acute rapid course, but in its typical form, it is a subacute or chronic disease. It manifests itself by diarrheal episodes separated by periods of constipation which may last for months. The stools characteristically contain tenacious mucus and flecks of fresh or altered blood. Fever and tenesmus are not conspicuous features. Localized abdominal pain and tenderness are characteristic of both the acute and more chronic form of the disease.

Diagnosis : The characteristic clinical features which serve to differentiate amebic from bacillary dysentery are the more chronic course, tendency to relapse, low degree of fever, the infrequency of tenesmus and the more conspicuous abdominal pain and tenderness in the former. During dysenteric attacks, the vegetative or active forms are seen in freshly passed stools. During periods of constipation, the cysts are found. Proctoscopic examination may show characteristic ulcers.

Treatment : For the acute attack use emetine hydrochloride in a dose of 1 mg./kg /day for 4 days and tetracyclines 40 mg./kg./day for 10 days. This treatment may be followed by two other amebicide drugs : carbarsone in a dose of 10 mg./kg./day for 10 days and di-iodohydroxy quinoline (diiodoquin) in a dose of 15 mg /kg./day for 10 days.

Metronizadole (Flagyl) is effective and may be given in doses of 35 mg./kg/ day divided on two doses during meals for 5 - 7 days.

— For hepatic amebiasis see chapter. XI.

BILHARZIAL DYSENTERY

This type of dysentery occurs following infection with *Schistosoma japonicum* and *S. mansoni* which cause the intestinal type of bilharziasis.

Clinical manifestations : The patient is usually acutely ill and in severe cases bed-ridden.

There is a prodromal toxic diarrhea. After a few weeks of rest, the dysentery is arrested, but on physical exertion it is reactivated. Digestive disturbances are increased as fibrosis of the intestinal wall develops. The liver may show signs of periportal fibrosis and the spleen progressively enlarges.

Diagnosis : There is a pronounced eosinophilia. Stool examination may show viable ova.

Treatment : See under Bilharziasis.

MALABSORPTION SYNDROMES

The diagnosis of malabsorption syndrome is made clinically in any infant or child showing the following manifestations :

1. Failure to gain weight, with wasting and stunting of growth.
2. Abdominal distension.
3. The passage of pale, bulky, foul-smelling stools. Malabsorption by the small intestine can result from one or more of the following mechanisms:
 - (a) Distortion of the normal continuity of the gastrointestinal tract, which impairs the efficient mixing of food with digestive juices.
 - (b) Alteration in the quality and/or quantity of digestive juices (bile, pancreatic juice . . etc.).
 - (c) Impairment and atrophy of enteric absorptive surface (due to disease, enteric shunts or resection).

Clinical syndromes associated with intestinal malabsorption :

I — Hepatobiliary diseases : Gross steatorrhea is expected during illness which severely impedes the flow of bile into the duodenum. The emulsifying effect of bile salts is essential for pancreatic lipase. Bile salts are also essential for fat absorption. This is present in :

1. Extrahepatic biliary obstruction.
2. Severe hepatocellular injury.

II — Pancreatic diseases : Severe diffuse disease of the pancreas can affect pancreatic enzyme production to a degree sufficient to cause an absorptive defect. Examples are : -

1. Mucoviscidosis (Fibrocystic disease of the pancreas).
2. Severe protein malnutrition (Kwashiorkor).

III — Small intestinal disorders : This includes a heterogeneous group of diseases affecting the small intestine and impairing fat absorption :

(a) Resections, (b) Shunts, blind loops, multiple jejunal diverticula, (c) Celiac disease (Gluten-induced enteropathy), (d) Tropical sprue, (e) Regional enteritis, (f) Severe protein malnutrition, (g) Intestinal parasites, (h) Drug injury, e.g. neomycin, (i) Congenital malabsorption of sugars either due to failure of epithelial monosaccharide transport involving glucose and galactose or to lack of epithelial disaccharidases, and (j) Inflammatory or neoplastic obstruction of mesenteric lymphatics.

Pathophysiology : The most serious feature is loss of fat resulting in progressive weight loss and general malnutrition. The hematologic defect is precipitated by iron, folic acid or vitamin B₁₂ deficiency due to malabsorption. Disturbances of calcium metabolism are common and may be very severe in malabsorptive states. There is failure to absorb ingested calcium and loss of endogenous calcium through increased digestive secretions. The bones suffer from osteoporosis and rickets.

Detection of malabsorption : Screening for steatorrhea begins with the two simple but least reliable methods :

1. Inspection of a stool specimen to detect the odour of excessive fatty acids and the creamy colour of severe steatorrhea.
2. Microscopic examination for excessive fat droplets. A more accurate screening test for fecal fat loss is determination of the proportion of lipid-soluble material to total dry solids in a random specimen of feces. Gross steatorrhea

shows greater than 25% fat. Other more accurate measures to prove malabsorption are ;

1. Oral administration of 20,000 I.U. of carotene in oil, daily for a week and determination of serum carotene level. A level less than 76 ug. per 100 ml. is due to lipid malabsorption.

2. D-xylose absorption test. Usually a 5 Gm. dose of xylose is given orally and the urine is collected over the next 5 hours and the excretion of xylose measured. Oral tolerance tests using glucose and vitamin A are grossly inaccurate and their interpretation should be done with care.

3. Analysis of fecal radioiodine in three-day collections following oral ingestion of radioiodine-labeled triolein or oleic acid.

4. Radiological examination of the small intestine, after the ingestion of a barium meal is useful to detect intestinal malrotation, dilated loops, regional ileitis and diverticulitis.

5. Peroral biopsy of the small intestine, a recently introduced technique, enables the small intestinal mucosa to be examined without resorting to laparotomy.

GLUTEN-INDUCED ENTEROPATHY

(CELIAC DISEASE)

This disease was formerly called idiopathic celiac disease. It constitutes the majority of children suffering from malabsorption syndrome.

Etiology : The offending agent is gluten or protein portion of wheat and rye flour.

Gluten is composed of two fractions; glutenin which is harmless and gliadin which is responsible for the injury. The mechanism of the harmful action of gliadin has not yet been fully clarified. Two hypotheses are of particular interest : a toxic, or an allergic action. Those who support the former, consider that there is an inborn error of metabolism with deficiency of a specific peptidase, resulting in incomplete digestion of gluten with the accumulation of an intermediate product thought to exert a toxic action on the intestinal epithelium. Supporters of the allergy hypothesis consider celiac disease to arise out of an immunological response to wheat and rye proteins.

Pathology : Peroral biopsy helped to reveal the exact pathologic picture. The mucosa is atrophic with fusion or absence of the villi; diminished goblet cells and infiltration of cells in lamina propria. These changes may be irreversible in long standing enteropathy.

Clinical manifestations :

1. Chronic or recurrent diarrhea, the stools are characteristically foul, bulky and greasy. Anorexia may be prominent.
2. Progressive malnutrition with secondary deficiencies.
3. Clinical examination reveals a nervous child, a greatly distended abdomen with extreme loss of subcutaneous fat. In contrast to the general picture of malnutrition, the face may be full and plump.
4. The age incidence when the condition starts is 6 to 18 months. Breast feeding delays the appearance of symptoms.
5. Episodes of dehydration and acidosis, termed celiac crisis, may interrupt the characteristic chronic course. These are often triggered by an upper respiratory tract infection. There are large, watery stools and copious vomiting.

Laboratory and X-ray findings:

1. Fat loss constitutes 75 to 85% of the ingested amount, usually in the form of soaps and fatty acids.
2. Low or flat oral glucose tolerance curves denoting intestinal malabsorption are obtained. There is impaired absorption of D-xylose.
3. Peroral biopsy reveals characteristic changes in the mucosa of small intestine.
4. Deficiencies may be manifested as rickets or osteoporosis with fractures evident in X-rays. Hypochromic anemia and hypoalbuminemia are common findings.

Treatment : The main principle is to eliminate wheat and rye products.

- I — In celiac crisis, repair the water and electrolyte balance. Antibiotics are given to combat infection and parenteral calcium is administered if there is tetany.
- II — Diet after the acute crisis should be high in protein, low in fat and starch-free. Initially, administer small feedings and increase gradually when appetite improves and there is no vomiting.
- III — The diet can be gradually increased, but care is given that wheat and rye products are not ingested for several years. Water-miscible oral preparations of vitamins A and D, and liver extract injections are given. Oral preparations of vitamin B complex, vitamin C and iron supplements are also administered.

FIBROCYSTIC DISEASE OF THE PANCREAS (MUCOVISCIDOSIS)

This is a hereditary recessive generalized disease characterized by the production of an abnormally viscid mucus which obstructs the small ducts of exocrine glands. The full picture includes chronic pulmonary disease, pancreatic insufficiency, abnormally high sweat electrolytes and occasionally cirrhosis of the liver.

Pathogenesis : The basic defect in cystic fibrosis is unknown. An inborn error of metabolism was put forward as an explanation.

Clinical manifestations :

- I — Pulmonary involvement : Bronchial and bronchiolar obstruction by abnormally viscous secretions is the cardinal feature. As a result, generalized obstructive emphysema is early and pertinent. Bronchial and bronchiolar infection is secondary to the obstructive process with resultant bronchiectasis. In long standing cases pulmonary hypertension with acute cor pulmonale may result.
- II — Pancreatic insufficiency is present in more than 80% of cases with absent trypsin, lipase and amylase in the duodenal contents.
- III — As a result of pancreatic insufficiency malabsorption with secondary malnutrition results. The abdomen is distended and the stools are increased in number, greasy and extremely foul.
- IV — In about 5 to 10 per cent of cases, intestinal obstruction within hours after birth results. This is called meconium ileus. The lumen of small intestine is plugged with hard meconium. Perforation may occur. Meconium peritonitis and congenital peritoneal adhesions are not uncommon as a result of perforation in utero.
- V — When multilobular biliary cirrhosis results due to obstruction in the biliary passages, persistent jaundice is present.

Diagnosis : The combination of chronic pulmonary disease and intestinal malabsorption suggests the disease. The helping points are : -

- 1. Increase in electrolyte concentration in sweat.
- 2. Absence of pancreatic enzymes.
- 3. Chronic pulmonary involvement.
- 4. A family history of the disorder.

X-ray of chest shows generalized obstructive emphysema, sometimes disse-

minated bronchopneumonia or atelectasis is found. X-ray changes of intestinal tract are of little help in mucoviscidosis and in the malabsorption syndromes in general.

Doudenal enzymes especially tryptic activity is absent in over 80% of cases. Serum electrolyte estimation may show hypoelectrolytemia.

Treatment :

- General care ; Vaccination against common infections is necessary.
- Control of pulmonary infection by antimicrobial agents. Selection of drugs is better based on bacterial sensitivity test.
- Dietary therapy A high caloric, high protein with moderate fat intake, with one of the products of pancreatic extracts.
- Salt and water loss especially in hot weather is treated by intravenous saline. Additional sodium chloride (2 to 4 Gm.) per day is added in hot weather.
- In meconium ileus relief obstruction by surgery.

INTESTINAL OBSTRUCTION

Congenital intestinal obstruction :

A — Intrinsic :

1. Atresia of the intestine and colon.
2. Stenosis of the intestine and colon.
3. Aganglionic segments (Hirschsprung's disease).
4. Meconium ileus.

B — Extrinsic :

1. Malrotation of the intestine and colon (Volvulus of midgut).
2. Duplication of the alimentary tract (Enteric and neurenteric cysts).
3. Diverticula (Meckel's).
4. Herniations : (a) Intra-abdominal (Omental, mesenteric defects).
(b) External (Inguinal canal).

Acquired intestinal obstruction :

1. Paralytic ileus (Pneumonia, peritonitis, uremia, electrolyte imbalance).
2. Mechanical (Strangulated inguinal hernia, intussusception).
3. Adhesions (Acute peritonitis, T.B. abdomen)
- 4 Foreign bodies and masses ; (Fecal concretions, tumours and cysts, mass of ascaris)

SOME FORMS OF INTESTINAL OBSTRUCTION

CONGENITAL ATRESIA OF THE INTESTINE AND COLON

This is an uncommon malformation in which there is complete obstruction of the alimentary tract.

Clinical picture : Babies with intestinal or colonic atresia show symptoms on the first day of life. There is frequent vomiting and the vomitus is bile-stained. In the stools failure to find cornified epithelial cells in the first forty-eight hours of life (Farber's test) or the failure to find milk curds at a later date is of great significance. Abdominal distension may or may not be present depending upon the level of atresia.

Diagnosis : A plain film will show a markedly distended duodenum or distended loops of small intestine. The use of barium meal or enema is risky, because the material can become inspissated and block the intestinal tract.

Treatment : For atresias of the duodenum or high jejunum, duodeno-jejunostomy is the treatment of choice. Attention must be paid to fluid therapy and regulation of feeding.

CONGENITAL STENOSIS OF THE INTESTINE AND COLON

Stenosis of the intestine and colon may give symptoms in the first week or two of life, less marked constrictions do not show up until later in infancy or even childhood years.

Clinical findings : In the newborn, there is persistent vomiting and abdominal distension, especially if the obstruction is low, together with loss of weight. In older patients, the symptoms may be mild as abdominal distension or occasionally vomiting.

Treatment : A gastro-jejunostomy or duodeno-jejunostomy is the safest procedure.

INTESTINAL OBSTRUCTION RESULTING FROM MECONIUM ILEUS

Meconium ileus is a rare cause of intestinal obstruction in the newborn infant. It is associated with cystic fibrosis of the pancreas.

Clinical picture : The clinical picture of meconium ileus simulates several other forms of intestinal obstruction in the newborn. Within the first day or two of life, vomiting becomes progressively more frequent. The abdomen is moderately or markedly distended. Palpation of the distended abdomen may reveal firm masses within the intestinal loops.

Röntgenologic examination shows gas and fluid-filled loops throughout the abdomen. Of importance is the fact that loops of intestines vary greatly in size in contrast to the picture of intestinal atresia or stenosis where all visualized loops are quite large. Another important fact is that meconium gives a mottled or granular appearance on some areas.

Treatment : Surgical removal of the terminal portion of the ileum by a Mickulicz resection with a temporary double ileostomy through which the intestine can be lavaged with dilute hydrogen peroxide solution, and pancreatic enzymes can be instilled to clear the bowel of its abnormal contents.

CONGENITAL MEGACOLON (HIRSCHPRUNG'S DISEASE).

This condition is due to congenital absence of parasympathetic ganglion cells from the intramural plexus of a portion of the intestinal tract, usually the rectum, rectosigmoid or lower sigmoid.

Pathology : The entire colon may be many times its normal caliber. The greatly dilated gut contains tremendous accumulations of gas and inspissated fecal material. The cecum and ascending colon are greatly hypertrophied. The rectum and rectosigmoid appear to have a normal caliber and thickness of wall in contrast to the sigmoid which is greatly distended and hypertrophied. Microscopic examination of the constricted portion of the rectosigmoid colon reveals absence of the parasympathetic ganglion cells of the intramural plexus.

Clinical findings : Hirschsprung's disease is a congenital lesion and the initial symptoms appear shortly after birth or in early infancy. The infant presents with obstinate constipation and marked enlargement of the abdomen. While constipation is the rule, at times diarrhea may appear, if fluid intestinal material is passed around inert fecal masses which lie in the colon. Vomiting is seldom an outstanding feature. Distension, fetid odour of the breath, anorexia, lassitude and malnourishment are the rule. The rectum is found commonly empty, but it may contain fecal material.

Diagnosis . In the newborn infant it is to be differentiated from meconium ileus. This is helped by barium enema injected slowly through a catheter passed in the anal canal. The sigmoid will appear tremendously enlarged,

usually with a characteristic narrowing of the recto-igmoid portion. In early infancy, where this narrowing is less definite, rectal biopsy is the only reliable method of diagnosis. X-ray examination of the urinary tract should also be obtained as megaloureters may coexist.

Treatment ;

- (A) *Conservative treatment* - Hirschsprung's disease can occur in variable degrees of severity. In the milder forms of the condition, control can be obtained by supervision of diet, the constant use of mineral oil and the use of colonic lavage.
- (B) *Surgical treatment* - After a preliminary colostomy, the operation of recto-sigmoidectomy, first described by Swenson, should be undertaken in which the whole of the aganglionic segment is removed while leaving the anal sphincter intact. The operation is followed by regular daily bowel actions and a gradual lessening of the abdominal distension. The results surpass previous medical and surgical measures.

INTUSSUSCEPTION

This is the most frequently acquired mechanical cause of intestinal obstruction in infancy. It is characterized by the telescoping of one portion of the intestine into a more distal portion, resulting in impairment of the blood supply, leading to necrosis of the involved segment of the bowel.

Etiology In 95 % of cases, no specific cause can be found, but viral infections (adenovirus) have been implicated as the cause of some cases. The condition is most frequent between the ages of five months and one year. Telescoping occasionally occurs around a Meckel's diverticulum.

Pathology Intussusception most commonly involves the telescoping of the ileum into the colon (ileocolic type). Gangrene of the intussusception occurs if the incarcerated bowel loses its blood supply for a period of about 3 hours.

Clinical findings

- A) *Symptoms* : A sudden onset of recurrent, paroxysmal, sharp abdominal pain in a well-nourished, healthy child suggests intussusception. The child perspires and draws up his legs to ease the pain. Vomiting frequently occurs after the onset of the abdominal pain. It usually becomes progressively more severe.
- B) *Signs* : The extent and severity of abnormal physical findings will depend on the duration of symptoms.

1. Shock, dehydration and fever : After one or two hours of recurrent pain, evidence of shock occurs with each episode and frequently persists into the interval between attacks. It is characterized by pallor, sweating and lassitude. After few hours, dehydration is noted and the eyes are sunken and soft. A low-grade fever is usually found as a result of dehydration and obstruction.

2. Mass : Careful palpation usually reveals a mass, sausage-shaped or ovoid. Its location varies, but it is frequently in the right upper quadrant. The right lower quadrant is characteristically less full than usual. Blood is frequently found on rectal examination.

C) *X-ray findings* : Barium contrast studies are usually not necessary if the history and physical findings are typical.

1. Plain film of abdomen : Dilated loops of small bowel suggest obstruction of the small intestine.

2. Barium enema : The intussusception is outlined as an inverted cap and an obstruction to the further progression of barium is noted.

Treatment ;

A) Specific measures :

1. Reduction by gentle administration of a barium enema is recommended in early ileocolic intussusception. The enema must reach above the ileocecal valve. Perforation can occur from the pressure of the enema if the bowel wall has been weakened due to impairment of its vascular supply. These patients need close observation after reduction.

2. surgical reduction is the method of choice if enema is not successful, or if there is evidence of peritoneal irritation, and in those whose symptoms have persisted for more than 24 hours.

B) Fluid and electrolyte therapy is necessary before the operation and parenteral feeding is needed after the operation.

INGUINAL HERNIA

In infants and children, inguinal hernias result from failure of obliteration of the processus vaginalis which accompanies the spermatic cord or round ligament into the scrotum or labium majus.

Clinical findings :

A) *Symptoms* : The history is usually classical with an intermittently appearing bulge in the inguinal area, larger when the child is straining.

- B) Signs :** The hernial bulge can usually be demonstrated. When the hernia is reduced, coughing or straining may demonstrate it. Occasionally, there are no signs on an initial examination and repeated examination is necessary. The presence of a mass in the groin, particularly if tender or inflamed, may suggest an incarcerated hernia.

Treatment It consists of early surgical repair. Small infants tolerate the operation well and recurrence is rare. Delay of operation in infants increases the risk of incarceration.

Incarcerated inguinal hernia :

Incarceration of inguinal hernias is common in children and occurs most often in the first six months of life. The infant is fretful and often vomits. Unless the incarceration is relieved, abdominal distension, cessation of movement, persistent vomiting and fever develop.

Treatment : The infant is sedated with barbiturates and is placed in the Trendelenburg position and ice bag is put on the affected side to decrease edema. After an hour or more, manual reduction is tried and frequently succeeds. If the incarcerated hernia cannot be reduced, emergency surgical correction must be tried.

DIAPHRAGMATIC HERNIA

Diaphragmatic hernia may be congenital or acquired. Acquired diaphragmatic hernias are usually traumatic in origin.

Congenital hernia of the diaphragm ; This hernia may occur through the esophageal hiatus, the canal of Bochdalek (posterior) or the foramen of Morgagni (anterior).

Clinical findings :

- A) Symptoms :** The severity and type of symptoms depend upon the degree of herniation of abdominal organs into the chest, the degree of displacement of the lungs and the presence or absence of obstruction of the intestinal tract.
- 1 — Cyanosis, dyspnea or vomiting of continuous nature in a newborn infant should suggest diaphragmatic hernia.
 - 2 — Respiratory distress may be constant or may appear only with feeding or after crying.
- B) Signs ;** Intestinal peristaltic sounds may be heard in the chest. Movements of the sides of the chest are asymmetrical. Dullness is noted on the affected side. Breath sounds may be absent.

C) X-ray findings : Chest X-ray will show a portion of the gastrointestinal tract in the thorax.

Treatment : Immediate surgical intervention is essential in extensive hernias.

In small hernias without respiratory distress, surgery may be deferred. In infants with eventration of the diaphragm without respiratory distress and with no mediastinal shift, surgery is not indicated.

HYDROCELE

A hydrocele is the presence of fluid anywhere within the course of the processus vaginalis.

There are two types of hydrocele, a common type of noncommunicating hydrocele and a communicating type in which the processus vaginalis remains open allowing peritoneal fluid to be forced into it. An inguinal hernia is often associated with the last type. The differentiation from an incarcerated inguinal hernia is difficult.

Treatment : Surgical repair, if the fluid is not absorbed during the first year of life, is done.

DISEASES OF THE LIVER

Acute Hepatitis

Acute hepatitis in children is due primarily to two viruses; designed as viral hepatitis type A (Infectious hepatitis) and viral hepatitis type B (Serum hepatitis).

Occasionally specific viruses as those associated with cytomegalic disease, herpes simplex and infectious mononucleosis are causally related to acute hepatitis in children.

The discovery of a unique antigen (Australia antigen, hepatitis B antigen) in the serum of patients with viral hepatitis type B and the identification by electron microscope of spherical particles in stools from patients with type A hepatitis serve as a useful marker in epidemiologic studies of type A and B viral hepatitis.

Clinical Manifestations : Hepatitis A transmission is by the fecaloral route.

Common symptoms are fever, malaise, chills, anorexia, vomiting and headache. Upper abdominal pain and hepatomegaly may be present. Jaundice appears in two to five days when fever is subsiding and may last several weeks. It is important to remember that the ratio of subclinical anicteric to icteric cases is as high as 10 : 1 in children. In icteric cases serum bilirubin is elevated usually not in excess of 15 mg./100 ml Transaminase (SGOT) level is increased early. It is a sensitive indicator of hepatocellular injury and is usually the only means of detecting anicteric cases.

The typical course of clinical symptoms and laboratory test abnormalities is for a period of no more than four weeks. Fulminant hepatitis and massive hepatic necrosis are rarely associated with hepatitis A infection.

Type B disease is often transmitted parenterally by inoculation of infective blood or blood products including fibrinogen, anti-hemophilic globulin and vaccines as well as by improperly sterilized needles or syringe.

Clinically type B virus infection is similar to hepatitis A except that the onset of symptoms is usually more insidious and serum transaminase activity usually reaches peak values about one month after onset of symptoms. The development of fulminant hepatitis is apparently more frequent with type B disease but children ultimately recover after a 4 to 6 weeks illness in over 90% of patients.

can also follow inspersion of proteins in cystic fibrosis of the pancreas. congenital malformations or external pressure on the extra-hepatic ducts. This may be due to 1. *Biliary cirrhosis* : follows chronic biliary obstruction. This may be due to

The following types can be recognized in infancy and childhood ; **Etiology** : Cirrhosis of the liver may be caused by a number of different agents.

Forms of cirrhosis : Cirrhosis is divided into portal (Laennec's cirrhosis) and biliary types. In portal cirrhosis, bands of fibrous tissue radiate from the portal triad and surround the hepatic lobules. Biliary cirrhosis is secondary to obstruction of the bile ducts is characterized by fibrosis radiating from the distended bile ducts.

The term «cirrhosis of the liver» has often been used in a loose sense to indicate varying degrees of fibrosis of the liver. In the strict sense, the condition may be defined as a pathological state of the liver characterized by diffuse inflammation accompanied by proliferation of connective tissue and by degenerative and regenerative changes in liver cells resulting in distortion of the hepatic architecture and the intralobular circulation. Severe or prolonged hepatic cellular damage is common to all known conditions predisposing to cirrhosis.

CIRRHOSIS OF THE LIVER

1. Reduce physical activity as long as there is evidence of active disease.
2. Balanced and palatable diet with adequate protein-sparing carbohydrate. Finally give full diet high in carbohydrates and proteins.
3. Supplement with vitamins, particularly B complex.
4. With severe hepatic disease and coma, reduce intestinal flora with neomycin and kanamycin and reduce protein intake.
5. In severely ill patients with anorexia, nausea and vomiting give corticosteroids for five days and then gradually reduce the dosage.
6. Treatment of complications: For haemorrhagic manifestations transfusion of fresh whole blood. In the rare event of acute yellow atrophy no specific treatment but transfusion and electrolyte replacement may help.

Treatment :

1. Chronic hepatitis : Impairment of liver function may be demonstrable for many years.
2. Hemorrhagic manifestations: Due to low prothrombin level.
3. Acute yellow atrophy : A rare fatal condition leading to hepatic coma.

Complications :

2 *Congestive cirrhosis* : following prolonged circulatory stasis as in chronic congestive heart failure and in constrictive pericarditis.

3. *Chronic infection* as syphilis, schistosomiasis, malaria and kala-azar.

4. Cirrhosis following *infections hepatitis* appears to be the most common cause during childhood. In most instances the initial episode of jaundice is followed by a quiescent period lasting from six months to few years during which the patients are free from jaundice and essentially asymptomatic. This is followed by recurrence of jaundice, ascites, esophageal varices and essentially the full picture of cirrhosis of the liver. The pathologic picture is that of postnecrotic cirrhosis.

5. Cirrhosis may follow recovery from acute *hepatic poisoning*, as for example with carbon tetrachloride.

6. Cirrhosis may follow long standing *chronic hemolytic anemias*, e.g. thalassemia and sickle cell anemia. Cirrhosis of the liver has also been described accompanying transfusional siderosis.

7. Cirrhosis may be a sequela of some *metabolic disorders*, e.g. Fanconi syndrome, galactosemia, Wilson's disease and very rarely glycogen storage disease.

Clinical manifestations : The liver is usually enlarged and firm and in later stages it may contract and shrink. The usual manifestations are due to : -

1. Failure of the liver in some of its physiologic functions. The functional reserve of the liver is great, cirrhosis may exist for years without evidence of deficiency of hepatic function. Jaundice is frequent. Hypoprothrombinemia with epistaxis is common. Anemia is usually present. Growth retardation is common and may be extreme.

2. When the pressure in the portal vein rises it gives the different manifestations of portal hypertension. These are enlargement of the spleen, gastric and esophageal varices, ascites and collateral venous circulation in the veins of the abdominal wall.

Diagnosis : The liver function tests may be normal or may show hepatic dysfunction, hypoalbuminemia, hypoprothrombinemia and retention of bromsulphalein. The cephalin flocculation, thymol turbidity and thymol flocculation tests become positive. Biopsy of the liver by needle aspiration is useful for diagnostic and prognostic purposes.

Treatment : A diet high in calories with liberal protein and fat content is given. Supplements of the B vitamins may be of value. Ascites is treated by salt restriction, diuretics and corticosteroids. Massive ascites may require paracentesis. In cases with impending liver failure, a diet containing little or

no protein is indicated together with administration of broad spectrum antibiotics and blood transfusion. Several surgical procedures have been devised to reduce the pressure in the esophageal or gastric varices by shunting blood from the portal circulation to the renal or portal veins.

CIRRHOSIS OF THE LIVER IN THE TROPICS

Liver cirrhosis is more prevalent in the tropics and subtropics than in the temperate zones. Two well defined types will be discussed, viz. veno-occlusive disease and Indian childhood cirrhosis.

I — Veno-occlusive disease

This is a disease of undetermined etiology occurring between the ages of 1 and 6 years in undernourished children. It has been reported from Jamaica, South Africa and Egypt.

Etiology : The exact etiology is unknown. Malnutrition of some degree is invariably present and is thought to play a subsidiary part. There is good evidence to suspect the role of toxins of plant or vegetable origin as bush teas which are infusions of herbs, seeds and roots used in West Indies both medicinally and for food. These contain senecio which is a hepatotoxic alkaloid.

Pathology : The initial histological lesion is confined to the central and next larger branches of the hepatic veins, leaving the rest of branches free. There is swelling of the intimal tissues of the affected vessels. The immediate sequelae are congestion of the sinusoids and a pressure degeneration of the hepatic cell cords in the centrilobular areas. Complete clinical and histological recovery may occur. In some cases there is centrilobular fibrosis with development of non-portal fibrosis. Progressive fibrosis with regenerating nodules ensue.

Clinical manifestations : Three often ill-defined and overlapping stages: -

1. *Acute* - A smooth, firm and often gross hepatomegaly is observed, usually with considerable ascites. Spontaneous subsidence may occur, but repeated paracentesis for several weeks may be necessary. There is splenomegaly and edema may appear either generalized or confined to the lower limbs. In some patients there is complete clinical recovery with liver function tests and liver biopsy findings becoming normal, but some children die in the acute phase of liver failure. Jaundice is uncommon. The acute phase may pass into the subacute stage or it may be subacute from the onset.

2. *Subacute* - There is persistent hepatomegaly and sometimes splenomegaly.

Acute episodes may occur but the disease often passes subclinically into the chronic stage.

3. *Chronic* : This is characterized by a cirrhosis clinically indistinguishable from other forms of cirrhosis. Repeated attacks of hematemesis occur and constitute the commonest cause of death at this stage, although some die of hepatic failure.

Laboratory data : There is non-specific derangement of the standard liver function tests.

Diagnosis : In the acute stage diagnosis is suspected from the history, the characteristic clinical picture and liver biopsy findings. In the subacute and chronic stages, diagnosis may be more difficult but readily confirmed by liver biopsy. When there is jaundice differentiate it from infectious hepatitis and leptospirosis.

Treatment : Improve the nutritional state by dietary measures and vitamin supplements. A high protein diet is recommended except when liver failure appears eminent. Salt and water are restricted if ascites is present. Cortisone was tried with apparently good results. Antibiotics are given to combat infection. Frequent paracentesis may be required.

11 — Indian childhood cirrhosis.

The frequent occurrence of cirrhosis of unknown etiology in many areas of India among children aged one to five years justifies the separate clinical designation «Indian childhood cirrhosis».

Etiology : The cause or causes of this type of cirrhosis are not exactly known.

Malnutrition, which was considered an important factor, seems to play no role since the condition is infrequent among the poorer classes. Progressive fibrosis of the liver is a rare sequela of kwashiorkor. The similarity of the histologic picture to those of chronic viral hepatitis together with the frequency of jaundice suggest a viral etiology. No hepatotoxin was found in the diet.

Pathology : There is postnecrotic scarring with regenerating nodules. Patchy or widespread liver cell damage is seen. There is no occlusion of hepatic vein radicles.

Clinical picture : Onset is insidious with poor appetite and slight abdominal distension. Enlargement of the liver variable in degree occurs, at first extends to the umbilicus, then it contracts and becomes more firm.

Jaundice is common in the late stages and occasionally the early phase. Portal hypertension, ascites and hematemesis are terminal. The course varies from few months to two years.

Treatment : Nutritious diet rich in protein and vitamins can help. Cortisone may be tried. Hematemesis may necessitate transfusion.

NUTRITIONAL LIVER DISEASES

I — Protein-calorie malnutrition:

The fatty liver which is an almost invariable part of the kwashiorkor syndrome is due to various causes such as the synthesis of large amounts of triglycerides from excess dietary carbohydrate, the transport to the liver of non-esterified fatty acid released from fat depots and inability to transport fat from the liver because protein-fat combinations cannot be made.

Fatty liver in kwashiorkor is of secondary rather than primary importance. The liver shows extensive fatty changes especially at the periphery of the lobules.

The presence of fat does not depress most functions of the liver with the notable exception of albumin formation. Follow-up studies have not shown evidence of progressive fibrosis, cirrhosis or other sequelae.

II — Veno-occlusive disease :

This liver affection as previously described is due to toxic substances in «bush teas» affecting children suffering from variable degrees of protein malnutrition.

III — Siderotic cirrhosis of the liver with protein malnutrition :

This condition occurs in native South African children whose diet consists of porridge fermented in iron utensils. Iron is deposited in the reticulo-endothelial cells throughout the body and in the parenchymal cells of the liver. Periportal hepatic fibrosis is common but cirrhosis may occur.

IV — Indian childhood cirrhosis :

A dietary or nutritional basis for this disease has been frequently suggested but the relative exemption of the poorest socio-economic group would point against malnutrition being a major factor. However, it is believed that poor nutritional background may be a contributing factor in association with viral hepatitis.

V Cirrhosis associated with malnutrition and parasitism :

The association of parasitic infestation as malaria, *schistosoma mansoni* and *schistosoma japonicum* with malnutrition is responsible for production of liver cirrhosis in many parts of the world.

E. HASANEIN

Chapter IX

INFECTIOUS DISEASES

ANTIMICROBIAL THERAPY

Antimicrobials are chemotherapeutic agents used against microorganisms, while antibiotics are substances synthesized by certain organisms and are toxic to other organisms. Sulfonamides, INH, PAS, ... etc. are therefore antimicrobials, but Penicillin, Tetracyclines, Chloramphenicol, ... etc. are antibiotics.

Antimicrobial therapy means the use of any chemotherapeutic agent for the treatment of an infectious disease, by attack upon its etiologic agent.

Spectrum of Activity :

1. Useful against Gram + & Gram - Cocci & Bacilli (Broad Spectrum) e.g. Sulfa drugs, Tetracyclines, Chloramphenicol and Ampicillin.

2. Useful against Gram + & Gram - Cocci & Gram + Bacilli (All cocci & G + bacilli) e.g. Penicillins, Erythromycin, Oleandomycin, Cephalosporins, Novobiocin, Vancomycin and Ristocetin.

3. Useful against Gram - Bacilli (Used in combination with previous group usually) e.g. Streptomycin, Neomycin, Kanamycin, Gentamycin, etc.

4. Useful against specific organisms.

Polymyxin B & Colistin, INH, Nystatin, and PAS.

STREPTOCOCCAL INFECTIONS

STREPTOCOCCOSIS

Streptococci are Gram + organisms that appear characteristically in chains. They are divided into :

1. Alpha hemolytic streptococci : these give an incomplete or green hemolysis on blood agar (*Streptococcus viridans*).

2 Beta hemolytic streptococci (commonly known as *Streptococcus pyogenes*) : give complete hemolysis on blood agar (Group A, B, C, D, ... etc). Group A Beta hemolytic streptococci are the most important pathogens in this series.

3. Gamma type, or Non-hemolytic streptococci these produce no visible hemolysis on blood agar (*Streptococcus fecalis*)

Common diseases caused by Beta hemolytic streptococci :

1. Nasopharyngitis, 2. Acute follicular tonsillitis (Exudative tonsillitis), 3. Suppurative otitis media, 4. Cervical lymphadenitis, 5. Erysipelas, 6. Cellulitis and 7. Scarlet Fever.

SCARLET FEVER (SCARLATINA)

Scarlet fever is an acute infection consisting of streptococcal pharyngitis plus a rash. The rash is due to an erythrogenic toxin, to which the child is susceptible, and is not due to a particular strain of streptococci.

Etiology : Any erythrogenic toxin-producing strain of Beta hemolytic streptococci mostly belonging to group A.

Clinical Picture : Incubation period 2 to 4 days. Age 3 to 8 years.

The symptoms are usually abrupt, with vomiting, fever and sore throat in the first 24 hours. Febrile convulsions may usher the onset in young children.

The throat (like any streptococcal pharyngitis), shows edema of the anterior pillars, beefy red appearance, exudative tonsillitis, with a white-yellow membrane. On the hard palate, an enanthem may appear as discrete red, sometimes hemorrhagic spots.

The exanthem (rash), appears 12 to 48 hours after the onset, in areas of warmth and pressure. It is characterised by pin-point diffuse erythema, with prominence of the bases of hair follicles and not involving the circumoral region. It fades on pressure, but the transverse red lines found at the elbow do not fade and constitute the Pastia's sign. The tongue at this stage is coated white, while the papillae show through as red points (the white strawberry tongue).

The exanthem starts to fade and desquamate in 3 to 7 days. The most characteristic is the peeling of the finger and toe tips. At this stage usually, the tongue loses its coat and is swollen, red, with studded prominent papillae (the red strawberry tongue).

Laboratory findings : 1. Leukocytosis (up to 15,000). 2. Antistreptolysin titer above 150 Todd Units and, 3. Throat culture positive for Beta hemolytic strepts.

Diagnosis : The typical case is easy to diagnose, but mild and atypical cases should be differentiated from :

1 Measles (catarrhal symptoms, morbilliform eruption and Koplik's spots).

2. German Measles (mild, enlarged occipital nodes, rash rapidly changes and desquamation is rare). 3. Exanthem subitum. 4. Infectious mononucleosis. 5. Drug rashes.

Complications : I Immediate :

1. Pyoderma, 2. Otitis media, 3. Adenitis, especially cervical, 4. Laryngitis, laryngotracheobronchitis, bronchopneumonia, and empyema. 5. Metastatic foci; as meningitis, arthritis, osteomyelitis, pericarditis... etc. and 6. Septicæmia.

II Delayed : (Non-septic, non-toxic) :

1. Acute diffuse glomerulonephritis (in 1% of cases and usually in the second or third week).

2. Rheumatic fever (also in the second to third week, as a hypersensitivity reaction).

Prophylaxis : No immunization is available (many strains). Antibiotic prophylaxis in certain cases (penicillin).

Treatment : 1. Symptomatic. 2. Specific — penicillin is the drug of choice, should be given 10 days i.m. followed by one benzathine (long acting). In cases of allergy to penicillin, erythromycin, or cephalothin should be given.

3. Treatment of complications (antibiotics, hot applications, incision,... etc).

DIPHTHERIA

It is an acute febrile specific infection, usually of the throat, caused by *Corynebacterium diphtheriae* (Gram positive pleomorphic rods). It is transmitted by droplet infection, or contaminated articles. The organism produces a powerful exotoxin responsible for the toxic and degenerative changes in the viscera and nervous system.

Etiology : Strains of *C. diphtheriae* capable of producing the specific exotoxin are virulent and can give rise to the disease.

Clinical Features : Incubation period is 2 to 7 days. — Infants up to 6 months, born to immune mothers are immune. Most cases are in children below 5 years.

1. *Pharyngeal (faucial) diphtheria :* Here there is mild sore throat, moderate fever, rapid pulse and severe prostration. Dysphagia, headache, noisy breathing and offensive odour from the mouth may be present.

The tonsils are congested and swollen and a pseudomembrane forms in the throat and spreads from the tonsils to the anterior pillars and uvula. The membrane is typically dirty grey when fully developed. Its edges are slightly elevated and if scraped off bleeding results (contraindicated procedure, as it may enhance toxin absorption). The cervical lymph nodes enlarge and the surrounding soft tissues are edematous, giving a characteristic «bull-neck» appearance. A nasal voice or regurgitation of liquids through the nose suggests palatal paralysis. The knee jerks are usually diminished or absent.

In severe malignant types, the sensorium is disturbed, hemorrhages from the mouth and nose are common, and petechiae may occur in the skin and mucous membranes. On the other hand, mild cases may be overlooked, as they may resemble catarrhal inflammation, or ordinary follicular tonsillitis.

2. *Laryngo-tracheal diphtheria* : (most serious). This is primary only in about 1/3 of the cases, and secondary to an extension from pharyngeal diphtheria in the rest. There is hoarseness of voice, or even aphonia, croupy cough, fever and marked prostration. The noisy breathing may progress to stridor, and will lead to respiratory obstruction and cyanosis. The neck is very much edematous. Anxiety and retractions of the suprasternal and subcostal regions occur and death may follow from suffocation or cardiac failure.

3. *Nasal diphtheria* : It is primary in about 2% of cases. It occurs more in infants. It is a potent source of infection to others. The constitutional manifestations here are very slight. There is usually a serosanguinous nasal discharge, that frequently excoriates the upper lip. The membrane may be visible on the turbinates.

4. *Cutaneous, vaginal, or wound lesions* with ulceration and membrane formation may occur. The vulva, conjunctivae, lips, face and umbilical cord are rare sites.

Laboratory findings :

1. Normal or slightly increased leukocytic count.
2. Smear of exudate stained with methylene blue, shows the diphtheria rods with midpolar bars.
3. Culture on Löffler's medium is positive.
4. Urine shows albuminuria and hyaline casts.
5. E.C.G. in myocarditis, shows T-wave changes and partial or complete heart block

Diagnosis : The clinical picture, and when in doubt, a smear and culture should be done. The following is the differential diagnosis of the different types of diphtheria :

1. **Faucial** — follicular tonsillitis, scarlet fever, infectious mononucleosis, herpes, thrush, leukemia and post-tonsillectomy wounds.

2. **Laryngo-tracheal** — acute laryngotracheobronchitis, spasmodic croup, foreign body, bronchiolitis, bronchopneumonia, bronchial asthma, retropharyngeal and peritonsillar abscess and tetany.

3. **Nasal** — ulcers from picking the nose, foreign body and congenital syphilis.

Complications :

1. **Respiratory** — bronchopneumonia, especially with laryngeal diphtheria, and atelectasis in laryngeal and tracheal diphtheria

2. **Cardiac and Circulatory** — circulatory failure may occur early (toxemia), or late (peripheral vasomotor changes). Cardiac failure is due to acute myocarditis (direct result of the toxin), with or without superimposed damage to the conducting system. Enlargement of the liver, epigastric pain, vomiting, feeble heart sounds (especially the first) and gallop rhythm are characteristic of cardiac failure.

3. **Renal** — albuminuria is present in most cases, but actual nephritis occurs in about 10% of cases.

4. **Nervous** — neuritis is usually a later development, and its degree depends on the extent of the primary lesion and the time elapsed before giving the anti-toxic serum. Paresis or paralysis may develop in about 15% of cases, it is both sensory and motor, it is rarely prolonged and complete recovery is the rule.

(a) **palatal paralysis** — most frequent and earliest, manifested by nasal voice, nasal regurge of fluids and dysphagia.

(b) **ocular muscles** — paralysis of accommodation is the usual, but squint and ptosis may also occur.

(c) **skeletal muscles** — legs and arms are the commonest, but trunk and neck muscles may also be involved. Guillain-Barré syndrome has been observed in some cases.

(d) **phrenic nerve** — this leads to diaphragmatic paralysis manifested by dyspnea, cyanosis, thoracic breathing and is usually accompanied by pneumonia and myocarditis.

If monoplegia or hemiplegia complicate the picture, it is usually due to thrombosis of cerebral arteries.

Prophylaxis :

1. Active immunization — best done at 3rd, 4th, and 5th months of life, usually by the triple antigen (DPT), or the diphtheria fluid toxoid.

2. Passive immunity - natural in the newborn (absolute for 3 months and partial from 3 to 6 months), and can be acquired at any age by diphtheria antitoxic serum.

3. Prompt treatment of cases and discovery and treatment of carriers.

Schick Test ; this consists in intracutaneous injection of 1/50 MLD (minimal lethal dose) of diphtheria toxin. Read after 24 hours. If positive (the tested person is susceptible, not immune), there will be a reddish-brown discoloration, or even vesiculation at the site of injection. If negative (non-susceptible or immune), no local reaction occurs, except if the person is allergic to some protein in the testing material. However, the allergic or false positive test occurs early (within minutes) and shows a wheal and flare reaction.

Treatment :

1. General — strict bed rest for 3 to 4 weeks, full attention for early discovery of any complication, ample soft diet and fluids i.v. if not taken by mouth.

2. Antitoxin — in sufficient amounts and as early as possible to combine with free toxin. Dose is 10,000 to 100,000 units for any age, depending on site, severity and duration of the disease. Test for horse serum sensitivity before giving the serum, 0.05 ml. 1/10 dilution intracutaneously, and read in 20 to 30 minutes. If not sensitive, give serum i.m. or i.v. according to the case. If positive (wheal and flare), resort to desensitization by serial injections of the antitoxin at intervals of 15 minutes. Adrenaline should always be ready. The antitoxin may be repeated in the severe case after 24 hours.

3. Penicillin or Erythromycin to attack the *C. diphtheriae*, (not to replace the serum), and treat secondary infection. They are also useful to treat the carrier state.

4. Active immunization in convalescence, as the attack does not confer immunity in many cases.

5. Treatment of complications : Myocarditis - oxygen tent, glucose i.v. and good fluid balance, digitalis cautiously, and diuretics.

Circulatory failure -- plasma, blood, ephedrine...etc.

Neuritis — splinting the paralysed limbs, and appropriate physiotherapy. Dysphagia may necessitate indwelling naso-gastric tube, phrenic or intercostal paralysis may require respirator.

PERTUSSIS (WHOOPIING COUGH)

It is an infectious disease of the respiratory system, caused by *Bordetella pertussis*. It is transmitted by droplet infection during the catarrhal and paroxysmal stages of the disease. It is communicable from one week before, to three weeks after the onset of symptoms.

Etiology : The *Bordetella* is present in the upper respiratory tract during the early stages of the disease. It is seldom found in persons without symptoms, and occasionally in immediate contacts of an active case.

Clinical Picture : Incubation period is 7 to 14 days. All ages including the newborn are susceptible however, rare after the 7th year of life. There are 3 stages of the disease each lasting about 3 weeks.

1. *Catarrhal or Prodromal Stage* — insidious onset with a mild cough, often nocturnal, with sneezing, lacrimation and slight fever (symptoms of coryza).

2. *Spasmodic, Paroxysmal or Whooping Stage* — the cough gradually becomes aggravated. In a typical case, there are repeated series of many coughs during one expiratory phase, followed by a sudden deep inspiration which may be accompanied by a characteristic «whoop». During the paroxysm, the face becomes red and congested, the lips and tongue cyanotic, and anxiety is apparent. At its end, vomiting or expectoration of thick, tenacious mucoid sputum, may occur. In violent spells, exhaustion or even convulsions may occur. Epistaxis, subconjunctival hemorrhages, and puffiness of the eye-lids are common.

The characteristic «whoop» may be absent in the very young, and disappears when bronchopneumonia complicates the picture. Almost all complications arise during this stage, and they are more frequent in the young and debilitated. Paroxysms are provoked by eating, excitement, sudden change in temperature or humidity and irritating fumes.

3. *Convalescent Stage* — the number and severity of the paroxysms decrease gradually. However, a habit pattern of coughing may be established which continues for many weeks or recurs with every common cold, resembling a new attack.

■ Laboratory findings •

1. Leukocytosis with a characteristic lymphocytosis.
2. Erythrocyte sedimentation rate may be low.
3. Positive nasopharyngeal culture taken by swab or cough plate on Bordet-Engou medium.

Diagnosis : Very easy in the «whooping» stage, while in the catarrhal and atypical forms it may be very difficult. The disease should be differentiated from :

1. Parapertussis resembles it so closely, though milder, that it can only be differentiated by culture.
2. Upper respiratory infections like pharyngitis, laryngitis, adenoiditis or sinusitis with post-nasal discharge may be confused with pertussis.
3. Lower respiratory infections like bronchiolitis and interstitial pneumonitis.
4. Bronchial asthma, foreign body and wheezy chest.
5. Enlarged mediastinal nodes.
6. Long uvula.

Complications :

1. *Respiratory* — otitis media, bronchopneumonia, atelectasis, emphysema and bronchiectasis may occur. Pneumothorax and empyema are infrequent. Dissemination of a previously existing primary tuberculosis can occur.

2. *Digestive* — severe and prolonged vomiting may lead to emaciation. Pro-lapse of the rectum and hernias may occur. Ulceration of the frenum of the tongue (if the incisors are present) usually occurs.

3. *Nervous* — convulsions are relatively common in infants and are probably due to cerebral anoxia during the paroxysms. Permanent brain damage may be a sequela. Tetany may occur if there is rickets or alkalosis from protracted vomiting. Intracranial hemorrhage is a serious complication. Encephalitis is also an undesirable complication.

4. *Hæmorrhagic* — usually mechanical in origin, and occur most often as epistaxis, subconjunctival, hemoptysis and seriously intracranial.

Prophylaxis :

1. *Active immunization* — best done at 3rd, 4th, and 5th month of life, usually by the triple antigen (DPT), or by Pertussis phase I fluid vaccine. The 3 doses should include 4 N.I.H. units (National Institute of Health) or 80 to 100 billion *B. pertussis*.

2. *Passive immunity* — absent in the newborn, and can be acquired by pertus-sis immune globulin (2.5 ml. i.m.).

3. In exposed immunized children, give an immediate booster dose of pertus-sis vaccine

Treatment :

1. *General* — bed rest if febrile, fresh air when not digestible diet, vitamins and if vomiting is severe, frequent meals and immediate feeding after vomiting may be helpful. Infants require constant attention, oxygen, suction and even artificial respiration.

2. *Symptomatic* — sedatives and antispasmodics are the most important. Phenobarbital in the young and codeine in the older child, together with expectorant bronchodilator mixture, are sometimes helpful.

3. *Specific* — erythromycin and ampicillin are effective if given early, and treatment of secondary infection helps to diminish the paroxysms. Pertussis immune gamma globulin can also be of help.

4. *Treatment of complications* : Pulmonary complications may need specific antibiotics.

Liberal use of oxygen in severe cases to decrease the incidence of convulsions and brain damage. Convulsions may need i.m. phenobarbital, or even lumbar puncture.

ACUTE BACTERIAL MENINGITIS

Acute bacterial meningitis is an inflammation of the membranes covering the brain and spinal cord with definite or presumptive evidence of bacteria and polymorphonuclear leukocytes in the cerebrospinal fluid.

Etiology :

1. In the neonatal period : *E. coli*, other Gram negative bacilli, and *Staph. aureus*.

2. In infancy and childhood : *H. influenzae* type B, *Pneumococci* and *Meningococci*. These 3 organisms are responsible for more than 90 % of bacterial meningitis.

3. At any age ; besides the 3 common pathogens, any of the following organisms can also be the cause : *Strept. hemolyticus*, *Pseudomonas*, *Proteus*, *Aerobacter* and *Klebsiella pneumoniae* (Friedlander's bacillus).

Clinical picture :

1. *Meningeal signs* — these include, stiffness of neck, (grades from simple guarding, to neck rigidity, to hyper-extension as in opisthotonus), stiffness of back (inability to sit up normally, and tripod sign), positive Kernig's sign (inabi-

lity to extend knee when leg is flexed anteriorly at the hip), and positive Brudzinski's sign (when the head is bent forward, flexure movements of the lower extremity are produced, and when one lower limb is flexed, the other one will also flex).

2. *Increased intracranial pressure* — bulging of the fontanel in small infants, irritability, headache, projectile vomiting, diplopia, «choking» of the optic disks and eventually blurring of vision, slowing of pulse, irregular respirations and sometimes «cracked-pot» percussion note over the skull.

3. *Change in sensorium* — from mild lethargy to coma.

4. *Convulsions* — usually generalized and more common in infancy.

5. *Fever* — may be absent or very high in infancy, but usually it is high with sudden onset, and low-grade with insidious meningitis.

6. *Shock* — in infancy, it may be the first and only sign.

7. *Other systemic signs of infection.*

There are few differences in the clinical picture produced by different organisms, but these are not conclusive. *H. influenzae* meningitis usually occurs below 2 years of age. The onset may be insidious, quite abrupt following an upper respiratory infection. Coma occurs within few hours, and young infants may have persistent unexplained fever, difficulties in feeding or a high-pitched cry. In Meningococcal infections, the onset is usually sudden, with high temperature, and petechial or purpuric rash. In Pneumococcal, Streptococcal, Staphylococcal, or meningitis caused by Gram negative bacteria, a history of upper respiratory infection, pneumonia, skull fracture, meningocele, infected umbilicus, pyoderma, or urinary tract infection is usually obtained.

Diagnosis : This is simple when the fully developed picture is seen. As early diagnosis is very important, lumbar puncture is obligatory whenever the question of meningitis is raised.

CSF Findings : (a) Increased pressure usually. (b) Naked-eye appearance—clear, cloudy to turbid. (c) Total cell — is usually over 100/c. mm., with evident predominance of polymorphs (pus cells). While a total count of less than 10/c.mm. is usually considered normal, the presence of any polymorph must be viewed with suspicion. (d) Sugar — is reduced in the majority of cases. (e) Proteins — are elevated usually above 100 mg.%. (f) Chlorides — not clinically useful in acute meningitis.

The diagnosis is difficult or delayed in :

- (a) newborns and very young infants, as the onset is atypical.
- (b) in the very early stage.

- (c) if meningitis occurs in the course of another severe illness.
- (d) inadequate antimicrobial therapy masking the clinical picture.

Bacteriology (1). *Gram stain* done to CSF and secretions of the upper respiratory tract. It is helpful to centrifuge the CSF before staining (2). *Culture* of CSF, blood and upper respiratory secretions, with sensitivity tests if necessary.

Complications :

1. Hydrocephalus especially in infants.

2. Subdural effusion, a collection of fluid (often sterile), in the subdural space may occur especially with *H. influenzae* & pneumococcal meningitis, and when initial therapy is delayed or inadequate. Symptoms include fever, vomiting, lethargy, or enlargement of the head in infants. Since the effusion may be unilateral or bilateral, proof of its presence needs bilateral subdural taps. In older children burrholes are required. If more than 2 ml. of fluid is recovered from the space, it is considered abnormal. It may be clear, slightly blood tinged, or cloudy.

It is indicated to tap the subdural space if :

- (a) the fever persists despite adequate therapy, or the fever returns after an afebrile period.
- (b) abnormal neurologic signs persist, or return despite therapy.
- (c) a full fontanel persists.
- (d) there is inability to render the CSF sterile.

3. Vascular collapse, most frequently seen with meningococcal infections. The shock-like syndrome (pallor, cyanosis, low blood pressure and diffuse skin hemorrhages) is due to the action of the endotoxins on the blood vessels and on the adrenal cortex (Waterhouse-Friderichsen Syndrome).

4. Metastatic complications like arthritis, pericarditis, peritonitis, empyema, ... etc.

5. Different forms of paralysis and or deafness.

6. Mental retardation.

7. Psychologic residua.

Prophylaxis : The patient should be isolated for 48 hours after the initiation of the antimicrobial therapy. Contacts and treating personnel should receive 0.5 to 1.0 Gm. of sulfadiazine by mouth daily for 3 days. This is also enough for the carrier state in meningococcal meningitis. There is no need for prophylaxis in the other types of meningitis.

Treatment :

1. *General supportive therapy* — this includes intravenous fluids, treatment of irritability and convulsions by phenobarbital, good nursing care, and frequent observations of the patient's condition. Diet may be given by naso-gastric tube,

blood transfusions may be needed to correct serious anemia, oxygen and anti-pyretics may be also required.

2. *Antimicrobial Therapy* — the principles of this therapy are

- (a) Prompt administration of at least one antimicrobial agent effective against the infecting organism.
- (b) use of the maximally tolerated dosage to maintain effective levels in the CSF.
- (c) Adjustment of the antimicrobial program in the light of the bacteriologic findings unless it is clear that the current therapy is effective.
- (d) Maintenance of the antimicrobial program until the clinical signs have disappeared, or the CSF has been sterilized.

In treating cases of unknown etiology, and in the initial stages before identification of the organism, the combination of Penicillin, Chloramphenicol, and Sulfonamides constitutes the most effective coverage. The effective doses in meningitis are : penicillin (crystalline) 100,000 to 200,000 u/kg/day divided, every 4 hours i.v., chloramphenicol 100 mg./Kg./day not exceeding 4 Gm. daily, and sulfadiazine 100 to 200 mg./Kg./day not exceeding 6 Gm. daily. Ampicillin alone can be also employed in a dose of 200 - 300 mg/Kg./day divided every 4 hours i.v.

The best combinations are two or more of the following :

<i>H. influenzae</i>	— ampicillin & chloramphenicol.
<i>Pneumococci</i>	— penicillin & chloramphenicol
<i>Meningococci</i>	— sulfa & penicillin.
<i>Streptococci</i>	— penicillin & chloramphenicol.
<i>Staphylococci</i>	— penicillin (or methicillin) & chloramphenicol.
<i>E. coli</i>	— kanamycin or gentamycin & ampicillin.
<i>Pseudomonas</i>	— kanamycin, gentamycin & polymyxin B.
<i>Proteus</i>	— kanamycin, streptomycin & penicillin.
<i>Aerobacter</i>	— kanamycin, chloramphenicol & sulfa.
<i>Klebsiella</i>	— streptomycin, sulfa & chloramphenicol.

9. *Treatment of complications*

- (a) Subdural effusion — daily tapping, on alternate sides, removing not more than 30 ml. per day. If the effusion does not clear up in 2 weeks, the child should be transferred to the neurosurgical service, where exploration may be necessary and membranes when found are removed.
- (b) Vascular collapse — maintain fluid and electrolyte balance. Small doses of transfused blood or plasma are given (5 ml./Kg.) and may be repeated 4 and 8 hours later. Corticosteroids (25 mg./Kg. /dose of hydrocortisone sodium succinate in the i.v. drip) are helpful. Pressor substances are recommended by some (4mg. in one liter fluid of levarterenol slowly i.v. checking the blood pressure).

TYPHOID FEVER

Typhoid fever is a systemic bacterial infection caused by *Salmonella typhi* and characterized by fever, gastrointestinal manifestations, systemic manifestations and at times localized lesions of an inflammatory nature.

Etiology : The causative organism is a Gram negative bacillus, and is transmitted by the fecal oral route, from a sick person or a carrier. Epidemics have been traced to contaminated water, ice, milk and various improperly prepared foods. Flies frequently carry the organisms.

Clinical Picture : Incubation period is 7 to 21 days (usually 14 days). In general, the disease in older children resembles typhoid in the adults, while in the young, it may be mild and confused with simple gastroenteritis. However, at any age fulminating cases are known to occur.

The disease begins with fever, headache, malaise, anorexia, vomiting and sometimes a chilly sensation. Dry cough is often present and diarrhea is variable. It may be mild, severe, or sometimes absent. Abdominal distension and a doughy sensation on palpation of the abdomen, together with gurgling when the cecum is compressed, are present. The spleen is often enlarged. There is relative bradycardia. At about the 5th day of the illness, rash may appear on the abdomen consisting of red macules which blanch easily (the rose spots). At this period, the child is usually very sick, with clouding of the sensorium which may progress to stupor and coma. Convulsions may occur.

Laboratory Findings: 1. Leukopenia early in the disease 2. Positive cultures from blood, urine, stools, or bone marrow. The blood culture is positive in about 90% of cases in the first week, then it decreases gradually. The stool culture is positive in 60% of cases in the first week, then it rises in the 2nd and 3rd weeks, followed by a gradual fall. 3. Widal Test — it is a serologic agglutination test. Antibodies in the serum agglutinate antigens of the causative organisms (O, H, and Vi). Of the 3 antigens, antibodies against O are the most indicative of present active infection. A titer of 1 : 160 or higher is considered diagnostic, but demonstration of a rising titer is more conclusive.

Diagnosis : Definitive diagnosis rests upon isolation of the organism or proper interpretation of the Widal Test.

In differential diagnosis, one must consider other types of *Salmonella* infection (Paratyphoid A, B, & C), brucellosis, bacillary dysentery, influenza, malaria, subacute bacterial endocarditis, miliary tuberculosis, infectious mononucleosis, rheumatic fever and sepsis.

Complications : 1. Dehydration and acidosis as in other diarrheal diseases.
2. Localized infections such as meningitis, osteomyelitis, or abscess in any organ.

3. Intestinal hemorrhage — is infrequent in children, occurs in 3rd week, evidenced by melena, or signs of shock, rapid and weak pulse, hypotension, fall in temperature, cold clammy skin, sweating, thirst and apprehension.

4. Perforation — is extremely rare in children. It leads to signs and symptoms of peritonitis.

Prophylaxis : Discovery and supervision of cases and carriers is very important to dispose of their excreta. It is also important to protect and purify water and food supply, and to control flies. Great care is necessary in supervision of food handlers.

Active immunization can be achieved by the T.A.B. vaccine. Usually 3 subcutaneous injections of 0.5 to 1.0 ml. each at intervals of one to four weeks, are effective. Booster injections consist of 0.1 ml. intradermally annually (less reaction), or 0.5 ml. subcutaneously.

Treatment : 1. *General* — control of high fever, soft diet and liquids are tolerated well in the acute stage, and if not, adequate fluid and electrolyte balance is imperative. Polyvitamins, good nursing and proper disposal of excreta are essential.

2. *Specific* — chloramphenicol is the drug of choice. It is given every 6 hours 50 to 100 mg./Kg./day orally, but i.m. or i.v. routes may be needed in severely toxic states or when vomiting is persistent. The course of therapy is 2 weeks or longer. Ampicillin and the tetracyclines come next in importance, and can be given for a similar period of time. In critically ill and toxic patients, steroids for several days, combined with antibiotic therapy may prove valuable.

3. *Treatment of complications :* — Treatment of shock. — Treatment of hemorrhage and perforation is surgical.

MEASLES (RUBEOLA)

Measles is a highly contagious viral disease characterized by acute onset of fever, coryza, conjunctivitis, cough, Koplik's spots and distinctive maculopapular rash.

Etiology : The causative filtrable «Measles virus» is transmitted by droplets and by contact with articles freshly soiled by nose and throat secretions of an infected child during the prodromal period of 3 to 5 days.

Clinical Picture : Incubation period : 7 to 14 days (usually 10 days). Age incidence highest between 2 years and 14 years. The infant is protected for a period of 4 to 6 months of age, if his mother had measles. Active immunity follows infection, and it is rare for an individual to have measles more than once. Those alleged to have had measles 2 or 3 times, have usually had measles, German measles exanthem subitum, or an ECHO viral disease with a rash simulating measles.

Measles characteristically begins with :

1. *The prodromal or catarrhal stage* — fever, general malaise, coryza, conjunctivitis and cough. The fever ranges from 38.5 to 40° C, tending to be highest just before the appearance of the rash. Coryza begins like common cold, and is associated with sneezing, mucopurulent discharge and a sore throat. Conjunctivitis is non-purulent, giving rise to bloodshot, bleary eyes with lacrimation and photophobia. It appears towards the end of the prodrome.

Cough is dry, «barking» and irritating. It becomes more frequent and hoarse as the disease progresses, and lingers more than coryza and conjunctivitis.

Lymphadenopathy of the posterior cervical lymph nodes may be noticed.

2. *The Enanthem and the Koplik's spots* — a day or two before the appearance of the rash, and 3 to 5 days after the onset of the disease, the Enanthem appears as small red spots on the inflamed hard and soft palate. More pathognomonic however, are Koplik's spots, first noted on the buccal mucosa opposite the molar teeth. They are rose-red spots, with a bluish-white speck in the center. After the first ones are seen, many others appear on the buccal and labial mucosa, and even in the caruncle of the eye.

3. *The Exanthem or Rash* — it appears usually on the 5th day of the illness. It begins as a maculopapular erythematous eruption at the hair-line on the forehead, back of the neck and behind the ears. It spreads downwards to cover the face, neck, trunk, arms and legs in about 3 days. The rash is blotchy, irregular and characteristically coalesces into larger red patches of varying size and shape. It may be accompanied by mild itching. It begins to fade in the same sequence as its spread, lasting from 4 to 7 days. It fades on pressure initially, but the subsequent brownish-stained ones do not. Branny desquamation, especially of the face and trunk, may follow lasting 2 or 3 days, and the skin returns to normal or leaving light-brown pigmentations for sometime.

Laboratory Findings : 1. Leukopenia is present during the prodrome and early stage of the rash. There is a sharp rise in the WBC count with the onset of bacterial complication.

2. Demonstration of multinucleate giant cells in the sputum and nasal secretions during the prodrome.

Diagnosis : A typical attack is easily diagnosed. In the pre-eruptive stage, measles can be confused with upper respiratory tract infections. German measles is not a severe disease like measles, and it causes a noticeable enlargement of the occipital lymph nodes with no conjunctivitis, photophobia, and no Koplik's spots. Exanthem subitum (*Roseola infantum*) gives a rash after the subsidence of a very high fever in small children, described as a «rainbow after the storm». Scarlet fever causes sore throat with exudative tonsillitis, cervical adenitis, strawberry tongue, diffuse blanchable rash, with circumoral pallor. Leukocytosis instead of leukopenia occurs. Drug rashes (phenobarbital and sulfonamides) may resemble measles. Serum sickness, presenting with a maculopapular rash, should also be differentiated.

Complications : Measles may produce a variety of complications, of which the most common are those of the respiratory tract. Complications occur more in the young, in the debilitated, and in the lower socio-economic classes.

1. *Respiratory tract* — the intense inflammation favours the development of sinusitis, otitis media, laryngitis, laryngotracheobronchitis and bronchopneumonia, with or without empyema.

2. *Cervical adenitis*, may occur and even mediastinal nodes may become enlarged and inflamed.

3. *Skin* — hemorrhagic rash may occur, bleeding from mucous membranes and purpura are seen. Impetigo, furunculosis and the rare cancrum oris can also occur.

4. *Digestive tract* — ulcerative stomatitis, vomiting, diarrhea with dehydration and acidosis may occur.

5. *Encephalitis* — occurs in 1 : 1,000 to 1 : 10,000. The first sign may be increasing lethargy or convulsions. It may prove fatal (15%) or may leave permanent damage (60%) reflected in personality changes, mental subnormality, epilepsy, neuromotor defects, or deafness. It usually appears within the first 6 days of the rash but may occur before or afterwards. Polyneuropathies are also reported to complicate measles.

6 *Aggravation of active pulmonary tuberculosis, or flare of healed primary lesion.*

Prophylaxis : 1. *Active immunization* — an attenuated live measles vaccine is now available and is used widely. It produces fever and mild rash in some cases, a sort of mild uncommunicable infection with persistence of immunity for a long time. The dose is 0.5 ml. of the reconstituted vaccine injected subcutaneously.

The inactivated measles vaccine should not be used now.

2. *Passive immunization* — with gamma globulin. This may prevent the disease (0.25 ml./Kg.) or result in a mild, modified rubeola syndrome with reduced incidence of complications (0.05 ml./Kg.), if given within 6 days of exposure to a case. The gamma globulin should be injected deep i.m.

Treatment : 1. *General* — isolation for one week from onset of rash, rest until afebrile, aspirin for fever and discomfort, diet as tolerated by the child hygienic care of the eyes and mouth (saline sponges and irrigations), cough depressing drugs at the beginning (codcine) and humid air for soothing. The skin also needs lotions to reduce the itching and discomfort.

2. *Specific* — none.

3. *Treatment of complications* — since bacterial complications are usually due to hemolytic streptococci, penicillin will be useful. Prophylactic antibiotics are only used in debilitated, or other high risk children.

Measles encephalitis is managed symptomatically by analgesics for headache, sedatives for irritability and anticonvulsants. Good nursing care, with proper fluid and electrolyte therapy, and protection from secondary infection is important. Opinion differs as to the value of big doses of gamma globulin and steroid therapy.

GERMAN MEASLES (RUBELLA)

German measles is an acute mild febrile viral infection characterized by minimal constitutional symptoms, swelling of posterior cervical, occipital and retroauricular lymph nodes, and the eruption of a rash.

Etiology : The virus of German measles is not as contagious as that of measles or chicken pox. The infection is by droplet route.

Clinical Picture : Incubation period : 12 to 25 days (usually 16 to 18). Age : any age, infants and young children do not have Rubella as frequently as older children and young adults.

Permanent immunity follows a single attack. Transplacental transmission to the fetus may also occur, producing malformations.

1. *The prodromal stage* — this consists of fever, low grade, general malaise, loss of appetite, headache and tender postero-occipital lymph nodes. In younger children, the prodrome may not be noticeable. The prodrome in any case is very short and may last only few hours.

2. *The Enanthem* — this may develop during the prodrome. It consists of rose red spots, chiefly on the soft palate, varying in size from pin-point to larger and sometimes blotchy.

3. *The Exanthem or Rash* — the rash of rubella lasts about 3 days. It begins on the face and spreads downwards, disappearing later in the same sequence. The lesions are pale rose maculopapules, generally discrete suggesting measles on the first day. On the second day the rash is usually confluent suggesting scarlet fever, and it generally disappears by the 3rd day.

Rubella without rash occurs as a febrile lymphadenopathy which may persist for a week or more (rubella sine eruptione).

4. *Lymph Nodes* — rubella causes generalized lymphadenopathy, but tender swelling of the posterior cervical, occipital and postauricular nodes are characteristic. Tenderness decreases after the appearance of the rash, but the nodes may remain enlarged for several weeks.

Laboratory findings : Transient leukopenia

Diagnosis : Typical cases are easy to diagnose. Measles should be differentiated by the more severe prodrome, and by the presence of Koplik's spots. Modified measles (by gamma globulin) may be very similar to rubella. Exanthem subitum and scarlet fever should be also differentiated. Infections mononucleosis with rash may simulate rubella, but the blood count, blood smear and heterophil antibody test help in differentiation. Drug rashes and rashes associated with ECHO viral infections may be very similar.

Complications : These are uncommon. (1) *Encephalitis* — once every 6,000 cases. Death may occur, but recovery is usual. (2) *Thrombocytopenic purpura* — also is rare. (3) *Polyarthrititis* — sometimes occurs on the 2nd or 3rd day of the rash, involves several joints painfully, and may cause effusion into one or more joints. It occurs more in persons over 16 years of age. (4) *Rubella in pregnancy* — when a pregnant woman contracts rubella during the first trimester, the virus may pass transplacentally to the fetus giving a 17% risk to develop the «rubella syndrome». Constituents of the Syndrome (not all present together in every case) are :

- (i) bilateral congenital cataracts and microphthalmia.
- (ii) deafness which causes mutism.
- (iii) mental deficiency, microcephaly, or hydrocephalus.
- (iv) malformations of the heart, usually PDA or septal defects.

This might be the basis of deliberate exposure of girls to rubella.

Prophylaxis : 1. *Active immunization* — a live vaccine is used now either alone or with Measles & Mumps.

2. *Passive immunization* — gamma globulin in big doses (20 ml. i.m.) has been claimed to prevent the disease.

Treatment : 1. General — isolation and symptomatic measures are rarely necessary. 2. Specific — none. 3. Treatment of complications — encephalitis is treated symptomatically, purpura by transfusion of fresh blood, and polyarthrititis by salicylates.

EXANTHEM SUBITUM (ROSEOLA INFANTUM)

This is a common acute infectious disease of infants and young children, probably caused by a virus, and characterized by a high fever for 3 to 5 days, followed by a precipitous drop to normal temperature and a pale rosy rash.

Etiology : The disease can be transmitted experimentally with bacteria-free serum, and this together with the long incubation period and leukopenia suggest a viral etiology. It is transmitted naturally by droplet or direct contact.

Clinical Picture : Incubation period : 7 to 17 days. Age : mostly in infancy, but can occur at any age. The onset is sudden with high fever, which may be sustained or spiky (41°C). Fever persists for one to five days, and is accompanied by malaise, irritability and even convulsions. In the majority of cases however, the child appears well in spite of the fever. Then the fever drops by crisis, the temperature may remain subnormal for few hours during which the rash appears.

This occurrence of the rash is described as «a rainbow following the storm». It is faintly erythematous, macular, very similar to rubella, favours the trunk and neck, fades on pressure and is very transient.

Laboratory Findings : Leukopenia as low as 3,000 and definite relative lymphocytosis (90%).

Diagnosis : Differentiate from rubella, measles, drug rashes and scarlet fever.

Complications : None. Convulsions may occur at the summit of the fever, and encephalopathy has been reported.

Prophylaxis : Not known.

Treatment : 1. General — rest, aspirin, sponges to control the fever and isolation. 2. Specific — none. 3. Treat convulsions by barbiturates.

ERYTHEMA INFECTIOSUM

This is a mild, afebrile contagious disease, usually occurring in family or institutional epidemics (close contact).

Etiology : Recent evidences indicate a viral etiology.

Clinical Picture : Incubation period : 7 to 14 days There is usually no prodrome and the first symptom is the rash, usually without any fever.

The rash appears first on the cheeks as very red macules which coalesce, are warm, slightly raised, and look as if the child has been wind-blown. There is circumoral pallor. This eruption fades within 4 days, giving a maculopapular erythematous rash on the extensor surfaces of the extremities, which spreads in 2 to 3 days to involve the flexor surfaces and the trunk. It gives a typical lace-like pattern of geographic lines. Palms and soles are rarely involved. This rash lasts 3 to 7 days and has tendency to recur with skin irritation or exposure to sunlight or extremes of heat and cold.

Laboratory Findings: WBC count is normal.

Diagnosis : The rash on the face must be differentiated from erysipelas, lupus erythematosus, drug eruptions and scarlet fever.

Complications : None reported.

Treatment : No treatment is indicated.

MUMPS (EPIDEMIC PAROTITIS)

Mumps is an acute viral disease which may involve many organs but commonly affects the salivary glands, and chiefly the parotids (60%). The virus has a certain affinity also to the nervous system.

Etiology : The virus is one of the myxoviruses (Influenza A,B,C, and Mumps are the most important myxoviruses), and is quite contagious, but not as much as measles and chicken pox. It spreads directly from person to person and by direct contact with contaminated articles.

Clinical Picture : Incubation period : 12 to 28 days (usually 16 to 18). Age : commonly between 5 and 10 years. Infants are protected up to 6 months if their mothers had had the disease. A single attack confers immunity, but the disease can occur without salivary gland involvement, in subclinical forms

and give also lasting immunity, explaining why many persons not known to have had mumps, do not contract the disease with close exposure.

A prodrome of one to two days may be present, and is characterized by fever, headache, malaise, vomiting and pain in or behind the ears on chewing or swallowing.

Involvement of the salivary glands follows in most cases, chiefly the parotid (unilaterally or bilaterally), but the submaxillary and sublingual glands may also be involved, or they may enlarge in absence of parotid involvement. In parotid swelling, the appearance of the child greatly changes. The ear is pushed upward and forward, there is brawny edema and tenderness. Pain is aggravated by opening the mouth, chewing, swallowing, or tasting sour substances. The skin over the gland is normal. The opening of the duct of the involved gland in the mouth may be edematous and red.

Orchitis rarely occurs before puberty, is accompanied by epididymitis, fortunately unilateral, and therefore sterility is not common. The testicle is swollen, very tender and the general symptoms are aggravated at this time. Oophoritis also is very rare before puberty, and gives symptoms of fever, abdominal pain, nausea and vomiting. Pancreatitis may occur producing severe abdominal pain (upper or mid-abdominal), vomiting, prostration, fever and chills. Full recovery is the rule. Nephritis may occur, but is rare and mild. Nervous system affection includes meningo-encephalitis, aseptic meningitis, or encephalitis, together with other rare affections like myelitis, neuritis and deafness. Meningo-encephalitis may occur as an isolated manifestation, but more commonly within a week or so following the onset of mumps.

Laboratory Findings : 1. Leukopenia with relative lymphocytosis is usual.

2. Complement fixation test, is the most useful in cases without gland enlargements. Antibodies against the S or soluble antigen rise rapidly during the first week and then fall rapidly. Antibodies against the V or virus antigen appear towards the end of the first week, rise higher later, then fall off, but persist for years.

3. Skin testing is of value in retrospect to demonstrate immunity in exposed persons, 0.1 ml. intradermally, read after 24 to 36 hours. Immunity is indicated by induration and erythema 1.5 cm. or more in diameter.

4. CSF findings : increased pressure, clear to turbid, 150 to 2000 cells per cmm. mostly monocytes, proteins 60 to 150 mg% and normal sugar.

Diagnosis : The glandular swelling should be differentiated from cervical lymphadenitis, and this is not difficult. Suppurative parotitis produces swollen, tender parotid, but the skin is usually red and hot, and pressure on the

gland forces pus from the Stensen's duct. Here, there are other signs of septic inflammation and polymorphonuclear leukocytosis.

Recurrent parotitis is a confusing condition, but the history of previous attacks helps to differentiate it. Calculus in Stensen's duct is a rarity in childhood, but must be thought of. Tumours of the parotid usually offer little difficulty in the differential diagnosis.

Prophylaxis : 1. *Active immunity* — there is a live vaccine which is used alone or with Measles & Rubella (MMR). 2. *Passive immunity* — mumps hyperimmune gamma globulin 2.5 to 5 ml. i.m. confers temporary protection to susceptibles. Its use is limited to adults to prevent orchitis and oophoritis.

Treatment : 1. General — isolation until salivary swelling is gone. Bed rest is advisable during the febrile period, aspirin or codeine for pain, local hot applications for discomfort, and hygiene for the oral cavity. 2. Specific — none. (3). Treatment of involvements other than salivary glands — Orchitis — suspension of the scrotum, analgesics for the severe pain and sometimes steroids are dramatic. — Oophoritis and Pancreatitis — symptomatic only. — C.N.S. involvement — symptomatic for mild encephalitis, lumbar puncture may be useful in reducing headache, prognosis is usually excellent.

HERPES SIMPLEX INFECTION

This is an acute and sometimes chronic disease caused by a dermatropic and neurotropic virus.

Etiology : It is caused by Herpes hominis virus, a common parasite of man, that can give rise to a variety of clinical pictures. Transmission is probably by direct contact with skin or mucous membrane lesions. Type 1 virus is responsible for most lesions of mouth and skin, while type 2 virus causes genital lesions and 95% of neonatal infections.

Clinical Picture : There is usually a history of exposure to a young child with stomatitis, or an adult with «fever or cold sores».

1 *Primary Herpes* : This may manifest itself as gingivostomatitis (most common form), vulvovaginitis, keratoconjunctivitis, meningoencephalitis, rhinitis, eczema herpeticum, or severe generalized disease of the newborn.

Herpetic stomatitis — commonest form of stomatitis under 5 years of age, onset insidious, with fever of 38 to 40°C, malaise and sore throat. The gums are

inflamed, red and swollen and bleed easily. The breath is very fetid, with evident drooling of saliva. Multiple small ulcers (ruptured vesicles of herpetic eruption) are present on the tongue, gums and palate. Feeding may be very painful and problematic.

2. Recurrent Herpes : This is the herpes febrilis « cold or fever sores ». The local lesions are mild, and there are no constitutional manifestations. Herpes may manifest as recurrent papulovesicular mucocutaneous eruption, recurrent ulcers on the mucous membrane of the mouth « canker sores », and recurrent eruption on almost any area of the body.

Laboratory Findings : There may be occasional leukopenia at the onset.

Diagnosis : The gingivostomatitis should be differentiated from other causes of mouth and throat affections, especially Herpangina (Coxsackie A virus), and in the very young and debilitated, from Thrush stomatitis (*Monilia fungus*).

Complications : Infection with Herpes is usually a self-limited disease, but fatalities may occur in the newborn, in eczema herpeticum and in meningoencephalitis. Herpes of the eye may proceed to dendritic ulcers or actual keratitis. Secondary bacterial infection may complicate skin or mucous membrane lesions.

Treatment : 1. *General* — for primary stomatitis, mouth hygiene is very important; mild antiseptics together with local analgesics (Benzocaine), and general sedation and aspirin, help the diseased child. Fluid and electrolyte balance is essential in severe cases and in eczema herpeticum. Lesions of the eye need a specialist, and recently thymidine analogues have been used locally in the eye. Steroids are contraindicated in the acute stage, otherwise corneal perforation may occur.

2. *Specific* — available as idoxuridine (IDU) systemically or locally.

3. *Treatment of complications* — secondary bacterial infection should be treated with an appropriate antibiotic.

VARICELLA (CHICKEN POX)

An acute, highly contagious and extremely common viral disease, characterized by constitutional symptoms and a specific rash. The immunity after the attack is life long except in rare exceptions.

Etiology : The causative virus is the Herpesvirus varicellae, responsible for chicken pox probably as a primary disease in the susceptible, and herpes zoster in the partially immune individual. It spreads from person to person by droplets from the respiratory tract or direct contact with freshly contaminated articles.

Clinical Picture : Incubation period : 14 to 21 days (usually 15 days). Age : most commonly 2 to 8 years of age, but newborns are infected occasionally, and even elderly individuals may contract it.

The Prodrome - is usually mild or inapparent, and is characterized by general malaise, fever, headache and anorexia for about 24 hours.

The Rash - is usually the first sign of illness. Lesions tend to occur in crops, 2 to 4 within 2 to 6 days (explanation of the pleomorphism of the rash). They occur first on the scalp, face, or trunk as small red macules and papules that quickly change into vesicles. The rash is heaviest on the chest, back and shoulders, and scarce on the extremities. It is seldom seen on the palms and soles. Successive stages of the rash are : (a) macular - small red blotches, (b) papular - raised skin eruption, and (c) vesicular - lesions are very

Table 13 : Differential diagnosis of Chicken pox from Small pox.

	Chicken pox	Small pox
History	— contact with case.	recent successful vaccination is against contact with case or fomites.
Prodrome	very mild and short.	long with severe constitutional manifestations.
Rash	in crops & hence pleo- morphic. centripetal. papules superficial. vesicles unilocular and superficial «tear drop» no scar tissue in healing except with secondary infection. no conspicuous «pustu- lar stage».	a single monomorphic crop. centrifugal. papules deep and firm. vesicles multilocular, deep and umbilicated. healing by scar tissue leaving disfiguring «pits». evident pustular stage.

fragile «tear drops», not umbilicated, excoriate very easily leaving scabs.

Crust formation follows. All scabs fall off by the 9th to 14th day. The rash occurs also on mucous membranes, with ulcerations in the mouth, vagina and conjunctivae. These lesions are painful and cause local irritation. Pruritis is minimal at the beginning, but may become severe in the late stage. In rare instances, hemorrhages may occur into the vesicles (hemorrhagic varicella). Congenital varicella may be manifest at birth, or appear within few days, if the mother has an active infection. Such infections are usually fatal. On the other hand, when a newborn infant contracts the disease postnatally from his mother, it is usually very mild.

Laboratory Findings : 1. Leukopenia early, but the count usually rises later.
2. Scraping of the floor of fresh vesicles reveals virus giant cells.

Diagnosis : Chicken pox must be differentiated from : 1. *Small pox* (see table 11)

2. *Herpes zoster*— This disease is produced by the same virus and is uncommon under 10 years of age. The individual lesions are very similar, but in distribution, they occur along the dermatome of peripheral nerves and the lesion is unilateral.

3. *Impetigo* — The lesions may look like those of chicken pox, however, they do not appear in crops. Mucous membranes are not involved, and there are no constitutional symptoms. The areas affected are chiefly skin areas accessible to scratching.

4. *Papular Urticaria* — The lesions here are mainly distributed over the extensor surfaces of the extremities, face and neck. They are formed of small papules which itch markedly, and may develop a vesicular component. They soon get excoriated and secondarily infected. They occur on the palms and soles.

Prophylaxis : 1. *Active immunity* — by contracting the illness, there is no available vaccine.

2. *Passive immunity* — gamma globulin has been reported to modify or prevent the disease. The dose is 1.0 ml./Kg. given once i.m. within 6 days of exposure. Zoster immune globulin is better if available.

Treatment : *Specific* : none. *General* : relieve itching by local application of calamine lotion, and general administration of an antihistamine. Cut nail short, restrict scratching and pay attention to mouth hygiene (especially if there are lesions in the mouth).

Treatment of complications — treat secondary infection by local, and if necessary, systemic antibiotic therapy. If encephalitis develops, supportive treatment is instituted.

ENTEROVIRAL INFECTIONS

Enteroviruses are a group of organisms having in common the following characteristics : All are very small viruses, they are resistant to adverse effects, they inhabit transiently the intestinal tract of man, they cause similar changes in tissue culture and they are world-wide in distribution and cause epidemics especially in warm months with a special predilection to the nervous system (table 12)

Table 14 : Enteroviruses and Associated Diseases.

Enteroviruses	Types	Associated Diseases
Poliomyelitis	1,2 and 3	Undifferentiated febrile illness Aseptic Meningitis Paralysis Encephalitis
Coxsackie Group A	1 to 24	Undifferentiated febrile illness Aseptic Meningitis Paralysis Herpangina Exanthem
Coxsackie Group B	1 to 6	Undifferentiated febrile illness Aseptic Meningitis Paralysis Encephalo-myocarditis of infants Pleurodynia
ECHO	1 to 28	Undifferentiated febrile illness Aseptic Meningitis Paralysis Diarrhea of infants and children Exanthem

POLIOMYELITIS

Poliomyelitis is an acute viral disease occurring both epidemically and endemically throughout the world, and characterized by different grades of neuronal injury, with special localization in the anterior horn cells and motor nuclei of the brain stem.

Etiology : The disease is caused by any one of 3 polioviruses; Type 1, Type 2 and Type 3 (Brunhilde, Lansing and Leon respectively). Each type is immunologically distinct, and infection with one type results in immunity only to that specific type.

Although the virus is present in the oro-pharyngeal secretions during the first days of the disease, and transmission by droplet infection may occur, the principal infecting route is the fecal-oral one due to massive multiplications of the virus in the intestinal tract and the large quantities passed in the stools.

Clinical Picture : Incubation period : is about 7 to 12 days. Age : may affect adults, but it is predominantly a disease of the young. The term « Infantile Paralysis » may imply this meaning. The age incidence has changed to young adults due to immunization of large segments of populations in many European countries. In Egypt, it is still a disease of infancy and childhood. This is also due to the lower level of sanitation, and the more intimate contact in crowded living premises.

There are different possible consequences of infection (Fig. 23) :

1. Clinically inapparent asymptomatic infection (silent).
2. Abortive poliomyelitis, an undifferentiated febrile illness.
3. Non-paralytic poliomyelitis, with the Aseptic Meningitis Syndrome.
4. Paralytic Poliomyelitis : (a) Spinal type, (b) Bulbar type, (c) Encephalitic type and combinations may occur.

Inapparent Infection — the most common. For every paralytic case, there are hundreds of individuals who have this inapparent infection.

Abortive poliomyelitis — the next most common. Here there is fever, headache, sore throat, nausea, vomiting, anorexia, malaise and vaguely localized abdominal pains.

The only physical sign may be mild injection of the throat.

Non-paralytic Poliomyelitis — next in frequency, and presents as Aseptic Meningitis Syndrome. In addition to the previous symptoms, there are signs of nervous system involvement. The clinical picture and the CSF findings here are similar to aseptic meningitis produced by many other diseases.

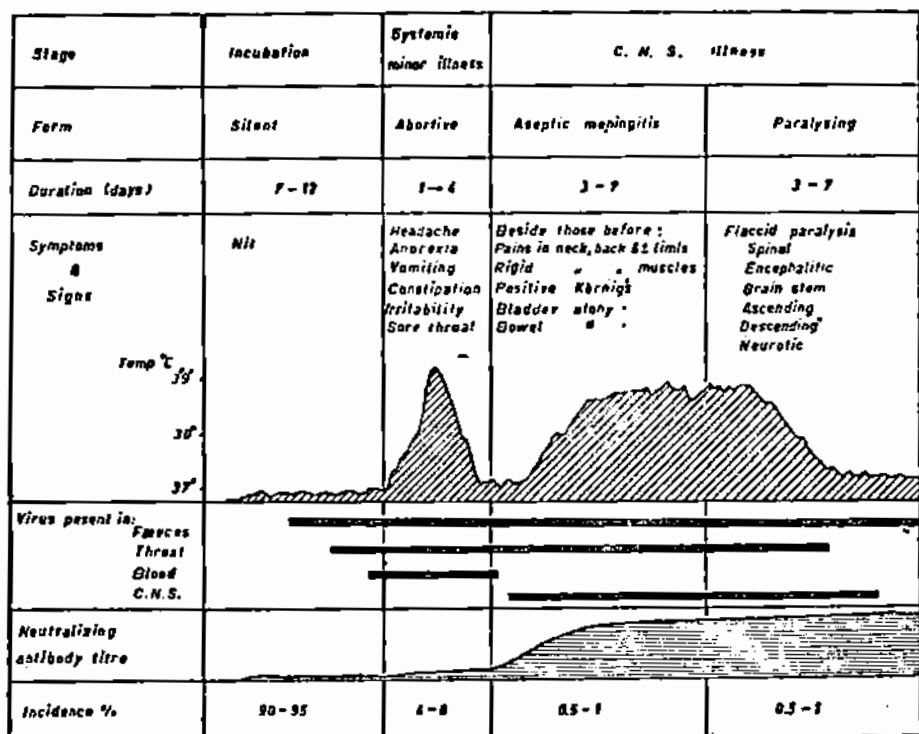


Fig. 23 : Possible consequences of Polio - infection.

Paralytic Poliomyelitis — this may begin with manifestations of the abortive type or the non-paralytic type.

Spinal — paralysis appears within a day or two after the above manifestations and 2 to 5 days from the onset. Muscle pain and spasm are present in the early stage, followed by lower motor neurone paralysis. Muscles of the limbs are the most commonly affected, but muscles of the chest wall (including intercostals), abdominal wall, diaphragm (phrenic nerve in cervical affection) and urinary bladder and bowel can be involved.

The distribution of paralysis is usually asymmetrical, and the legs are more commonly affected than the arms. The large muscles are more prone to paralysis and therefore the muscles mostly affected are :

— In legs, the anterior tibial group, the peroneal group, the quadriceps femoris and the hamstrings.

— In arms, the shoulder girdle especially the deltoid. The paralysis, being

lower motor, should be differentiated from upper motor types by being flaccid, by absent deep tendon jerks, together with early muscle atrophy and R.D.

Bulbar — more life threatening, and manifests itself as neuronal damage of cranial nerve nuclei, vital centers of respiration, circulation and temperature control. The involvement of the 10th cranial nerve leads to interference in swallowing, regurge of fluids through the nose and inability to swallow saliva which puddles in the pharynx. If not continuously aspirated, it may interfere with respiration through frequent choking and aspiration.

Encephalitic — manifesting as encephalitis, and is only diagnosed as poliomyelitis if bulbar and spinal affections, one or both are present. Disturbances of personality occur, sensorium is interfered with and gross tremors or convulsions may be added to the picture.

Laboratory Findings : 1. - Rise in antibodies in paired serum samples, one in the acute and one 2 to 3 weeks later. 2. Isolation of the virus. 3. Blood count not distinctive. 4. CSF shows normal or increased pressure, clear or opalescent, with 15 to 400 cells (early polymorphs and later mononuclear cells), 30 to 60 mg % protein (later may rise to 100 — 600) and normal sugar.

Diagnosis : The disease should be differentiated from :

1. Other causes of «flu» syndrome. 2. Other causes of «Aseptic Meningitis Syndrome». 3. Pseudo-paralysis — which occurs in scurvy, congenital syphilis, unrecognized trauma, toxic synovitis, arthritis, osteomyelitis and other conditions characterized by pain interfering with movements of a part. 4. True paralysis — may occur in rare instances of other Enteroviral infections, though usually very mild. The Guillain-Barré Syndrome may present a diagnostic difficulty. 5. Other causes of Encephalitis.

Respiratory Difficulty in Poliomyelitis.

It may occur in : 1. Intercostal muscle paralysis. 2. Diaphragmatic paralysis. 3. Obstruction of the pharynx and trachea in pharyngeal and or palatal paralysis. 4. Respiratory center damage. 5. Change in the sensorium.

Contributing factors are : Pulmonary complications (pneumonia, atelectasis, etc), Panic, Gastric dilatation, Oversedation and inadequate management.

Complications . *Gastrointestinal* — acute gastric dilatation, perforations and melena.

2. *Cardiovascular* hypertension, hypotension, arrhythmias, myocarditis and acute cardiac failure

3 *Urinary* transitory paralysis of the bladder nephrocalcinosis (immobilization and hypercalcemia) and calculi (hypercalcuria).

Prophylaxis : 1. Active immunization (Salk and Sabin vaccines).

2. Passive immunity (0.25 ml. of Poliomyelitis immune globulin/Kg. body weight i.m.)

3. During «Polio» season, or in epidemics, avoid overexertion, fatigue, injections and keep patients in bed during any febrile episode

Salk Vaccine (formaldehyde-inactivated vaccine to be given by i.m. injection).

Advantages : (a) effective in preventing poliomyelitis. (b) has a reasonable long life when kept refrigerated.

Disadvantages : (a) has to be injected. (b) difficult in mass campaigns. (c) person immunized may still harbour the poliovirus in the alimentary tract and transmit the disease.

Sabin Vaccine (living attenuated vaccine to be given orally).

Advantages : (a) ease of administration, especially in mass campaigns. (b) confers a substantial degree of resistance to the alimentary tract towards reinfection with wild polioviruses.

Disadvantages : (a) short life of the vaccine. (b) other enteric viruses, more prevalent in summer months, may interfere with the effectiveness of the vaccine.

Treatment : 1. *General* : — bed rest, may limit paralytic involvement.

— heat, may relax tender and tight muscles, ligaments and fasciae and can be applied by hot packs or hot tub in mild ambulatory cases. Dry heat may be used in mild affections.

— diet, simple, nutritious and attractive.

— aspirin, to control the fever, headache and pains.

— physiotherapy, most important single factor in treatment. Passive movements at first, then active exercises when pain subsides.

— orthopedic measures, special boards, splints, braces, or surgery.

2. *Specific* : none. 3. Treatment of special problems and complications :

— Respiratory difficulty, may need respirator, and or eletrophrenic stimulation.

— Tracheostomy, is done in paralysis of muscles of swallowing, and is needed to use tank respirator — Irritability and apprehension, need tranquilizers.—

Enemas and laxatives, for constipation. — Urecholine, and or intermittent catheterization, with prophylactic use of sulfonamides, in bladder paralysis.—

Gastric aspiration, and ice bags, in gastric dilatation. — Anticonvulsant therapy may be needed. — Digitalization may be resorted to. — Psychologic guidance.

Galal H. Aref

Chapter X

TUBERCULOSIS

It was previously understood that Egyptian infants and children as well as those of developing countries are usually infected with tuberculosis in their early months of life. Campaigns against tuberculosis in adults, who were the main source of infection to children, have been in the last few years successful and at present many children could in this way escape infection especially during the preschool age. Adequate preventive measures by B.C.G. vaccination are also being carried out by public health authorities, and would be of the greatest help in the battle against the disease.

Etiology : The disease is caused by the acid fast bacillus *Mycobacterium tuberculosis*. In man it can be produced by the human or the bovine type.

All pathological forms of tuberculosis can be produced by the bovine type of bacillus, but it usually causes primary abdominal or primary pharyngeal tuberculosis, with involvement of the mesenteric and cervical lymph nodes respectively. It may also be transmitted aerogenously as a pulmonary infection. The differentiation of human type and bovine type of infections can be only made by cultural methods after isolation of the bacilli.

Mode of infection : There are two main types of primary tuberculous infection, the air borne and the alimentary. The former is the more frequent. Air borne infection may be by droplets or by dust.

Droplet infection : This depends on the expectoration of minute droplets containing tubercle bacilli by coughing of patients with open pulmonary tuberculosis.

Dust infection : The larger droplets contribute chiefly to the contamination of dust. When it is agitated, a dust cloud reforms in the air. Desiccation, however, decreases the virulence of the bacilli.

Alimentary infection : This occurs by ingestion of infected milk or by swallowing other contaminated matter. The common sites of entry are the small intestine and the tonsil. Although the mucosa of the intestine has a greater local resistance against tuberculosis than that of the small bronchi or the cell layer of the alveoli, contaminated food or milk may contain abundant tubercle bacilli and thus often cause infection.

Allergy to tuberculosis: This reveals itself by sensitivity to tuberculin. Before infection and during the incubation period (4-6 weeks) there is complete tolerance to tuberculin. At the end of the incubation period this suddenly changes into a high degree of sensitiveness demonstrated by local inflammatory reactions. The same type of reaction occurs spontaneously near the foci of the primary complex, and the degree of specific sensitiveness is responsible for the extent of the primary tuberculous lesion.

Immunity to tuberculosis : A certain degree of specific resistance to tuberculosis is known to develop after the first infection. This specific resistance so far as is known at present, consists in the power to arrest the multiplication of the tubercle bacilli, to prevent their penetration into the body, and to check their activity by proliferative reactions. Specific acquired resistance seems to be set up about the end of the incubation period, that is almost simultaneously with the development of tuberculin sensitivity. There is, however, no parallelism between the degree of immunity and that of hypersensitivity. Experimental work has shown that the specific acquired resistance is not always great enough to resist strong new infections.

INTRATHORACIC TUBERCULOSIS

Sources of Infection : By far the most usual source of infection in infancy and childhood, is adult contact who is suffering from open pulmonary T.B.

Pathology of Primary Complex : When a person of any age inhales tubercle bacilli for the first time, the TB bacilli reach down to the alveoli and pass to the interstitial tissue where they will set a reaction. At first there is an accumulation of polymorphonuclear leukocytes, which is followed by proliferation of epithelioid cells (RES). These surround the TB bacilli forming the typical tubercle. Tubercles are usually surrounded by lymphocytes. Some of the epithelioid cells conglomerate together forming giant cells. Central caseous necrosis is commonly present. This is due to avascularity of the centre, and the tissue necrotizing capacity of the protein fraction of the TB bacilli. This primary focus in the lung is called "Ghon's lesion." Ghon's lesion is usually single, occasionally multiple, and most often situated subpleurally. The site is more likely to be in the lower lobe, the size is usually small, (1 cm in diameter in the majority of cases). The bacilli travel via the peribronchial lymphatics towards the bronchopulmonary and tracheobronchial glands on the same side, which become enlarged. The Ghon's focus, lymphangitis and hilar adenitis, constitute the "primary complex".

Clinical picture of the primary complex : In the majority of patients this will pass unnoticed. When symptoms do appear they coincide with the development by the tissues of an allergic sensitivity towards tuberculo-proteins. This takes about 4-6 weeks to develop and may be demonstrated by means of a positive tuberculin skin test which is the first sign of TB infection. In some patients spontaneous manifestations of this allergic state appear in the form of : —

- a) *Fever* : It is usually low grade and commonly attributed to teething in infancy and may last for 3-4 weeks.
- b) *Phlyctenular conjunctivitis* A tuberculin positive phlycten is usually a sign of primary tuberculosis.
- c) *Erythema nodosum* : This condition should always be presumed to indicate tuberculous infection in children until they are proved to be otherwise caused.

Fate of the primary complex : —

A) Healing : Will take place if (i) virulence of the organism is low. (ii) Resistance of the host is high. This depends on : —

- a) Genetic inheritance.
- b) Age; infants are less resistant.
- c) Nutritional status.

Healing will take place by proliferation of fibroblasts forming fibrous tissue surrounding the tubercle, and by deposition of calcium salts in the caseous material in the primary focus as well as in the regional lymph nodes and this is the happy end.

However, if the resistance of the host is diminished by, undernutrition, measles, whooping cough and recurrent streptococcal infection the dormant TB bacilli which may be present then flourish and lead to various complications.

B) Complications :—

1. *Locally extending Ghon's lesion* (progressive primary TB) : In this condition, the TB bacilli proliferate and the initial lesion in the lung is not confined to a small focal area but extends into the surrounding lung tissue, involving part of a lobe or even a whole lobe. Manifestations are :—

- Toxic symptoms such as fever, loss of weight, night sweat, fatigability, irritability are the usual presenting symptoms.
- Physical signs vary considerably; they include, impaired note, diminished air entry and fine crepitations. Signs may not be detected clinically.
- X-ray shows irregularly demarcated area of infiltration. If the lesion becomes liquified it may evacuate its content in a bronchus leaving irregular cavity with ill defined wall (acute cavity).

2. *Enlarged Mediastinal glands* : The mediastinal glands first to be affected are those which lie along the main bronchus of the lobe containing the primary focus. The infection may spread to infect the big glands at the bifurcation of the trachea and so crosses to those on the opposite side or spreads upward to involve the glands alongside the trachea (para-tracheal) until eventually a large conglomerate mass of caseous glands surround the trachea and main bronchi. Manifestations are :-

- General symptoms of tuberculosis are minimal, as the pulmonary focus is usually minimal and the glands are relatively avascular.
- Respiratory manifestations : paroxysmal cough which may simulate whooping cough, D'espine sign is positive.
- Rarely cyanosis of the face, engorged neck veins owing to compression of the large blood vessels are seen.
- X-ray : enlarged mediastinal glands.

3. *Segmental lesions* : Segmental lesions may result from partial or complete obstruction by an adherent enlarged TB gland with or without erosion of the bronchial wall. When the TB gland extend through the bronchial wall it forms an endobronchial granulomatous lesion. The granuloma may pour a liquified caseous material containing living and/or dead bacilli into the lobe drained by the eroded bronchus. Thus the manifestations would be :

- a) *Obstructive emphysema* : due to partial bronchial obstruction (chapter XII). On clinical examination there are, diminished breath sounds, localized wheeze and a resonant note over the affected lobe. X-ray shows hypertranslucency of the affected area. Fluoroscopically shows shift of the heart and mediastinum towards the opposite side during expiration.
- b) *Atelectasis* : Due to complete bronchial obstruction (chapter XII). Manifestations, vary with the extent of atelectasis; it may be asymptomatic if the atelectatic area is small or there may be cough, dyspnea and shallow rapid respiration. Breath sounds may be absent or decreased over the atelectatic areas. The trachea and or heart may be shifted to the side of the lesion
- c) *Atelectasis + allergic consolidation* :- due to pouring of the liquified caseous material which does not contain living T.B. bacilli into a previously sensitized lung.
- d) *Atelectasis + T.B. Pneumonic consolidation* :- due to pouring of liquified caseous material containing viable TB bacilli This type is distinguished from the previous allergic variety by the severity of toxemic manifestations although they are similar in the X-ray picture

4. *Spread via Bronchial tree* : (TB Pneumonia and/or Broncho-pneumonia) :-

When a caseous mediastinal gland or pulmon-overary lesion discharges its content over the neighbouring area of the lung or even both lungs, it gives rise to tuberculous pneumonia or broncho-pneumonia. The manifestations are :-

- Cough, listlessness, flushing of the cheeks, sweating, rapid loss of weight and hectic temperature are generally very evident.
- The signs are those of an ordinary bronchopneumonia and may consist of an impaired percussion note, fine metallic crepitations and sometimes patches of tubular breathing (chapter XII).
- X-ray shows fluffy opacity in the lungs.

5 *Spread via the Blood stream* : Hematogenous dissemination due to erosion of blood vessel (vein) in the vicinity of a caseous lesion is much more frequent in the first few years of life and is most likely to occur during the early stages of tuberculous infection. The fate may be :-

- If the resultant TB bacillema is mild it can be dealt with by the R.E.S.
- If the bacillema is moderate, It usually results in focal tuberculomata.
- If the bacillema is severe, it results in miliary tuberculosis in which multiple tubercles are practically found in all organs of the body. Rarely tubercles are confined to the lungs and this could be the result of invasion of a pulmonary artery.

a) *Acute miliary tuberculosis of the lungs* :-

- General symptoms are very severe and consist of wasting, anorexia, tachycardia and high swinging temperature.
- Symptoms of lung involvement are sometimes remarkably few while in other cases there may be frequent short cough and rapid respiration rate out of proportion to the signs obtained over the lungs.
- Examination of the chest may show only a few fine crepitations and at times wheezes. There is as a rule no impairment of percussion note nor alteration of the breath sounds.
- Spleen and the liver are usually enlarged.
- Choroidal tubercles may be detected on fundus examination.
- X-ray shows a fine mottling over both lungs described as a snowstorm appearance.

b) *Tuberculous Meningitis* : This is the principal cause of death from tuberculosis in the first years of life. Generalized miliary tuberculosis is associated with it in about 25 per cent of cases.

Pathology : The meninges are rarely directly infected by the hematogenous route, but are commonly secondarily involved by the discharge of tubercle bacilli

into the cerebrospinal fluid from older caseous foci such as a tuberculoma in the brain or spinal cord or osseous lesions of the vertebrae or calvarium.

Tubercles are scattered over the pia and the surface of the brain. The dura is tense, the convolutions are flattened and the arachnoid space and ventricles contain serofibrinous exudate.

Clinical Manifestations : This may be divided into 3 stages : 1. a prodromal stage of irritation, 2. a transitional stage of increased intracranial pressure and meningeal symptoms, and 3. a terminal stage of paralysis and coma. These stages may not be sharply demarcated and not all may be present in every case.

Prodromal Stage : The onset is usually slow with little or no fever. The initial manifestations are indefinite and often vague. Changes in the personality of the child are frequent. Periods of drowsiness are common, but sleep is restless. Older children complain of headache. Anorexia, vomiting and constipation are common.

Transitional Stage : Convulsions may occur during this stage, and drowsiness becomes much deeper. Evidences of meningeal irritation are present. There is neck rigidity with stiffness of the back and extremities. When this is severe opisthotonus is produced. Kernig's and Brudzinski's signs are positive. The deep reflexes are exaggerated. There is bulging of the fontanel. Ocular paralyses are common and there may be nystagmus or strabismus. The pupils are normal or contracted. Occasionally the discs may show choking and tubercles may be seen along the choroid vessels. There is usually a well marked *tache cerebrale* and because of vasomotor disturbances irregular flushing of the trunk and face may be present. The temperature is usually elevated, the course is progressive and drowsiness is gradually replaced by stupor.

Terminal Stage : The evidences of meningeal irritation are replaced by those of paralysis. There is coma with dilated and unresponsive pupils and insensitivity of the cornea. Paralyses become widespread, the pulse becomes irregular and either slow or rapid and the respirations irregular and at times Chyne Stokes in type. The temperature rises and there may be hyperglycemia and glucosuria. Death may occur without recovery of consciousness.

Diagnosis : A positive tuberculin reaction is suggestive. In the terminal stages it may turn negative. The cerebrospinal fluid provides the most important data. The fluid is turbid with the so called ground glass appearance. The pressure and amount are increased. The cell count ranges from about 20 to 500 per cubic millimeter and cells are principally lymphocytes. A predominance of polymorphs may be occasionally met with at the onset of the disease. The protein content of the fluid is increased and is often more than 100 mg. per 100 ml., the glucose

content is usually decreased, and the total chlorides are usually markedly reduced. On standing the C.S.F. forms a fibrinous web in which tubercle bacilli can be demonstrated by direct examination or by culture or guineapig inoculation.

The differential diagnosis is chiefly from other conditions responsible for an increase in lymphocytes in the C.S.F. It has also to be differentiated from the various types of purulent meningitis.

c) Tuberculous Pleurisy : Is rare in infancy and uncommon in young children.

Infection reaches the pleura either by direct extension from a contiguous caseous focus in the lung or via blood stream. Serous effusion is the common reaction to this infection and is usually unilateral. Depending upon the amount of fibrin and leukocytes, the fluid is clear to slightly turbid.

The physical signs are the same as any pleural effusion (chapter XII). The fluid is absorbed gradually, but pleural thickening and adhesions usually follow.

The prognosis is generally governed by the pulmonary lesion, but is generally good.

Treatment is that of the underlying tuberculous disease. Rarely an effusion may become so extensive that aspiration, other than for diagnostic purposes, is indicated.

Diagnosis of Intrathoracic TB : The diagnosis is established with certainty by demonstration of tubercle bacilli in the sputum, aspirated bronchial or pleural secretions, gastric contents or fecal matter. In the absence of such information, the diagnosis is based on the history, the physical examination, the reaction to tuberculin and on X-ray examination.

1. *History :* History of contact with an adult known to be suffering from open tuberculosis.
— History of previous negative tuberculin test makes a recent positive one more significant i.e. recent conversion of the reaction to tuberculin.
2. *Physical examination :* — The various signs that arise in each variety of tuberculous infection of the chest have already been detailed.
3. *Tuberculin test :* — Tuberculin test is an allergy skin test, to detect the state of hypersensitivity to tubercle bacilli, (its protein).
— At present two tuberculins of the human TB bacillus are available; old tuberculin (OT) and purified protein derivative (PPD).
OT is now not recommended because of the variation in potency of different batches.

- *Technique* : — There are various methods for performing tuberculin testing. These are scarification test, Vollmer's patch test, multiple puncture method, intracutaneous test of Mantoux, and the jet test.

Intradermal (Mantoux) test is the most widely used test. It is performed by intradermal injection of 0.1 ml. of the desired concentration of PPD or O.T. into the cleansed skin of either the flexor or extensor surface of the forearm. The injection is made with a short sharply beveled needle with special tuberculin syringe. A pale elevation of the skin, 6-10 mm. in diameter should be produced, or the injection should be repeated at another site.

The standard dose of tuberculin is 5 TU (5 tuberculin unit).

- *Interpretation* : — The reading is made 48-72 hours after the test : -
- A 10 mm. or more of induration = positive reaction.
- 5-9 mm. of induration = doubtful reaction, and is indication for repetition of the test preferably together with skin test for atypical mycobacteria. If the person with doubtful reaction has history of contact with open TB or has clinical evidence or X-ray compatible with TB, he should be managed in the same manner as with positive reaction.
- 0-4 mm. of induration = negative reaction.

Significance of positive tuberculin reaction : -

A positive tuberculin reaction indicates that the person has been infected with the tubercle bacillus and is hypersensitive to its protein. However, it does not mean an active lesion unless the child is under 5 years of age or had a recent conversion.

Causes of false negative tuberculin test : -

- Pre-allergic stage «early weeks after the infection» i.e. incubation period.
- Advanced tuberculous disease e.g. miliary TB & or TB meningitis.
- Severe wasting and dehydration.
- Acute infectious diseases especially measles, rubella and mumps.
- Corticosteroid administration.
- Vaccination with live attenuated virus vaccines e.g. measles, vaccinia or small pox.
- Malignancy and lymphomas particularly Hodgkin's disease.

Causes of false positive tuberculin test : -

- Infection with unclassified mycobacteria may give positive tuberculin test. However, it is usually a doubtful reaction and a simultaneously done specific test will rule out this possibility.

4. *X-ray examination*: The findings according to the nature and extent of the lesion (as mentioned before).
5. *Isolation of TB bacilli*: either from gastric lavage, sputum, pleural effusion, or aspirated bronchial secretion. This is done by direct smear stained with Zeil-Nelson stain, culture, or guinea pig inoculation.

EXTRATHORACIC TUBERCULOSIS

Tuberculous infection of Tonsils and cervical lymph nodes :

Tuberculous glands in the neck are usually the result of tuberculous infection of the tonsil. The tonsillar gland at the angle of the jaw is the first to be affected, followed by enlargement of glands lower in the neck. At first the glands are discrete, firm and usually freely movable; later they tend to become matted together and eventually they may liquefy, and may rupture into the overlying skin forming chronic sinuses. Not all tuberculous lymph nodes undergo such a course; resolution may take place before extensive caseation occurs, or the caseous mass may become calcified. There may be low grade fever and other evidences of chronic infection.

Treatment : If the glands are discrete, surgical excision of the glands under cover of high doses of antituberculous drugs followed by I.N.H. for 12 months in doses of 10-20 mg./Kg/day is advisable.

Abdominal Tuberculosis :

This term includes *tabes mesenterica*, tuberculous enteritis and tuberculous peritonitis. They are considered as stages of a continuous process, and indeed all three stages may co-exist in the same patient. The mode of infection is chiefly by the ingestion of TB bacilli which may be of either bovine or human strains. Children with tuberculous lesion in the lung are also likely to infect their intestine secondarily, by swallowing sputum containing the organism.

Pathology : —

a) *Tabes mesenterica* : The mesenteric glands in the right iliac fossa are usually the first to be affected. These glands become enlarged and they either heal by fibrosis and calcification or cause complications. They become adherent to neighbouring loops of intestine and they may also liquefy and discharge their content in the peritoneum leading to TB peritonitis.

They may open into a blood vessel to produce either focal tuberculomata or generalized miliary tuberculosis according to the dose of the infection.

b) Tuberculous enteritis : Tuberculous ulceration usually starts in the Peyer's patches of the terminal ileum or the cecum. The ulcers then spread in a circular direction around the gut following the line of lymphatics.

c) Tuberculous peritonitis : May occur by : —

- i — Direct penetration of TB bacilli from the lumen of the gut.
- ii — Direct spread from T.B. ulcer.
- iii — Direct extension from caseous T.B. lymph node.
- iv — Via blood stream.

At first there is formation of miliary tubercles, to which the peritoneum may react by producing effusion "ascitic variety". The fluid is clear, straw colored and has a lymphocytic cell reaction. In other cases ascites does not occur, and the coils of intestine become matted together so that it is often impossible to separate the intestinal loops from each other at the post mortem. This variety is called the "plastic variety". Caseation and liquefaction may occur resulting in abscess formation which may ulcerate through the skin or remain localized, this variety is called caseous or "ulcerative variety".

Clinical Picture : Clinical manifestations of the three stages may be coexisting.

— General symptoms of tuberculous infection (fever, anorexia, loss of weight, sweating, . .) are usually marked in TB enteritis and plastic peritonitis and usually mild in isolated *tabes mesenterica* and ascitic TB peritonitis.

Tuberculous enteritis is characterised by persistent diarrhea with loose, slightly offensive stools, containing shreds of undigested food and mucus and occasionally blood streaks. On examination, there is severe emaciation and the abdomen is somewhat tumid and may be tender on palpation.

Tabes mesenterica is characterised by attacks of abdominal pain, failure to thrive, mild attacks of diarrhea alternating with constipation, occasionally passage of fatty stools (due to obstruction of the lacteals) and above all the presence of palpable glands in the abdomen. They are usually multiple, firm, slightly mobile and little tender.

Ascitic TB peritonitis : is characterised by progressive enlargement of the abdomen. On examination there are evidences of accumulation of free fluid in the peritoneum (fullness of the flanks and shifting dullness on percussion). Aspiration of the fluid is of diagnostic help.

Plastic TB peritonitis : is more common than the ascitic form. It is characterised by swollen abdomen, which feels doughy to the palpating hands (as if lightly packed with cotton wool) and occasionally a rolled up tuber-

culous omentum can be felt as a sausage shaped mass across the epigastrium. In advanced cases caseation and liquefaction may occur resulting in abscess formation. Such an abscess may remain localized in between the adherent loops of the gut, or it may ulcerate through the skin.

Prevention : Prevent contact with open cases. Such cases should be isolated and treated.

B.C.G. Vaccination : The aim of inoculation with *Bacillus Calmette — Guérin* is to produce a controlled primary lesion in previously uninfected persons. By so doing, the risk of the development of an overwhelming primary pulmonary lesion is lessened. It is presumed that if the inoculation is followed by a positive tuberculin reaction, an increased immunity to tuberculous infection results.

Inoculation is therefore of the greatest value for persons exposed to special risks of infection like doctors, nurses and butchers.

The B.C.G. vaccine is prepared from a strain of attenuated bovine, tubercle bacilli.

Technique of inoculation into the skin : oral administration of B.C.G. has not proved satisfactory, and inoculation into the skin is the method practiced at present. This is carried out by means of the multiple puncture method, by scarification or by intradermal injection.

Multiple puncture : The skin is smeared with B.C.G. vaccine and then pricked with a needle in 20 — 60 places.

Scarification : The scarification technique is similar to that used for small pox vaccination.

Intradermal injection : For this 0.1 ml. of vaccine is injected intradermally usually in the deltoid region or in the anterior aspect of the thigh. There is no constitutional disturbance following the inoculation, and there is little change at the site of injection, until after 3 weeks when redness and induration develop. This is usually followed by slight ulceration and some discharge. A scab forms after an interval varying from a few days to several weeks and the lesion gradually heals leaving a small tissue paper scar. There may be palpable enlargement of the lymphatic glands draining the area at the height of the reaction.

Preliminary testing : Before inoculation it is important to carry out satisfactory tuberculin tests to confirm that no previous infection has taken place. It is recommended that after a negative reaction has been obtained, the child should be isolated from any source of tuberculous infection for 6 weeks before inoculation.

and then retested after that period in order to avoid the possibility of inoculation during a time when allergy is developing. It is also recommended that there should be strict isolation from infected persons for 6 weeks after inoculation, that is while hypersensitivity is developing.

Reactions and immunity : Hypersensitivity to tuberculin usually develops 4 — 6 weeks after inoculation. A further tuberculin test should be carried out after this interval. Those few cases (2%) in which positive reactions do not develop will require a second vaccination.

Chemoprophylaxis : It has been shown that the daily administration of isoniazid to children who are exposed to tuberculous infection reduces the incidence of their developing the disease. This procedure is therefore at present extensively used with great success. The disadvantage of this form of prophylaxis is the need for continuous therapy. Its great advantage is the absence of any effect on the child's reaction to tuberculin, so that the test can continue to be useful in detecting infection if it is acquired.

Treatment: It is generally agreed that children with active lesions of tuberculosis in any location of the body should receive general and antimicrobial therapy. In addition, it is recommended that all tuberculin positive children up to 4 years of age, all children who are known to have become tuberculin positive within recent months, and all contacts with patients having open tuberculosis should receive isoniazid for about one year. The reasons for this policy are the effectiveness of isoniazid in the control of progressive lesions, the low degree of its toxicity, and in particular its effectiveness in the prevention of hematogenous dissemination.

General treatment :

Bed rest : This is indicated until the general condition improves. The child can be nursed in a hospital or at home and adequate isolation procedures should be maintained.

Fresh air and sunshine : This is important in improving the psychological attitudes of the child. It gives him a sense of well being and improves the appetite.

Adequate diet : The diet should be adequate but forced feeding is not beneficial and should be avoided. Special attention should be given to the protein, mineral and vitamin content of the diet.

Drug therapy : The most important drugs in use against tuberculosis are isoniazid, streptomycin, and para-aminosalicylic acid.

Isoniazid : This is given orally or parenterally. Its dose is from 10 to 20 mg.

per kilogram body weight per day. Drug resistance is not rapidly produced. Prolonged therapy with isoniazid may lead to convulsive disorders. These reactions can be minimized by the simultaneous administration of pyridoxine.

Streptomycin : Its combined use with niazid is probably always indicated in all serious tuberculous infections. It is given intramuscularly in a dose of 20-40mg. per kilogram per day. The total daily dose is given in one injection and should not exceed 1 Gm. Long term therapy is occasionally complicated by disorders of the labyrinth and less often by deafness. Dihydrostreptomycin is not recommended as deafness is more commonly produced by its use. Streptomycin therapy may lead to rapid emergence of resistant strains of tubercle Bacilli.

Para-aminosalicylic acid : It is given in a dose of 0.2—0.5 Gm. per kilogram per day. Drug resistant organisms may be infrequently met with after a prolonged course of treatment. Its main toxic manifestation is gastric irritation which may be severe.

A combined use of 2 or 3 drugs is usually made according to the severity of the tuberculous lesion.

Corticosteroid therapy : This is of accepted value in the treatment of pleural effusion and endobronchial lesions of tuberculosis. It may also be of help in the prevention of hydrocephalus in cases of tuberculous meningitis. In such cases corticosteroid therapy is usually continued for 2 weeks.

M. K. BADR-EL-DIN

Chapter XI

PARASITIC INFESTATIONS

OXYURIASIS (ENTEROBIASIS)

The worm is called *enterobius vermicularis* 5 — 10 mms. in length and lives in the cecum. The worm migrates down the bowel and deposits its eggs in the perianal skin during the hours of sleep and cause intense itching which may disturb the sleep of the patient. The eggs become infective in two hours.

Epidemiology Children are usually susceptible. Infection is by scratching the skin around the anus where the eggs are laid. When viable eggs are swallowed and pass down the digestive tract, they hatch in the duodenum and the larvae migrate to the cecum and within 2 — 4 weeks complete their development into adult worms.

Clinical picture: Asymptomatic infestation with oxyuris is a common disease. Symptoms occasionally do occur and may require treatment. Pruritis ani is the most common symptom and is usually most intense at night. Massive infestation may cause abdominal pain or even appendicitis as well as vague nervous symptoms.

Diagnosis : By swabbing of perianal skin, best in the morning before bathing or defecation.

No eosinophilia because there is no tissue migration of the larvae.

Treatment : Piperazine citrate syrup given in the same dosage as for ascariasis or in smaller doses over a week. Pyrvinium pamoate (vanquin) has proved by far the most reliable drug given as a single dose of 5 mg. / Kg. body weight on empty stomach. No saline purgative is needed. All members of the family or contacts must be examined and treated. Treatment must be repeated after a period of 14 days because the drug kills only the adult worms and not the developing eggs or larvae.

Pyrantel pamoate (Combantrin) is a new and very effective drug. It is given in a single dose of 10 mg./kg. body weight without previous preparation.

Personal hygienic measures are very important. White precipitate ointment should be applied around the anus in the morning and at bed-time.

ROUNDWORMS (*ASCARIS LUMERICOIDES*)

The large worms (9 inches long) live through all the length of the small intestine. Ingestion of fertilized eggs results in release of larvae which after migration through the lungs reach the small intestine and mature into adult worms. The adult ascaris lies free in the lumen of the small bowel, absorbing nutrients from the diet of the host. When the diet is already deficient in protein, large numbers of such worms may utilize amounts of protein sufficient to upset the balance of nutrition in the host with resultant protein malnutrition. Heavy worm infections are not uncommon in children presenting the syndrome of kwashiorkor.

Clinical picture : 1. A few roundworms in a well-fed child usually produce no ill effects and are not noticed until a worm is either vomited by the child, or passed in the stools, or a routine microscopic examination of the stools shows eggs to be present. Sometimes occasional mild abdominal pain, loose stools or vomiting may be produced.

2. Very occasionally one or more roundworms may migrate through small orifices, particularly under stress, as when the child has febrile illness, undergoes anesthesia or is receiving treatment for a hookworm infection. Invasion of the biliary or pancreatic ducts may produce obstructive jaundice, intrahepatic abscess, pancreatitis or pancreatic abscess. A single worm may cause an acute respiratory death when it migrates up the esophagus and obstructs the upper respiratory tract. Partial or complete intestinal obstruction, most common in the jejunum, intussusception, most common at the ileocecal valve, and volvulus may result from a tangled bolus of worms. If roundworms enter the peritoneal cavity by perforating the intestine, peritonitis occurs.

3. In very heavy infections with up to hundreds of worms, these large parasites become dangerous nutritionally especially in poorly fed, rapidly growing young children as they use up a considerable portion of the food taken by the child.

Diagnosis : The diagnosis of ascariasis should be suspected in any child with vague intestinal symptoms, poor growth or nutrition, or a history of vomiting or passage of a large worm. Stool examination will confirm the diagnosis.

Treatment : Piperazine derivatives (adipate, citrate or phosphate) are used for the treatment of roundworm infections. The dose is 150 mg. per kilogram, not to exceed 4 Gm. A single-dose treatment is frequently effective. It can be repeated on 3 occasions at 2-day intervals if necessary. The mechanism

of action of the piperazine salt is paralyzing the parasite so that it can no longer maintain its place in the lumen of the small intestine resulting in the passage of a live but flaccid worm.

- Hexylresorcinol (crystoids) : A safe highly efficient ascaricide is given in a dose of 0.1 or 0.2 hard gelatin pills to be swallowed without being chewed. After an evening saline purge, next morning, a single dose of 0.1 Gm./year (maximum one gram) is given on empty stomach, to be followed two hours later by another saline purge.
- Pyrantel pamoate (combantrin) is the drug of choice now. For dosage see Oxyuriasis.

HOOKWORM (ANKYLOSTOMA DUODENALE)

These worms which are about one inch long, live in the first part of the small intestine (especially the duodenum). Their heads are stuck into the wall of the intestine by means of cutting plates or teeth. An anticoagulant aids in the pumping of blood. Each worm may remove over 0.75 ml. of blood and plasma per day. Surgical and autopsy specimens have demonstrated that the worms move frequently to new mucosal attachment, leaving behind oozing sites as a further source of blood loss. Eggs are found in the stools and develop into active larvae, if feces are passed on to warm moist ground. The larvae penetrate the skin, usually between the toes, but in small children playing on contaminated soil, the area of entry may be any part of the body. Once in the small capillaries, the larvae progress to the lungs, rupture from the alveolar capillaries and pass up the tracheobronchial tree to descend to the small intestine, where they mature into adult worms.

Clinical picture : The main picture of hookworm disease is caused by prolonged loss of blood. The degree of anemia produced depends on the size of the worm burden, the body iron stores and the dietary intake of iron. Children who have large amounts of iron stores in their diet can tolerate a larger hookworm burden of longer duration without manifesting iron deficiency anemia than those who have a poor iron intake. In addition to red blood cells, the hookworm also ingests plasma; an amount of albumin equivalent to 3 ml. of plasma per 100 worms may be lost in 24 hours. This places an additional stress on the patient with borderline nutrition, and since dietary deficiencies are common in areas where the hookworm is endemic, frequently there is associated evidence of malnutrition and protein deficiency. Severe hookworm disease may be associated with a frank intestinal malabsorption syndrome with increase in fecal fat, abnormal D-xylose tests and low levels of vitamin A. Gastrointestinal disturbances include anorexia, nausea, diarrhea or constipation, vague abdominal

pain and in severe cases tarry, viscid stools. Many children have no gastrointestinal complaints and present primarily as a diagnostic problem of iron deficiency anemia.

Diagnosis : Three findings are needed to diagnose hookworm disease :

1. A definite anemia (as shown by clinical examination and by a low hemoglobin usually below 4%). 2. Many hookworm ova in the stools. 3. The presence of blood in the stool as shown by chemical test (positive occult blood test).

Treatment : I — *Anemia* : If severe, a small intravenous blood transfusion using sedimented red cells may be given slowly, if blood is available. If moderate in degree, iron may be given by mouth (as ferrous sulphate mixture) or intramuscular injection (Imferon).

II — *Deworming* : Tetrachloroethylene (T C E) 0.1 ml. per kilogram by mouth is given in a liquid form on an empty stomach with no preliminary starvation or subsequent purgatives. It can be repeated on 3 occasions at 2-day intervals. If the hemoglobin is very low, it should preferably be raised to 40% by transfusion or iron before deworming. In mixed infections that include ascaris, the ascarids should be eliminated first and then treatment with tetrachloroethylene administered.

- Bephenium Hydroxynaphthoate (Alcopar) is effective against both ascaris and hookworm. A single dose of 5 grains with 40 ml. of water is given fasting. Children under two years and weighing less than 10 kg. are given half the dose. Food is given after 0.5 to 1 hour. No saline purgative is necessary. The dose may be repeated after 10 days if needed.
- Combantrin is effective against ankylostoma duodenale, ascaris and enterobius. Because mixed infestations are common, this drug is of special value.

SCHISTOSOMIASIS (BILHARZIASIS)

Bilharziasis is a disease of childhood rather than other periods of life, but is seldom seen in infancy. It reaches its maximal incidence at the age of 10 or 12 years. In an endemic region, all children should be suspected of getting the infection.

The pathological effects of the illness depend on :

1. The duration of the illness.
2. The degree of infestation.
3. The type of parasite. This indicates the part of the body liable to be attacked.
4. The site of selection by the parasite for the deposition of ova.

Clinical features : 1. The itch is the earliest lesion and appears within few hours to few days after exposure to infected water. The condition quickly disappears in 2 — 3 days.

2. Bilharzial fever is uncommonly encountered. It appears 4 — 10 weeks after exposure to infected water and usually before ova are found in the excreta. This fever last for a variable time from few days to one or more weeks. A constant sign is the high blood eosinophilia 20 — 60%.

3. Stage of localized disease occurs when ova are excreted. At least half the children in this stage do not suffer from intestinal or urinary trouble, but rather from constitutional symptoms as debility, indigestion, poor appetite, nervousness and loss of weight. The main symptoms in the other half of children are those of intestinal or urinary involvement :

— Urinary : most characteristic is terminal hematuria. Occasionally, the stream is uniformly discoloured or may be clear urine with microscopic hematuria. Some patients get dysuria or discomfort over the epigastrium. Examination of urine shows bilharzial ova with R.B.Cs.

— Bowels : In *S. mansoni* there is a chronic diarrhea, often associated with blood and mucus, which may be overlooked as amebic disease or ulcerative colitis. Some cases may be constipated.

4. Stage of complications, may set early or many years after reinfection. Stricture and dilatation of the ureter is often found in its lower third and may be complicated by hydronephrosis.

I — Parenteral therapy : Trivalent antimony compounds are effective in both *S. hematobium* and *S. mansoni* infections. Routine modes of treatment are contraindicated in advanced renal, cardiac, pulmonary and hepatic diseases. Each dose is given with the patient in the fasting state; thereafter he must rest or avoid physical exertion for two hours.

1. Stibophen (Fouadin, Repodral) : supplied in the form of 6.3% sterile solution. We start by a dose of 0.5 ml. for every 10 kilograms given daily for 3 days, then 1 ml. for every 10 kilograms on alternate days for 10 — 15 injections, to be given intramuscularly.

2. Tartar Emetic : is potassium antimony tartrate. It is not usually used for children because of difficulty in administration and due to its highly toxic effect. The individual dose is 2 mg./Kg. body weight. It is given intravenously in the form of a freshly prepared 6% sterile solution for 6 days. All trivalent antimony compounds must not be repeated before the lapse of at least three months, otherwise side effects are common if intensive therapy is attempted.

3. Anthiomaline or Pentostam : is given by both intravenous or intramuscular route. For children, start by 0.5 ml., maximum 1.5 ml. for 12 — 20 injections.

II — Oral therapy : 1. **Miracil - D** (Lucanthone hydrochloride) : The dose is 10 mg./Kg. body weight daily for 20 consecutive days or every other day for 20 doses. It is of moderate efficiency in *S. hematobium* and of low efficiency in *S. mansoni* infections. It is contraindicated in severe renal insufficiency and in advanced hepatosplenomegaly.

2. **Ambilhar** (Niridazole) : is a nitro-imidazolidinone compound recently introduced in tablet form in the oral therapy of bilharziasis. It is very effective in both *S. hematobium* and *S. mansoni* infections in the dose of 25 mg./Kg. body weight for 5 — 7 days. Side effects are anorexia, nausea, vomiting, insomnia, headache and excitation.

3. **Bilarcil** (INN Metrifonate) : This new drug is easy to administer but is effective against *S. hematobium* only. The tablets are swallowed with some liquid in a dose of 10 mg. /Kg body weight once every 2 to 4 weeks to a maximum of 3 doses.

TENIASIS (TAPEWORMS)

A disease produced by beef or pork tapeworm : *Tenia saginata* is common in beef-eating people and *T. solium* in pork-eating people.

Infection is contracted by eating insufficiently cooked beef or pork. Ingestion of an encysted scolex or head of the tapeworm leads to its attachment to the small intestine and generation of many many segments that form a worm of up to 10 meters length.

Diagnosis : Stool examination shows the proglottids or their ova.

Clinical findings : The nutrition of the child may suffer, or the first complaint may be the passage of proglottids per rectum. Man is subject to infection with the cysticercus stage of *T. solium* by swallowing eggs in contamination. These cysticercariae lodge in soft tissues of liver and brain.

Treatment : 1. **Niclosamide** (Yomesan). For children over 5 years old, a single dose of 2 Gm. after a light breakfast is given. For younger children the dose is 0.5 Gm. per year of age. Saline purgative is given after 2 hours. If the first course of niclosamide is ineffective, it can be repeated after one week.

2. **Quinacrine hydrochloride** (Atabrine).:

Dosage : Four to eight years 0.5 Gm. in three or four divided doses five minutes apart. Over eight years, 0.8 Gm. in four doses, five minutes apart. Two hours after therapy, give saline purge of 15 to 30 Gm. sodium sulphate in water.

The cysts which are formed from cysticercus stage are not affected by drugs and need surgical removal.

AMEBIASIS

Amebiasis is found in all parts of the world especially in the tropics. Its prevalence correlates more with standards of personal hygiene and sanitation than with climate. Infection is passed from person to person by cysts in feces which contaminate food and water.

Pathology : For amebic dysentery see Chapter VII.

The hepatic lesion is more characteristic. Trophozoites diffusely distributed through the liver parenchyma produce multiple microscopic areas of necrosis which may coalesce to form a macroscopic lesion, the amebic liver abscess. It usually contains a characteristic pasty brownish material. Occasionally, this material is mixed with purulent exudate, and the demonstration of ameba, essential for positive diagnosis is more difficult.

Clinical manifestations : For intestinal amebiasis see under amebic dysentery. The presence of an amebic abscess of the liver is suggested by chills, fever, leukocytosis and right upper quadrant tenderness or pain. The demonstration of colonic amebiasis would confirm the diagnosis.

Treatment : For amebic dysentery see chapter VIII.

For hepatic amebiasis chloroquine phosphate (Aralen) is given in 10 mg./kg/day doses divided on two doses for 10 days. Emetine hydrochloride may be used in a dose of 1 mg./kilogram per day for not more than 10 days.

Metronidazole (Flagyl) is a very useful drug. Dose is 50 mg./kg/day divided on three doses and given during meals for 7 days.

— Therapeutic aspiration of the abscess may be necessary in a treated patient who has obvious clinical improvement, but whose liver mass does not recede promptly.

GIARDIA LAMBLIA

This flagellate has been assumed to be a saprophite inhabiting the duodenum and was therefore ignored. The infection is acquired through the ingestion of cysts passed in human feces. Although many infected persons are asymptomatic, others develop protracted severe diarrhea often associated with fever and loss of weight. The most dramatic manifestation of giardiasis is a picture of malabsorption syndrome.

Diagnosis : is based on finding *Giardia* trophozoites or cysts in the stools duodenal fluid or in the biopsied mucosa.

Treatment : Either metronidazole or quinacrine is effective in about 80% of patients.

- Metronidazole (Flagyl) is given in 15 mg./kg / day doses divided on two doses for 5 days. If there is therapeutic failure, a second course of the same drug is likely to be effective.
- Quinacrine Hcl (Atabrin) is given in 5 mg. / Kg / day doses divided on two doses for 10 days.

MALARIA

All species of malaria have two distinct phases : intracorporeal and extracorporeal. Each species has its special intracorporeal erythrocytic life-cycle that may last approximately 48 to 72 hours. The extracorporeal stage is undergone in the body of an anopheles mosquito.

In the intracorporeal life-cycle, the parasite grows inside the red cell and the protoplasm becomes divided into segments (merozoites). When the cycle is complete, the containing corpuscle breaks down and liberates the merozoites which attach themselves to other red corpuscles, enter them and grow at the expense of hemoglobin. The extracorporeal or mosquito stage consists in formation of the sexual cells or gametocytes.

Four well-established species of malarial parasites are met with : *P. vivax* the cause of tertian malaria with 48 — hour periodicity, *P. malariae*, causing quartan fever with 72 — hour periodicity, *P. falciparum* causing malignant or pernicious malaria and *P. ovale* derives its name from the oval shape of infected red blood cell.

Symptoms : In children over 6 years of age, the clinical features of malaria resemble those seen in adults. The first paroxysm is usually preceded by vague prodromal symptoms : low grade fever, malaise, lassitude and vague pains in the bones and joints which may last for several days. The paroxysms are generally well marked. There is sudden exacerbation of the constitutional symptoms with headache and sometimes vomiting followed by a shaking chill. This is followed after 1 to 3 hours by a hot stage during which the temperature markedly rises. The sweating stage commences as the fever subsides, usually accompanied by disappearance of symptoms.

In infants and very young children, a well-marked intermittent fever with distinct stages is often absent, many cases assuming more of a remittent type or

an irregular intermittent form. Malarial chills are rarely witnessed in children under five years old. They are replaced in infants by cold hands and feet, blue lips and nails, sometimes pallor, drowsiness, prostration accompanied by vomiting and in many cases convulsive seizures. Enlargement of the spleen is present in the majority of cases. The white count is variable but there is often monocytosis and leukopenia.

In *P. falciparum* infection, the onset is sudden with convulsions; mental symptoms commonly develop such as active delirium, coma or a semicomatose state. Headache is severe and severe pains in the arms and legs are common.

Diagnosis : The diagnosis rests upon the demonstration of the parasite in the blood. Thick and thin films could be made at regular intervals. With failure to demonstrate the parasite, malaria can be suspected from a history of exposure in a district known to be malarial. The periodicity of symptoms coupled with splenic enlargement is always suspicious. The therapeutic test may be of value. The fever and recurring chills of pyelitis are often mistaken for malaria.

Treatment : Immediate therapy of all forms of malaria must be directed towards eradication of the erythrocytic forms of the parasites.

- Chloroquine phosphate (Aralen or Resochin) is the best drug for this purpose. It is given orally in a dose of 17 mg./kg body weight immediately, and half this quantity twice daily for 2 days.
- Amodiquine HCL (Camoquine) can replace chloroquine phosphate and is equally effective. It is given orally in a dose of 10 mg./kg immediately, and 2/3 this quantity daily for 2 days.
- Primaquine phosphate (8-aminoquinolin Co) should follow or is added to either chloroquine or amodiquine in plasmodium vivax and *P. ovale* infections for the eradication of the exoerythrocytic cycle. The dose is 0.2 mg./kg/ day given by mouth daily for 14 days. Children on primaquine should be under medical supervision for early detection of toxic symptoms viz. methemoglobinemia, hemolytic anemia especially in children with glucose 6-phosphate dehydrogenase deficiency, neutropenia, colicky abdominal pain and renal obstruction from crystallization.

This drug is not necessary in the cases of *P. falciparum* and *P. malariae* infection because there is no exoerythrocytic cycle in their patients.

Parenteral therapy is used essentially in the treatment of cerebral malaria caused by *P. falciparum*, but also in other emergency conditions. One of the following may be used : -

Chloroquine phosphate is given I.M. in a daily dose of 17 mg./kg body weight. Half this amount is given immediately, and the other half after 6-8 hours.

Quinine sulfate is given I.V. in a daily dose of 20 mg./kg. Half this is given immediately, and the other half after 6-12 hours.

Prophylaxis : Chloroquine phosphate is given by mouth- 35 mg./kg body weight once every week, beginning two weeks before arrival in a malarial zone and continued for two months after the last possible exposure.

E. HASANEIN

Chapter XII

THE RESPIRATORY SYSTEM

Introduction

Among all childhood diseases, those of the respiratory system are second only to gastrointestinal disorders in Egypt. The mortality rate of these diseases takes also the second place among others in the age period 0-5 years.

It is mostly infants who are subject to respiratory disorders. This is due to anatomic and physiologic features, as well as immaturity of their central nervous system and of their immunological responses beside the various environmental factors which may influence the type and/or the severity of the illness.

Accordingly both the incidence and the clinical patterns of respiratory disorders differ from one age level to another throughout the pediatric period. Evidently, these contrasts deviate more and more when compared with those of older children or adults. Therefore, before starting to discuss the various respiratory disorders, it is worth to mention :

The Important Normal data in Infants and Children.

At birth and during infancy the antero-posterior and lateral diameters of the chest are equal. With a rounded chest like this in the position of inspiration, the *type* of breathing can be diaphragmatic only. After infancy and due to development and action of the postural muscles attached to the chest wall and employed in sitting and standing, the shape of the chest changes gradually to become oval as in adults. Now, the ribs can rotate moving up and down and so respiration becomes abdomino-thoracic about the age of seven years.

Again, because of the same peculiarity concerning the shape of the chest, the infant compensates his needs in face of the smaller volume of inspired air per act by increasing the *rate* per minute. At birth the respiratory rate is 45 — 35/min., by three years it is 35 — 25, at the age five to seven it drops to 25 - 20 and after that it approaches the adult rate of 18 - 16/min.

However, this *rate is irregular* except during sleep. This is due to immaturity of the nervous system.

Breath sounds are harsh in infants and young children due to the intact and healthy elastic tissue of the lungs.

The normal *rhythm* of breathing during the first 2 - 3 years of life may become inverted i.e. the pause follows inspiration instead of expiration. This occurs when breathing is quickened in the presence of high fever.

The normally *hypertrophied adenoids* and tonsils may partially obstruct breathing especially when inflamed.

The soft *flabby larynx* may collapse easily leading to laryngeal stridor.

The excess of *areolar tissue* in the submucous layer of the larynx allows edema and inflammatory exudate to accumulate and obstruct the airway.

The *thin-walled* bronchioles may be easily plugged and closed by inflammation in and around them.

The *soft chest cage* may be easily deformed by rickets leading to diminution in the capacity of its cavity and this helps collapse of the lungs and secondary infection.

Lack of immunity to the huge number of respiratory viruses and bacteria makes of children an easy victim of recurrent and complicated respiratory infections and allows easy and rapid dissemination as in cases of tuberculosis etc.

AGE AND OTHER FACTORS INFLUENCING RESPIRATORY DISORDERS

I — Neonatal period : During this period (0 - 4 weeks) the most important factors that influence respiration (initiation and continuation) and respiratory disturbances are : -

- (a) Chemical (O_2 & CO_2) and
- (b) Mechanical (obstruction or malformation), while the role played by
- (c) Infection is a very slight one due to rarity, of exposure. Therefore, the respiratory diseases which we may meet in these critical four weeks of life are :

Apnoea neonatorum, congenital atelectasis, congenital laryngeal stridor, hyaline membrane disease, aspiration pneumonia, pneumothorax, pneumonia and empyema (chapter V).

II - - Period of infancy : During this period (1 - 24 months),

- a) Infection becomes the most important factor while,
- b) Aspiration of foreign bodies or of lipoid substances start when the infant begins to move and tries to discover the world around him.

- c) Complications of upper respiratory infections are particularly common during this age.

Most of the diseases which occur in this age period are vital and are rarely met with at later age and these are :

Herpangina, pharyngoconjunctival fever, pharyngitis, acute laryngotracheo-bronchitis, bronchitis, atypical pneumonia, bacterial pneumonias, pertussis, aspiration pneumonia, and tuberculous infection and may be disease. Complications of the forementioned diseases e.g. otitis media, sinusitis, retropharyngeal abscess, quincy, acute cervical adenitis etc. are common.

III -- Period of childhood (after 2 years) : During this period and due to more exposures to droplet infections,

- a) Recurrent respiratory infections take place particularly the syndromes of common cold and certain problems emerge as :
- b) The problem of tonsils and adenoids and whether to be removed or saved.
- c) Allergic respiratory disorders.
- d) Tuberculosis especially in developing countries.

Thus the diseases and disorders which may occur are : -

Influenza, common cold, enlarged adenoids and/or tonsils with or without recurrent inflammation, sinusitis, bronchitis, asthma, pertussis and pulmonary tuberculous affections.

VIRAL AND BACTERIAL INFECTIONS OF THE RESPIRATORY TRACT

In the past the elucidation of this complex problem has been difficult because of the diverse etiology of the group as a whole and the lack of any experimental animal for viral studies. With recent improvements in laboratory methods progress is being made in the differentiation of these disorders into etiological types as well as clinical syndromes.

Although the general symptoms are almost the same in the group as a whole (i.e. fever, chills, malaise, headache and cough), yet the clinical picture differs and this depends on ; -

1. **Maximum area involved:** i.e. localising symptoms and signs : -

Because the mucus membrane of the respiratory tract is continuous from the nose down to the bronchioles, inflammation spreads easily, but usually one part is affected more. Thus nasal catarrh or obstruction is due to (rhinitis), sore throat (pharyngitis and/or tonsillitis), hoarseness of voice, aphonia or croup (laryngitis), irritating dry cough (laryngotracheitis or tracheobronchitis), productive cough and rhonchi (bronchitis), productive cough and crepitations (bronchiolitis or pneumonia). The forementioned entities may overlap and usually more than one part of the respiratory tract is affected by one or more agent. That is why the illness is best described by terms of the anatomical area which is affected.

2. Age of patient : Because the nose, pharynx, larynx and bronchi of the newborn and infant are very narrow, therefore any inflammation, allergic reaction or foreign body can produce symptoms of obstruction in the respiratory tract, the severity of which differs from early infancy to late childhood. For example simple coryza in young infants interfere with feeding and sleeping because of more dependence on nose breathing. In late infancy the associated high fever may cause also meningism and convulsions. In childhood the symptom become mild and at a later age they are minimal with short course and no fever. Immunity also plays a part beside the anatomical differences due to age.

3. Causal agent : It has been found that rhinitis and nasopharyngitis are almost solely caused by viruses while the pharynx and larynx are mostly affected by viruses but bacteria also share. Acute chest diseases are usually caused by bacteria but viruses may play a prominent part also as in bronchiolitis.

It is well known that uncomplicated viral infections run a short course than that of bacterial. But since viruses devitalize the mucus membrane of the respiratory tract, invasion of tissues by bacteria may occur and lead to complications as sinusitis, otitis etc.

In such complex and acute situations, the physician may be forced to make immediate diagnosis. In an attempt to reach this, accurate history and a careful physical examination are to be made and they usually yield enough information.

X-ray study of the respiratory tract of a child suffering from difficult breathing is often invaluable except in the case of an opaque foreign body.

Endoscopic study is sometimes a very necessary diagnostic procedure especially when the obstruction is suspected of being in the region of or below the larynx.

Bacteriologic examination of any material secured from the nose or throat is often helpful. It may be necessary to establish an airway for the child immediately before any investigative procedures are carried out to arrive at the possible diagnosis of which clinical syndrome exists.

CLINICAL SYNDROMES OF THE RESPIRATORY TRACT ILLNESSES.

Although overlapping is common, yet the following categories can be differentiated from each other -

1. — Common cold (nasopharyngeal symptoms and signs but little or no constitutional reaction).
- 2 — Influenza (well recognized course and epidemicity).
- 3 — Influenza-like disease (U.R.I.).
- 4 — Acute tonsillpharyngitis.
- 5 — Obstructive laryngotracheobronchitis, croup or stridor of infants.
- 6 — Acute bronchitis of infants and children.
- 7 — Acute bronchiolitis of infants and young children.
- 8 — Atypical pneumonia.
- 9 — Lobar, lobular and broncho-pneumonias.

Before proceeding to discuss the individual syndromes, their relation to the known offending agents can be made clear through table 15.

Table 15 : Respiratory syndromes and causative viruses, bacteria or agents.

Respiratory Syndromes	Infl. A, P vir.	Para-infl. vir.	Resp. sync. vir.	Adeno-vir.	Rhino-vir.	Cox. A & B vir.	Echo vir.	H. Infl.	Strep. tococ.	Pneu-mococ.	Staph. coc.	Kleb-sella pn.	Dipn-theria	Sec. bac-teria	Mycoplasma pn.
Common cold	+	+	+	+	++++ ++++	++	++								+
Influenza	++++														
Infl.-like dis. (U.R.I.)	++	++++	+++	+++	++++	++	+	+	+						+
Tonsillopharyngitis				++		++	++		+++				+		
Croup	+	+++	++	+	++	+		++	+				+		
Bronchitis	+	++	++	++	++	+				+				+++	
Bronchiolitis	+	++	++++ ++	++	++	+		+							+
Primary Pneum.				-				+		+++ ++	+	+			+
Secondary Pneum.	+	++	+++	+	+++	+		+	+	+++	++	+		+++	
Atypical	+	+	++	+					+						++++ ++

DISEASE OF THE NOSE, EAR AND THROAT

COMMON COLD (ACUTE RHINITIS, CORYZA)

An acute illness of a few days duration with or without low grade fever, accompanied by inflammation of the mucus membrane of the nose and may be of the pharynx. It is usually manifested by watery nasal discharge, sneezing, mouth breathing, nasal quality of the voice and cough. The nasal secretions—sometimes dry and form crusts in the nares which small infants may be unable to expel. Because of consequent nasal obstruction, the infant becomes fussy, irritable, sleepless and feeds poorly.

The condition usually disappears in 24 to 48 hours, but if it persists for days, secondary bacterial infection is to be suspected and complications may arise e.g. otitis media, bronchitis, pneumonia etc.

Etiology : Rhinoviruses (89 serotypes) are the common offenders, but others share (table 15). Immunity is of 1 - 2 years duration, but recurrences may occur in the same year due to other viruses or to allergy.

Treatment : Prophylaxis by open air, sunlight and adequate nutrition. Nursing mothers and adults with colds should not be allowed to care for young children unless they put masks on their mouth and nose.

Treatment is symptomatic i.e. nose drops, aspirin and when necessary sedation for cough and / or irritability.

The Catarrhal Child (Sino-bronchitis) :

The catarrhal child is one of the common and unsolved problems of pediatrics. Little is known about the etiological factors in this type of children. It is well known that an ordinary child during the age period 3 - 8 years usually experiences 3 - 6 attacks of colds a year each of which is followed by complete recovery. It can be assumed that these colds are caused by a variety of viruses and that in this way a child develops immunity gradually. The catarrhal child, on the other hand is one who suffers more attacks and who retains some of his symptoms between the acute episodes, sometimes in the form of persistent rhinitis, nasal obstruction and sinusitis; frequently in the form of an unproductive barking cough that may be accompanied with wheezes and rhonchi. These children are also prone to attacks of acute otitis media, chronic adenoiditis and cervical lymphadenitis. Spontaneous recovery usually takes place after the age of 7 or 8 years.

Management : Immediate relief is not available. The most useful role of the pediatrician is to explain the nature of the problem to the parents and to assure its relatively benign nature and good long-term prognosis. Parents must be dissuaded from over protecting the child by keeping him indoors, overclothing him or keeping him unnecessarily away from school.

In acute febrile episodes, the treatment is essentially that of common cold. Sooner or later the parents will raise the question of removal of tonsils and adenoids. This has certain clear indications (page 255) In those cases where tonsillectomy was done, the results were disappointing.

INFLUENZA-LIKE DISEASE (U.R.I.)

As a rule, the onset is often insidious with symptoms similar to those of common cold for some days to be followed by fever, pharyngitis, adenoiditis and enlarged tender cervical lymph nodes. The voice becomes hoarse and the chest may show scattered rhonchi.

Etiology : Many viruses are responsible (table 15), the most common are adenoviruses (31 types), rhinoviruses, para-influenza and respiratory syncytial (R.S.) viruses.

The bacteria which share are the hemolytic streptococci and may be hemophilus influenza bacillus.

Antibody studies show that infection with these viruses commonly takes place early in childhood and that further infection with new strains continues throughout life.

Beside infection, contributory factors include age, susceptibility, malnutrition, fatigue, chilling, dampness, dust and other respiratory irritants.

Treatment : Prophylaxis by avoiding exposure and the predisposing conditions.

A vaccin against adenoviruses 3,4,7 is on trial. Otherwise, treatment is symptomatic. Chemotherapy or antibiotics are to be given for bacterial infection and for complications.

ACUTE TONSILLOPHARYNGITIS

Under this heading a variety of different clinical and etiological conditions are included and more will be discovered with identification of other offending viruses or agents. In general, the systemic manifestations are the same being similar to those of acute upper respiratory disease with the addition of others

related to the local lesion. The following conditions are the most important among this group : -

Acute Tonsillopharyngitis (exudative or membranous) : The common causative organisms are streptococcus hemolyticus, and adenoviruses (Table 15).

Beside the general symptoms this condition is characterised by dysphagia, thick voice and the presence of catarrh, follicles, membrane or pseudo-membrane on the tonsils and may be pharynx. Inspection of the oropharynx at times reveals purulent mucus on the posterior wall, representing drainage from the adenoids, nasopharynx and/or paranasal sinuses above. The lymph follicles on the posterior wall become hypertrophied and present red inflamed elevations of few to several millimeters diameter.

Peritonsillar abscess (quinsy) may complicate tonsillar infection. It forms in the anterior part of the arch of the soft palate on one or the other side thus causing asymmetry of the soft palate.

To differentiate bacterial from viral affections on clinical grounds only is not always easy, but the following table may be helpful so that the appropriate treatment could be started without delay.

Table 16 : Bacterial and viral affections of the throat.

Tonsillopharyngitis	Bacterial	Viral
Onset	Sudden	Gradual
Course	Severe	Mild
Temp.	High	Moderate
Voice	Normal	Hoarse
Cough	Late	Early
Sore throat	Lags	Early
Follicles & / or membrane	Both	± membrane
Cervical nodes	+	±
L. C.	> 10,000	< 10,000
Complications	+ + +	±

Acute vesicular or ulcerative tonsillopharyngitis — «Herpangina» . Is a common febrile children's summer illness characterized by papular, vesicular and then ulcerative lesions on the anterior pillars, soft palate, tonsils, and pharyngeal mucus membrane. The fever remains 1 — 2 days accompanied by headache, myalgia, dysphagia and occasional vomiting and/or abdominal pain. There is no cough, coryza or otitis media.

Studies showed definite relation with Coxsackie-A-viruses which were isolated from stools of 85% and throats of 45% of cases. Neutralizing antibodies against homologous strains can be detected in all cases. More recently the studies suggested other enterovirus etiologies as Coxsackie B and many ECHO viruses (table 15).

Coxsackie A₉ and A₁₆ may cause vesicular lesions on the hands and feet also and then the condition is termed «hand foot and mouth disease».

These diseases are benign and self limited. Treatment is symptomatic.

Pharyngoconjunctival fever : A febrile epidemic or sporadic illness which lasts 1 - 10 days and is characterized by sore throat, non-purulent conjunctivitis, posterior cervical lymphadenopathy beside the general manifestations of headache and lassitude.

There is no cough, lung affection or rash, but vomiting and/or diarrhea may occur. Otitis media is a frequent complication.

The disease is produced by the adenoidal - pharyngeal - conjunctival (A.P.C.) group of viruses (18 immunological types). Type APC₃ is the commonest cause and can easily be recovered from the throat. Infection leads to antibody formation and complement fixation test.

Acute Lymphonodular Pharyngitis : In this condition beside fever, headache, malaise and anorexia there is sore throat with discrete white to yellow nodules surrounded by a zone of erythema on the uvula, palate, anterior and posterior pillars. These lesions do not ulcerate. They appear and disappear for 4 - 14 days and may be accompanied with mild submandibular lymphadenopathy. Coxsackie A₁₀ virus is the cause.

Treatment of tonsillopharyngitis :— Streptococcal infections respond to various antimicrobial agents, but penicillin has been proved to be the drug of choice. It eradicates the infection, and drug resistance has not been observed after its use. Erythromycin and the broad spectrum tetracyclines are also effective. Sulfonamides may produce clinical improvement, but they frequently do not eradicate the organism from the patient.

The duration of therapy is extremely important, and an effective drug should be continued for ten days in order to minimize the development of acute rheumatism, acute glomerulonephritis or a recurrent streptococcal infection.

In addition to specific therapy, symptomatic treatment should be instituted as analgesics, antipyretics, sedatives, compresses, enough fluid intake... etc.

ACUTE PARA-NASAL SINUSITIS

Inflammation of the mucus membrane lining the accessory cavities of the nose occur in most cases of upper respiratory tract infections, but sinus infection usually does not persist after the nasal infection has subsided. However, in cases of obstruction to the normal drainage of the sinus, or of continuous irritation of its mucus membrane the infection may persist. Among the causes of obstruction hypertrophied adenoids, deformity of nasal septa, allergy and edema of the mucus membrane from nasal infection are the prominent ones.

Symptoms : Fever, headache, malaise and nasal voice. Usually there is mucopurulent nasal discharge and post-nasal discharge also.

Signs : Edema around the orbit and may be cellulitis. Tenderness over the involved sinus and may be cellulitis also. Failure of transmission of light through the affected sinus.

X-ray shows clouding of the affected sinus region and may be a fluid level inside the sinus.

Treatment : Proper management of the original respiratory infection may abort acute sinusitis.

For treatment consider : -

1. *Ventilation and drainage :* Humid atmosphere, 0.25% neo-synephrine nose drops or better as spray three or four times daily. If no success is obtained, puncture of the antrum, irrigation to remove the secretion and antibiotic instillation is indicated.

2. *Specific treatment :* Systemic broad spectrum antibiotic to which the organism is sensitive is given.

3. *Symptomatic treatment :* Aspirin for fever and discomfort. Hot fomentations help in relieving pain. Corticosteroids or other anti-allergic drugs may be helpful especially in allergic subjects.

ACUTE OTITIS MEDIA

Acute infection of the middle ear is common in infancy and childhood. Thanks to antibiotic therapy which has diminished the possibility of progression to perforation and chronicity. Acute otitis media is primarily an obstructive disease; when the eustachian tube becomes obstructed during the course of an upper respiratory tract infection (particularly with measles, scarlet fever, influenza etc..) or by grossly enlarged adenoids, a transudate rapidly appears in the middle ear cleft. The tympanum, the mastoid antrum and mastoid air cells (if any) become simultaneously involved. Organisms ascend the eustachian tube into the middle ear and flourish in the transudate. Acute otitis media is, therefore, acute infection of the entire middle ear cleft : namely, the nasopharynx, the eustachian tube, the middle ear space, the mastoid antrum and adjacent air cells (if present). Acute surgical mastoiditis is a late stage of this process in which the entrance to the mastoid antrum is obstructed and the walls of the mastoid air cells are broken down.

The most common pathogens are the pneumococci, H. influenza, beta-hemolytic streptococci, and staphylococci; the first two being the chief bacterial pathogens in infancy. In one third of the cases no bacteria can be found.

Symptoms : Fever, irritability, sudden shrill cries which are more during night, head rolling, pulling or rubbing on the ear and may be convulsions.

Signs : In suspected cases, pressing on the mastoid process evokes sharp pain, the baby cries out loudly and becomes restless. However, the more reliable method is to examine the ear drum with a speculum for distortion or absence of the light reflex, redness and bulging or perforation of the drum with drainage of pus.

Treatment :

- a) *Establishment of ventilation and physiologic drainage :* The nasal mucosa should be kept shrunken by using 3 drops, two hourly of 0.25% neosynephrine solution. If history or findings are suggestive of allergy, a combined antihistaminic and vasoconstrictor are indicated. These measures will help opening the eustachian tube and drainage of the middle ear in the physiologic way.
- b) *Specific antibacterial therapy :* If the ear is draining, a culture and sensitivity test are done to choose the proper therapy. However, the drug of choice is

ampicillin 50 - 100 mg/Kg/day, or the combination of erythromycin (25 - 50 mg./ Kg/day) and sulfa drugs.

- c) *Symptomatic treatment* : Ear drops are not used because they obscure physical findings, but they may be used to give local relief of pain after the diagnosis has been made. Aspirin may be given to reduce the discomfort and fever.

Duration of treatment : Antibiotics should be continued for five days after all signs of acute infection have subsided. Nose drops, however, should be continued until hearing returns.

- d) *Surgery* : Myringotomy is indicated if there is no response to the medical treatment.

THE PROBLEM OF TONSILLECTOMY AND ADENOIDECTOMY

The adenoids and tonsils form an important part of a fortress of protective tissue against invasion of infection to the respiratory tract. As regards their possible role in the development of immunity or in hormonal secretion we are still very much in the dark inspite of the many critical studies. Therefore, it will be clear that no hard and fast indications can be deduced for saving or sacrificing tissues that might play an active role. But there must be no breaches in such defenses so long as they can perform their function. It should be remembered that we can help these tissues to restore their integrity and function by using chemotherapeutic agents and antibiotics. On the other hand, the fact exists that the morbidity of tonsillectomy and adenoidectomy is still a major problem and the number of complications is probably high. In addition, there is distinct risk of operative mortality.

Therefore, indications for tonsillectomy and adenoidectomy should be subject to the most thoughtful and critical investigations.

Many studies were done to find out the indications and contraindications for tonsillectomy and/or adenoidectomy. The value of such studies is limited because of the lack of controls. However, there was general agreement on some indications.

Recommendations for Tonsillectomy : The studies show that there are never any absolute indications for tonsillectomy. Before removing the tonsils we must be sure that : (a) they have themselves become the seat of continuing infection (red pillars and cervical nodes), (b) that they have lost their resiliency (c) that the child fails to respond to

adequate medication and (d) that the barrier of the tonsils has broken down resulting in recurrent or chronic otitis media etc. Peritonsillar abscess is another indication because it is not worth the risk of recurrence.

Such conditions as serious systemic diseases, tuberculous cervical glands, fever of unknown origin, being a diphtheritic carrier, asthma, rheumatism and general debility are indications only after the child has been followed long enough to establish clearly the relation between the symptoms and the tonsillar infection : generally a minimum of one year is needed.

Recommendations for Adenoidectomy : Chronic infection causing repeated or long standing otitis media, sinusitis or pyrexia because of the retained pus in their crypts. Huge obstructive adenoids which cause mouth breathing and/or early impairment of hearing.

Follow up studies have shown that it is probable that cases with recurrent or chronic tonsillitis and also adenoiditis benefit for a few years only after operation. Residual tissue may rapidly hypertrophy in 20% - 80% of cases leading to recurrence or even worsening of symptoms.

Contra-indications of Tonsillectomy and/or Adenoidectomy :-

- I — *Absolute* : Hemophilia and other disorders of coagulation, agranulocytosis.
- II — *Relative* : Diabetes, congestive heart failure, advanced tuberculosis, mild forms of agranulocytosis, active rheumatic fever, active glomerulonephritis and nephrosis.

Early age, family history of allergic manifestations, lack of history of repeated infections for more than one year should be considered as relative contra-indications to removal of tonsils and adenoids.

Age for Operation :-

Adenoidectomy : Not to be performed under one year, preferably about 3 - 5 years. Before that there is appreciable chance that the adenoids may recur, and after that there may be a cosmetic defect in the upper jaw which may affect the position and shape of the permanent teeth.

Tonsillectomy : Not under 2 years, preferably at 4 - 5 years.

Time of year for operating : Never operate during an epidemic of poliomyelitis. Where this disease is endemic minimize the number of tonsillectomies performed with due regard to the endemic areas. Immunization against poliomyelitis in such localities diminishes the risk. Also

postpone the operation if there is a local epidemic of contagious disease and during hay fever season if the patient is allergic.

Deaths and severe complications during and following operations :-

Death : From anaesthesia, hemorrhage or sudden unexplained.

Complications : Late hemorrhage, pneumonia, stomatitis, septicemia, bulbar poliomyelitis, psychological trauma, dry or stiff throat, easily recurrent attacks of sore throat and laryngitis and the occasional change of the tone of voice.

Results of operation :

1. Frequency of upper respiratory infections : The improvement is not impressive. The members of the operated group seem to be helped during the first 3 years after operation, while they become worse between the fourth and tenth year. The actual reduction might be due to the normal decline in frequency that is a function of the passage of time which is noticed in non-tonsillectomised as well as in tonsillectomised children.

2. Prominent mouth breathing : Complete cure in 2/3 of the cases, improvement in most of the rest and failure in about 2%.

3. Chronic cervical adenitis : Complete cure occurs in half of the operated cases and reduction of the condition takes place in the great majority of the rest.

4. Recurrent or chronic otitis media : Improvement in about 70 — 90% of cases was reported in two studies, the results were questionable in the other four studies.

5. Hearing impairment : Good results are gained in half of the cases while improvement is noticed in the other half.

6. Rheumatic relapses : Results are contradictory. While in two studies improvement is claimed in 70 - 90% of cases, no difference was found between the operated and non-operated group in the other four studies.

7. Asthma : The results have been so unsatisfactory. However, occasional brilliant results have been seen in those with a clear history that tonsillar infection always preceded the attacks of asthma.

8. Pneumonias : Were found to occur more frequently after the operation in two out of six studies.

9. Appetite and the nutritional state : Anorexia improves in more than 2/3 of the cases. Marked gain in weight following tonsillectomy has long been noticed.

Thus it can be concluded that so long that there is still no evidence of any long term benefit of tonsillectomy and/or adenoidectomy, these procedures may

remain of benefit only in properly and strictly selected cases. The operation should not be easily or reluctantly advised or pressed on the people; the question should be thoroughly studied by the pediatrician and otolaryngologist in every individual case and benefits and losses should be accurately weighed before embarking on the operation.

It is to be stressed that the decision for their removal can be arrived at only after a sufficiently long period of observation has excluded other causes for the complaints, and after trial of non-operative treatment has proved to be ineffective.

Non-operative treatment : It has been observed long ago, that the great majority of children who do have considerable trouble with tonsillitis build up an immunity and become almost entirely free from further affection after 6 or 7 years of age. Here comes the use of antibiotics which help to pull such children over the difficult periods until immunity develops and spontaneous cure is obtained. The fact that there is a marked reduction in the number of tonsillectomies performed today, as compared with ten years ago confirms this view. Some workers (California group) found out that since the sulfonamides and antibiotics have been introduced the need for tonsillectomy has been reduced by 90% and that for adenoidectomy by 50%.

DISEASES OF THE LARYNX, TRACHEA AND BRONCHI

LARYNGEAL AND LARYNGOTRACHEAL OBSTRUCTION

- CROUP IN INFANTS -

Under this heading, a group of diseases is discussed, all the members of which have a broad common etiology i.e. laryngeal obstruction which produces a common symptom i.e. stridulous, croupy or noisy breathing.

Though having this common symptom, yet the members of the group differ in the cause of obstruction, clinical picture, prognosis and management. While the result is safe in some conditions, it is serious and may be fatal in others.

Obstruction in the region of the larynx frequently has an acute onset and justifiably causes more concern to both parents and physician than does obstruction in other parts of the respiratory passages. The nature of such obstruction may be mechanical, inflammatory or spasm. One of these predominates but usually the others share in particular diseases. The result is a sort of clinical spectrum including a group of diseases the most important among which can best be illustrated as follows :

Table 17 : Mechanisms of laryngeal obstruction.

Disease	Mechanism of Obstruction		
	Mechanical	Inflammatory	Spasm
Congenital laryngeal stridor	+ + +		
Congenital web or neoplasm	+ + +		
Angioneurotic edema	+ + +		
Foreign body	+ + +	+	
Acute epiglottitis	+	+ + +	
Acute catarrhal laryngitis		+ + +	±
Acute spasmodic laryngitis		± +	+ +
Diphtheritic laryngitis		+	+ +
Laryngismus strudulosa			+ + +

Congenital Laryngeal stridor : Very shortly after birth the infant exhibits noisy breathing on each inspiration. It is less when the child is quiet. It is due to congenital deformity or flabbiness of the epiglottis and supraglottic aperture. The condition spontaneously disappears by the age of one year. No treatment.

Congenital Web or papilloma : Give symptoms similar to the previous condition. The treatment is surgical.

Angioneurotic edema : Angioneurotic edema of the larynx may be an allergic response to food or the environment. If marked it leads to obstruction, stridor and may be suffocation. Prompt treatment with ephedrine and antihistamines help to reduce the obstruction to the flow of air into the lungs. Desensitization of these patients should be considered also.

Laryngeal Foreign Body : Causes hoarseness, a cough which soon becomes croupy and aphonia. Inflammation with edema follows which, together with the foreign body, may cause obstruction and prove fatal.

Treatment : Removal of the F.B. and chemotherapy or antibiotics for the inflammation.

Acute Epiglottitis : Is a fulminating inflammation of the epiglottis and neighbouring structures, usually caused by *H. influenza* type B and rarely by other organisms as strept. -or staphylococcus. Onset is sudden with moderate to high fever, marked prostration and severe supra-glottic obstructive manifestations. Interference with respiration proceeds rapidly often to alarming degree. The child struggles for breath, uses his accessory muscles and may become cyanosed. The throat is red, and the epiglottis as seen by depressing the base of the tongue, is greatly inflamed and swollen.

Acute Catarrhal Laryngitis or Laryngotracheobronchitis : Is perhaps the most frequent cause of serious acute respiratory difficulty caused by infections in infants and young children. This condition begins with a cold but the inflammation, croupy breathing and dyspnea steadily increase without intermission. There is high temperature, hoarse voice or aphonia, cyanosis and spasmodic stridulous cough that later becomes loose. The supra-sternal fossa and intercostal spaces are retracted during inspiration due to laryngeal obstruction by the inflammation, edema and possibly spasm also. The important etiological agents are the common cold viruses. The condition may be a complication of measles, scarlet fever or influenza.

Acute Spasmodic laryngitis, (mid-night croup) : Is an acute, self-limited, but usually recurrent, catarrhal inflammation of the larynx in which the severity of laryngeal spasm is out of proportion to that of inflammation. The attack which is usually preceded by slight coryza comes on suddenly after sleeping. The child awakens with a characteristic barking metallic cough and severe inspiratory and expiratory spasmodic respiration that forces him to sit in bed struggling for breath. The crisis gradually subsides after 1 - 4 hours to recur in the same or next night usually with less severity. This condition runs in families of nervous constitution but allergy may also be an underlying factor.

Diphtheritic Laryngitis : In this specific type of laryngitis, which is usually secondary to faucial diphtheria, the temperature is not high but the toxemia is marked and the color of the child is grey. There is brassy cough and hoarse voice. The croup at first is inspiratory due to spasm alone, but later on it is inspiratory and expiratory due to the added mechanical obstruction by the diphtheritic membrane. The condition is progressive and the cervical lymph nodes are enlarged.

Laryngismus Stridulosa : This condition occurs in rachetic children of nervous constitution. It is one of the manifestations of tetany (page 123). The baby suffers from spasmodic closure of the glottis which leads to temporary asphyxia that occasionally proves fatal. The attack comes early in the morning or at night and can easily be precipitated by external irritation or emotion. For treatment refer to tetany (chapter VII).

Treatment of Epiglottitis, Acute Laryngitis and Acute Laryngotracheo-bronchitis

a) Confine to bed.

b) To relieve the anoxia :-

- (i) High humidity : The purpose is to reduce the viscosity of secretions and thus to reduce the obstruction and establish patent airways. Cold humidification is preferable to steam. Emetics as syrup of ipecac 2 - 4 ml. to be repeated after 4 hour help also in clearing the obstructing exudate.
- (ii) Oxygen inhalation : Bubbled oxygen administration should be started when the patient starts to use his accessory muscles of respiration. Do not wait until cyanosis develops.
- (iii) Tracheostomy : may be indicated as an emergency in late cases or may be done as an elective procedure in those cases which either show no much improvement on conservative treatment or become worse again after some improvement.

Thus when inspiratory effort is accompanied by retraction of the suprasternal, epigastric and infracostal regions, the decision to perform tracheostomy will rest upon rising respiratory rate, rising heart rate, increasing stridor, increasing retractions and especially evidence of developing exhaustion as seen by anxious facial expression or a falling respiratory rate in the face of a continuing tachycardia. With progress, if cyanosis develops, the operation may have already been delayed too long.

The post operative measures aim at keeping the air ways clear by

1. Continuous nursing care, 2. Suction and clearing the inner tube,
 3. Saturating the inspired air with vapour, 4. Treating dehydration and,
 5. Guarding against and adequately treating any pulmonary infection.
- e) To relieve dehydration : Fluids should be administered either orally or intravenously.
 - a) To combat infection : Broad spectrum antibiotics as ampicillin or penicillin and chloromycetin.
 - e) To relieve irritability and insomnia : Give sedatives as phenobarbital and avoid respiratory depressants.
 - f) If heart failure develops : Digitalisation is indicated.
 - g) Corticosteroids are supposed to be of some value especially in cases of spasmodic laryngitis with allergic background.
 - h) In diphtheritic cases the antitoxic serum should be given on mere suspicion as early as possible and as much as 25,000 to 100,000 units in order to neutralize the circulating toxins. Penicillin is of value and it reduces the carrier state also. Tracheostomy may be needed.

ACUTE BRONCHITIS

Catarrh of the bronchi is an inflammatory process of the bronchial mucosa accompanied by mucoid exudate. It is often associated with a similar condition in the trachea; therefore tracheo-bronchitis is a more suitable definition.

Pathology : The tracheobronchial mucosa is red and swollen, sometimes with hemorrhagic spots. It is covered by tenacious mucus exudate, at times it is purulent.

Etiology : It is usually secondary to acute nasopharyngitis or to such specific infections as measles, pertussis, influenza etc.

Many organisms have been isolated (table 15), the more common are the rhino-and other common cold viruses, pneumococci, and H. influenza. Chronic

infection of the U.R.T., allergy, rickets, undernutrition, dust and other chemical and physical irritants are among the predisposing causes.

Symptoms and Signs Cough is the most constant symptom while rhonchi* is the most important sign. The cough usually dry at first becomes loose later on. Infants and young children swallow their sputum which is often ejected with vomitus. Mild or moderate fever may or may not be present. There may be coarse moist rales in cases of abundant secretion, but the presence of medium-sized crepitations indicate involvement of the bronchioles also. Older children recognize retro-sternal pain especially during coughing due to tracheitis. The course is 10 to 15 days but in young infants it may be more.

The chest X-ray of a patient suffering from acute bronchitis, whether viral or bacterial, is usually negative but it may show increased bronchial markings.

In chronic cases, beside the increased hilar shadow there may be moderate generalized emphysema.

Treatment : Fresh air, moderate environmental temperature, and bed rest if the patient is febrile. Expectorants and change of position facilitate drainage of the mucus. Proper antibiotics are usually indicated. Sedatives may be needed. Treat the original disease as measles etc.

ACUTE BRONCHIOLITIS IN INFANTS

(Capillary bronchitis, Interstitial pneumonia)

Is a syndrome which occurs during the first two years of life and usually below six months. It is characterized by rapid laboured respiration, audible wheezing, cyanosis and prostration.

There is exudate in the bronchioles causing obstructive emphysema and dyspnea that sometimes lead to terminal asphyxia.

Pathology : The walls of the bronchi and bronchioles are thickened and infiltrated by inflammatory cells. There is also involvement of the interstitial tissues. There is no or minimal exudate in the alveoli.

(*) Dry rales or rhonchi are due to local narrowing of the bronchi or bronchioles. The cause may be in the lumen (exudate), walls (swelling) or around the bronchus (pressure). The sound produced by the passage of air is musical and continuous in character. It may disappear or change on violent coughing.

If originating in large bronchi they are low-pitched or *sonorous rhonchi*. The smaller tubes produce high-pitched or *sibilant rhonchi*. When the narrowing affects a longer segment of the bronchioles as in case of bronchospasm, wheezes are produced.

Etiology . Failure to isolate a single causative organism, poor response to anti-bacterial therapy and frequent presence of a normal leukocytic count point to viral etiology (table 15).

Respiratory syncytial virus was found to be the most frequent etiologic agent.

Clinically . The condition usually follows U.R.I. The onset being gradual with slight malaise and irritability that progress rapidly to cyanosis, marked restlessness and great respiratory distress followed by apathy. Fever is not a prominent feature early in the disease but is usually so later on. Cough is dry and persistent. Respiration is rapid (60 - 80/minute), shallow and accompanied with expiratory effort and grunt. Respiration becomes more laboured with intercostal, supra- and infra-sternal retractions and expiratory prolonged wheezing. The accessory respiratory muscles are used in an effort to overcome the obstructive emphysema. The chest is hyper-resonant and there is widely scattered fine and medium sized crepitations (*) and wheezing. Cardiac sounds are rapid and feeble. Gallop rhythm may develop secondary to the anoxia and the toxemia. Dehydration is usually present.

X-ray of the chest shows hyperinflation of the lungs due to generalized obstructive emphysema, increased bronchovascular marking and may be small scattered areas of opacity due to pneumonic and atelectatic patches (Fig. 24).

Course : Is variable, rarely it is less than two weeks, sometimes it is protracted, with periods of exacerbations and remissions. Fatality used to be high but it has been controlled by chemotherapy and antibiotics.

Treatment :

— Keep in bed, moderate temperature and good ventilation.

Light diet or even clear fluids for the first day. Then beside adequate supply of fluids, milk pudding, potatoes, bread etc. are to be added gradually.

(*) Moist rales or crepitations are due to bubbling of air through fluid. It indicates the presence of fluid secretions in the air cells or tubes. The sound produced by the passage of air is composed of many individual small explosions of different intensity. It survives several coughing bouts.

Fine crepitations are caused by the opening up of collapsed alveoli whose walls have been agglutinated by the exudation of a little fluid secretion as in the case of early pneumonia. They occur at or near the end of inspiration. *Medium and coarse crepitations* occur in the small and larger bronchioles respectively by the air bubbling through fluid secretion, which has been poured out in their lumen. The presence of consolidation or cavitation close to the site of their production intensifies very much the pitch and so are heard *resonating in character*.



Fig 24 Acute Bronchiolitis.

- If the patient cannot take enough fluids by mouth, the calculated needs are given I.V. as 5% glucose initially to be followed by saline glucose solution to combat dehydration and liquify bronchiolar exudate.
- Oxygen in 50% concentration for anoxia. Packed cells transfusion increases the oxygen carrying power and combats the toxemia.
- Humidity for bronchiolar plugging is very helpful.
- Chemotherapy and antibiotics for primary or secondary bacterial infections or if corticosteroids are given.
- Bronchodilators for bronchiolar spasm may be needed as adrenaline and aminophylline. Corticosteroids may be used. Both are of doubtful value.
- Sedatives as phenobarbital may be given for irritability. Give paraldehyde or chloral hydrate and avoid respiratory depressants.
- Digitalise the patient if there is heart failure
- Abdominal distention can be relieved by applying warmth to the abdomen rectal tube, doing small enema or giving prostigmine.

DISEASES OF THE LUNGS

BACTERIAL PNEUMONIAS IN INFANTS AND CHILDREN

The clinical aspects of pneumonia in children are so variable and different that attempts to classify them is very confusing. Moreover, it is often difficult and not helpful to refer a particular case to one class or the other because cases of similar clinical picture may be of different etiology, pathology, course and sequelae and vice versa.

An etiological classification of bacterial pneumonias would be of more practical value to the clinician who is now armed with effective antibacterial drugs than the traditional subdivision into lobar (alveolar) and bronchopneumonia (lobular with or without bronchial involvement).

Therefore, to avoid confusion and to provide basis for therapy it is better to classify bacterial pneumonias of children into primary and secondary.

Primary pneumonia is one in which infection has occurred in a previously healthy lung. For example, the pneumococcus is inhaled and pneumonia follows by pouring of inflammatory exudate in the alveoli.

In secondary pneumonia or bronchopneumonia the damage occurs primarily in the bronchi and bronchioles, followed by spread of the inflammatory lesion to the surrounding peribronchial and interstitial tissue and into the alveoli supplied by the affected terminal bronchioles.

PRIMARY BACTERIAL PNEUMONIAS

PNEUMOCOCCAL PNEUMONIA :

It is an infectious disease, endemic in large cities with an annual winter epidemicity reaching a maximum in spring. Infection being spread by cases, contacts and convalescent carriers as well as freshly contaminated utensils.

Etiology : The responsible organism is practically always the pneumococcus but few others share (table 15). It is the exciting cause but factors such as chill, exposure and over exertion are predisposing causes.

Pathology : Pneumococci gain entrance to the lungs by way of the respiratory passages. Edema fluid containing the pneumococci fills the alveoli and rapidly spreads to others. Consolidation usually develops first in the

periphery of the lobe or lobule and then spreads towards the centre. Blood invasion may occur in the first few days following lung affection leading to bacteremia or septicemia. The affected lobe or lobules pass through the same well known pathological stages characteristic of lobar pneumonia in adults i.e. congestion, red and then gray hepatisation and at last resolution.

It is difficult to explain why in sometimes the pneumococcus causes lobar pneumonia while in others it causes the lobular type. It is possible that there is some relation between the greater frequency of lobular pneumonia in infancy and the relatively higher incidence of pneumococci of the high types. Type 14 and other high types being the most frequent in infancy unlike adults and older children where type 1 and other low types of pneumococci predominate.

Symptoms : Fairly sudden onset with rapidly rising temperature which may be accompanied by convulsions or by chills in older children. The respiratory rate is greatly increased but usually without distress. Cough is usually a late feature except when it is due to pleural pain. Delirium may occur.

Signs : The traid of inverted breathing, expiratory grunt and inspiratory acting alac nasi:s diagnostic of pneumonia if associated with the forementioned symptoms. Chest signs usually appear late and are sometimes misleading. The first abnormal sign detected may be diminution of breath sounds over the affected area as contrasted with the harsh peurile breathing over the healthy lung. This may lead to the erroneous diagnosis of pneumonia on the healthy side. Limitation of movements and impaired note or dullness on percussion appear early and are more constant features of lobar pneumonia than of lobular or bronchopneumonia. Signs of consolidation appear later in children than adults. The breath sounds become tubular or bronchial with bronchophony. At this stage few crepitation may be heard. During resolution which usually begins after crises or during lysis, these signs fade gradually while coarse crepitations make their appearance. The crises occurs earlier in children than adults being on the fifth to seventh day i.e. pneumococcal pneumonia tends to be self-limiting disease. Pseudo-crisis is not uncommon in children. It can be differentiated from a real one by the fact that true crisis is accompanied by fall of respiratory rate to normal while in pseudo- the temperature only falls while tachypnoe persists.

The typical course described above is not always followed, but may be modified according to the clinical type present. Thus apical pneumonia gives meningitic signs, right basal pneumonia may simulate acute appendicitis, central pneumonia exhibits symptoms but no signs while massive pneumonia in which the bronchi are also plugged with fibrinous exudate may simulate pleural effusion.

In a typical case, chest X-ray shows homogenous opacity of a part of a lobe, a whole lobe or even a complete lung due to consolidation (Fig. 25). In the



Fig. 25 : Lobar Pneumonia. (Rt. upper lobe).

stage of resolution, clearing of consolidation usually starts at the periphery of the segment or lobe but it may be patchy and scattered. In the lobular type, the initial appearance is usually that of scattered areas of clouding.

Laboratory Findings : High leucocytic count, positive nose and/or throat cultures and positive blood culture in 10 - 20% of cases.

Differential Diagnosis : Before localization, some of the cases should be differentiated from acute specific fevers, acute abdominal disease and meningitis. The local lesion may be differentiated from massive atelectasis, pleural effusion, pericardial effusion, thickened pleura, bronchiectasis, tuberculosis, bronchopneumonia and fibrosis of lungs.

Complications : Prolonged pyrexia may occur without apparant cause, but slow resolution may be the cause and in such cases fibrosis may follow. Empyema is more frequent but less fatal after the age of five years. It may be syn - or meta-pneumonic, the last being more common. Lung abscess, bronchiectasis and otitis media are less common. Suppurative pericarditis, meningitis, peritonitis, arthritis are complications of pneumococcal bacteremia. Heart failure is not a common complication in primary pneumonias in children.

Prognosis : Antibiotics have revolutionized the therapy of pneumonia. If the patient is above one year, then an uncomplicated primary pneumonia is almost a safe disease without bad sequelae. Complications however, present considerable therapeutic difficulties.

Prophylaxis : Unfavourable conditions which predispose to pneumonias should be combated. Most important among these is bad housing, poor nutrition and exposure to infectious diseases as influenza, measles and pertussis.

Cases of pneumonia should be isolated to avoid spreading the disease among other children.

Treatment .

General Measures : Fresh air, proper nutrition, and good care. Bed rest and frequent change of position should be observed during day, while ample sleep by night should be our aim. The diet should be soft and readily digestible as milk, egg, toast etc. Avoid forcing the child to eat beyond his desire. Supply adequate amounts of fluids to avoid renal trouble, help secretion of toxins and lower the temperature.

- Oxygen is indicated to avoid and combat respiratory distress.
- For abdominal distention, enema may be enough, otherwise give prostigmine 0.5 - 1 cc of 1:1000 solution to infants 1 - 2 years old. It may be repeated after 2 - 3 hours.

Specific Measures : Antibacterial therapy is the most important measure.

The choice of the chemotherapeutic agent or the antibiotic will depend on the type of the organism. Since we cannot postpone the treatment until we get bacteriological diagnosis, it is recommended to give penicillin 25000 to 50000 units/Kg /day to cases of pneumococcal pneumonia. Benzyl penicillin 600,000 units may be an alternative.

STAPHYLOCOCCUS AUREUS PNEUMONIA

This is the commonest type of primary pneumonia during early infancy. In most cases these organisms have colonized the infants' nose in the maternity unit and almost always they are penicillin and may be also tetracyclin resistant.

At a latter age, staph. aureus pneumonia is usually preceded by a viral U.R.T. infection. Therefore, its incidence is higher during influenza epidemics than during corresponding non-influenzal periods. Further, the occurrence of fulminating infection with this organism is more common and the mortality is higher especially if the patient has some underlying disease.

Pathology & Pathogenesis . In cases of staph. pneumonia, beside the consolidation there is destruction of the lung tissue. The latter is due to a variety of toxins and enzymes which are produced by this

organism and which cause hemorrhagic necrosis, irregular abscess cavities and frequently emphysematous bulloe that may rupture leading to pneumothorax, pyo pneumothorax and/or bronchial fistula due to erosion into a bronchus.

Symptoms & Signs : These depend on the underlying pathology whether lobar consolidation broncho-pneumonia, pleural effusion, pneumothorax or pyopneumothorax and the extent of the lesion as well as the general toxic manifestations.

X-ray shows patchy clouding in one or more lobes. Pneumatocoles appear as thin-walled, rounded translucencies varying in size (Fig. 26). Pneumothorax (Fig. 27), emphysema or pyopneumothorax with a fluid level may be observed.



Fig. 26 : Staph. Pneumonia.

Prognosis : Is not bright, being poor in infants, debilitated children and in the complicated cases.

Treatment : When staph. pneumonia seems likely and especially when pneumonia due to gram negative organisms cannot be excluded, a combination of cloxacillin (50 mg/kg/day) and ampicillin (50-100 mg/kg/day) is given intramuscularly initially in 6 hourly doses. If no response within 72 hours, change to cephaloridine (50 mg/kg/day), erythromycin (50 mg/kg/day) or fucidin (20 mg/kg/day).

Combined medical and surgical treatment may be necessary.
General treatment should be carried on as mentioned before.

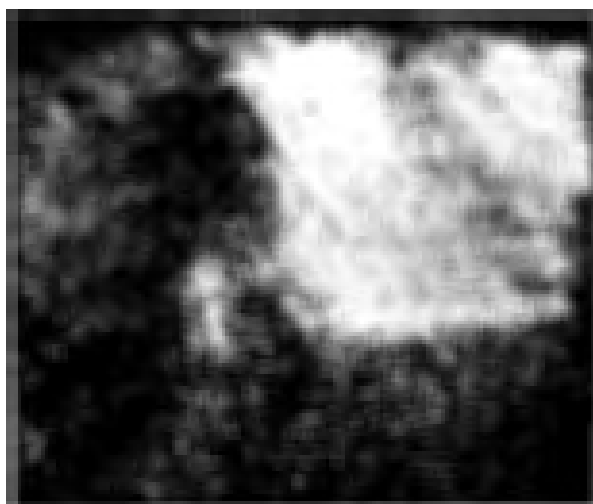


Fig. 27 : Same case of fig. 26 after rupture of pneumatocele or abscess, leading to pneumo-thorax and partial lung collapse.

HEMOPHILUS INFLUENZAE PNEUMONIA :

It is usually preceded by U.R.T. infection and may be meningitis. It causes marked destruction of bronchial and bronchiolar epithelium, interstitial infiltration and hemorrhagic edema.

The lesion is usually lobar and is difficult to be differentiated from pneumococcal pneumonia. However, the onset of the disease is usually gradual and the course moderate and prolonged.

The X-ray picture is usually one of lobar pneumonia.

The diagnosis is not easy. There is moderate leucocytosis with relative lymphopenia. Isolation of the organism from the blood or pleural exudate is necessary to establish the etiology.

Complications are common especially during infancy.

The therapy of choice is ampicillin 150 mg/kg/day. General, symptomatic and supportive measures are necessary.

KLEBSIELLA PNEUMONIAE PNEUMONIA :

This kind of pneumonia occurs in nurseries. Its course is fulminating while the distribution is lobar. The affected area breaks into multiple abscesses similar to those of staph. aureus pneumonia.

The treatment of choice is kanamycin 15 mg/kg/day given I.M., 12 hourly for two weeks. Friedlander's bacillus is also sensitive to gentamycin and polymyxin.

BRONCHOPNEUMONIA

(Secondary Pneumonia)

Bronchopneumonia tends to attack infants and young children already debilitated by some disease. It is not common after the first two years of life, but during this period any bronchitis may quickly develop into bronchopneumonia.

Etiology : Bronchopneumonia is always secondary, the so called primary is usually due to overlooked nasal catarrh. The infection is essentially endogenous, the organisms spreading along and then through the bronchial mucus membrane. The disease follows or complicates : -

- A) *Infectious fevers* : as measles, scarlet fever, pertussis, influenza etc... The organisms of these diseases invade and destroy the mucus membrane and so the organisms which are normal inhabitants of the air passages attack it and lead to bronchopneumonia.
- B) *General debilitating diseases* : as malnutrition (wasting and kwashiorkor), severe rickets, gastro-enteritis, miliary tuberculosis, prolonged skin diseases etc.. Here all the body is weak and the chest is included and is attacked by the organisms which are usually present, bronchopneumonia develops often with fatal result. The common organisms responsible beside the pneumococcus are the para-influenza, respiratory syncytial, adenoviruses, staphylococcus, H. influenza and klebsiella pneumoniae (table 15).

Pathology : The respiratory tree and its supporting tissue are affected in varying degrees. The essential element is severe bronchitis which extends to the finer bronchioles and later to many alveoli. The walls of the bronchi and bronchioles are thickened and infiltrated with lymphocytes, plasma cells and neutrophils. The lumens contain mucus and neutrophilic exudate.

The interstitial tissue around the bronchioles is thickened by an inflammatory infiltrate similar to that present in the bronchiolar walls.

The alveoli are affected in three different ways : -

- a) Owing to blocking of the bronchioles by secretions or exudate, small areas of collapse of lobular distribution are produced.
- b) The inflammatory process extends to some of these alveoli as well as to others and areas of lobular consolidation result.
- c) The adjacent groups of alveoli may become distended with air i.e. emphysematus.

Symptoms & signs Onset is usually gradual and is preceded by signs of bronchitis. The outstanding feature of bronchopneumonia is rapid distressed breathing, dyspnoea or orthopnoea, cyanosis and cough. There is inverted breathing, grunt and active dilatation of the alae nasi. The chest reveals signs of bronchitis with the addition of those of areas of consolidation and presence of crepitations of various kinds according to the underlying pathology. Cardiac distress is often present.

X-ray of chest shows patchy mottling of the lung fields or diffuse involvement with nodular lesions or pseudo-lobar consolidation. Increased bronchovascular markings, usually in the lower lobes, is noticed (Fig. 28)



Fig. 28 : Bronchopneumonia.

Clinical types :

- a) Fulminating or suffocating type where the lesion is wide spread with blocking of the bronchioles that often ends fatally.

- b) Acute bronchopneumonia as described above or the lesion may be pseudo-lobar instead of being bilaterally scattered
- c) Latent type which is not diagnosed during life but is discovered at autopsy. It occurs in marasmic and cachectic babies who cannot react to infection either by fever or cough and thus nothing attracts the attention to bronchopneumonia.

Differential Diagnosis : To be differentiated from severe acute bronchitis, acute bronchiolitis, primary atypical pneumonia, lobar pneumonia, acute exacerbation in bronchiectasis, patchy atelectasis, pulmonary tuberculosis and chronic passive pulmonary congestion in heart failure.

Complications : Similar to those mentioned under primary pneumonia with predominance of suppurative lesions. Fibrosis of lungs, bronchiectasis or flaring of tuberculous focus, may follow.

Prognosis : Bronchopneumonia taxes the patient's strength so much so that none is left to deal with complications. Cardiac failure is a common termination.

Treatment : Prophylaxis and general treatment as mentioned under primary pneumonia. As for specific therapy, two agents instead of one i.e. penicillin plus chloramphenicol, sulphonamide or tetracyclines should be administered until bacteriological results are obtained.

Mild expectorants and digitalis may be needed.

VIRAL PNEUMONIAS

As mentioned before, the same viruses may affect the respiratory tract at different levels producing different clinical syndromes.

Certain viruses are known to be capable of invading the lower respiratory tract in children. The most frequent and severe affections are due to the respiratory syncytial virus, but many others share as the adenoviruses, para-influenza, myxoviruses, influenza, measles etc. On the other hand, virus infections of the respiratory tract render the patient more susceptible to bacterial invasion and thus a secondary pneumonia develops as a complication.

Pathogenesis : Viral pneumonias are usually interstitial. There is invasion of the walls of the alveoli and bronchi as well as the surrounding tissues with round cells, mainly of the mononuclear type. Necrosis of the

tracheal and bronchial epithelium may occur and pave the way for secondary bacterial invasion.

Symptoms & signs : The onset may be acute or gradual. There is coryza, mild to moderate temperature and cough. If the bronchi are plugged with necrotic material or the bronchioles are also affected respiratory difficulty usually appears. Breath sounds are normal to harsh. Rhonchi and/or fine crepitations may be only heard because there is too little exudate inside the alveoli.

X-ray shows areas of diffuse or patchy clouding that tend to have peribronchial distribution (Fig. 29).



Fig. 29 · Viral Pneumonitis.

Laboratory investigations reveals normal or a slight leucopenia and growth of non-specific organisms from nasopharyngeal cultures.

Treatment : No specific treatment, symptomatic management by moisture and oxygen inhalation. For secondary infection, the proper antibiotic should be given.

PRIMARY ATYPICAL PNEUMONIA

Is a syndrome characterized by distressing cough, little dyspnoea, mild fever and malaise. The x-ray shows pneumonic involvement of special distribution and is out of proportion to the physical signs.

Etiology Mycoplasma pneumoniae Eaton agents are probable for most cases (table 15).

Epidemiology : It occurs usually as sporadic or endemic disease but epidemics have been reported in institutes and camps. The disease is met with everywhere with no geographical limitations, no special season though more in winter, no particular climate, and no special age. It is not easily diagnosed in infants and there is evidence that some of the cases of bronchiolitis may belong to this syndrome.

Clinical features : Incubation period is 10-20 days. Onset is usually gradual with mild fever, malaise and cough which soon becomes severe and distressing. The cough is initially dry and paroxysmal like that of pertussis and the sputum may be streaked with blood. Dyspnoea and cyanosis are either absent or mild.

The contrast between the incidence of symptomatology and the physical findings can be shown in the following diagram.

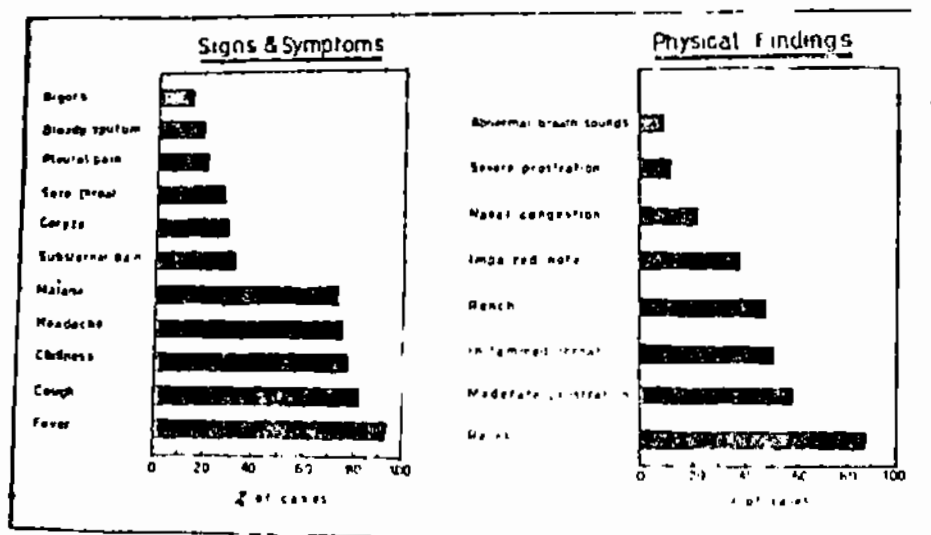


Fig. 30 - Symptomatology and physical findings of atypical pneumonia.

X-ray findings occur early before symptoms and signs appear and the changes are out of proportion to the physical findings. It reveals enlarged hilar shadow with patchy type of peribronchial or pulmonary infiltration. The lesion may be either homogenous, nodular or patchy but occasionally with sharp margin and often basal. The lesion is not limited or related to anatomical structure. In infants there may be widespread, generalized obstructive emphysema.

Laboratory findings :- W.B.C. count is within normal range. Sedimentation rate is usually increased. Cold agglutinins against group-O-human R.B.C.s and/or agglutinins for streptococcus MG appear during the second week and persist for several weeks in 50 - 75% of cases and are of diagnostic value.

The course of the acute phase averages 8 - 10 days or more. Complications are not common and prognosis is good.

Treatment :- Is mainly supportive and symptomatic like that of bronchiolitis.

The broad spectrum antibiotics especially the tetracyclines and erythromycin are effective against this agent.

ASPIRATION PNEUMONIAS

Aspiration of amniotic fluid, blood, foreign body, food, powder, kerosene, oils etc., may lead to pneumonia. The severity of pulmonary reaction depends upon the kind and size or amount of inhaled material, and whether it initiates hypersensitivity or not.

KEROSENE PNEUMONIA & POISONING

Kerosene when ingested is rapidly absorbed from the stomach. The main organs which may be affected are :-

1. The central nervous system, because in children it is very susceptible to its toxic effect.
2. The lungs are usually affected by aspiration of kerosene either during its ingestion or vomiting, or through blood after its absorption and excretion into the lungs.
3. The liver, heart, kidneys and/or spleen through vascular damage.

The clinical pictures that we may meet depend on which of the fore-mentioned organs is severely affected and thus we may get :-

- I — *Acute toxicity with depression of the central nervous system and minimal respiratory changes* : Drowsiness, vomiting and cough. These may be followed by stupor or coma. Although pulmonary signs are minimal, yet x-ray may reveal infiltrations in 50% of these cases. Recovery is usually rapid.
- II — *Severe pneumonia* : Vomiting, choking, cough, hyperpyrexia, tachypnoea, cyanosis and tachycardia. There are rales in the lungs especially bases and fluid may develop in the pleural cavities. X-ray shows patchy mottling which becomes later confluent. Recovery is prolonged.
- III — *Severe pneumonia with evidence of degenerative changes in the myocardium, liver, kidneys and/or gastro-intestinal tract* : Clinical picture is similar to the preceding one but with dilatation of the heart, enlarged liver and spleen, urinary findings (alb., cells, casts) and occult blood in stools. Prognosis is poor. Recently partial hyaline membrane was found in most of the fatal cases.

X-ray shows various degrees of ill-defined homogenous or patchy clouding in the affected segments.

Treatment :

If the patient is seen early and the amount of ingested kerosene is thought to be much, give 100 ml. of liquid paraffin and do stomach lavage using 2% sodium bicarbonate solution.

If the patient comes late give him saline cathartic only.

In both cases do not induce vomiting for fear of aspiration. Oxygen inhalation may be needed.

Antibiotics at first I.M. and then orally are given for about 10 days. Hypertonic glucose I.V. for pulmonary edema may be needed. Circulatory and/or respiratory stimulants may be needed also.

BRONCHIAL FOREIGN BODY

Inhalation of a foreign body usually produces immediate and severe respiratory distress with choking, coughing, gagging, stidor and cyanosis but rarely death. On the other hand, such respiratory manifestations may be mild or missed and the aspiration of the foreign body is followed by a silent period before symptoms and signs of secondary bacterial infection in the obstructed bronchus make their appearance.

The changes produced by settling of a foreign body in a bronchus depend

upon the nature of the foreign matter and the degree of obstruction of the air passages.

In the former respect, foreign bodies of vegetable matter result in early, severe and recurrent bronchitis and/or pneumonia, and in some cases formation of lung abscess. Metallic or plastic foreign bodies may remain without giving any trouble or secondary infection for a long time.

As regards obstruction, if the foreign body is non-obstructive it may produce no or few symptoms even after a long time. If it is obstructive, it produces symptoms and signs, and the underlying pathology depends on whether the obstruction is partial or complete.

Partial obstruction which permits air to pass in both directions but with some difficulty causes *wheeze* only.

When a primary bronchus is partially obstructed to a degree which permits the entry of air into the alveoli, but hinders its exit during expiration i.e. "check valve", the result is *obstructive emphysema*. The physical signs of obstructive emphysema are bulging, limited expansion, hyper-resonance and diminished breath sounds on the affected part. In marked cases the mediastinum is shifted to the other side. X-ray may identify the foreign body if opaque. Distal to the site of obstruction the lungs are overinflated with air. In marked cases the mediastinum is displaced to the healthy side, the intercostal spaces are wider and the diaphragm is flat and at a lower level on the affected side (Fig. 31)



Fig. 31 : Obstructive Emphysema of the left lung caused by non-opaque foreign body.

Complete obstruction i.e. «stop valve» is followed by resorption of air from the obstructed pulmonary segment or lobe and the result is *collapse* of that area. In such a case, beside the diminished movement there may be diminished size of the affected side of the chest together with decreased note and vocal resonance and decreased or absent breath sounds. In marked cases the mediastinum may be shifted to the affected side and the diaphragm higher in position.

X-ray shows the atelectatic lobe or segment to be small, opaque and retracted towards the midline, the apex of which is at the hilus of the lung. The leftover area is in part filled by compensatory emphysema of the other lobes of the lungs, in part by mediastinal shift to the affected side, by rise in the level of the diaphragm and by approximation of the ribs and some falling inwards of the chest wall (Fig. 32)



Fig. 32 - Collapse of the left lower lobe.

Treatment. Bronchoscopy is essential for diagnosis and possibly removal of the foreign body. Suitable antibiotics are used. Postural drainage preceded by isoproterenol aerosol has been successful in removal of a variety of foreign matter. Rapid re-expansion of the collapsed part must be achieved if bronchiectasis is to be avoided.

PULMONARY SUPPURATION

LUNG ABSCESS

Lung abscess is a localized area of suppuration of the lung accompanied by marked constitutional disturbances and profuse foul purulent sputum.

Etiology : It usually follows (1) aspiration of foreign body or infected material (associated with tonsillectomy or extraction of teeth), (2) an infected embolus, (3) pneumonia, (4) neoplasm or (5) it may be idiopathic without apparent cause.

Pathology The common site is the right lower lobe. At first there is necrosis of the pulmonary tissue (closed abscess), followed by liquefaction and evacuation of big amount of purulent material and cavity formation (open abscess). The walls of such a cavity are ragged in the early stage but later become defined by dense fibrosis. Evacuation of the abscess contents may occur in the pleura producing putrid empyema.

Symptoms : Malaise and anorexia together with gradual rise of temperature occur a few days after infection. The temperature is usually hectic. Cough without sputum makes its appearance and when the abscess opens foul purulent sputum is discharged.

Signs . The chest becomes flat and later on retracted over the abscess area with limitation of respiratory movements. Fremitus is decreased if there pleural reaction or collapse of lung; and increased if there is consolidation around the abscess cavity. The note is impaired to dull if there is pleural reaction or inflammation about the cavity, but tympanitic over the cavity if at the periphery and contains air. Breath sounds are usually cavernous or an phoric and the intensity depends on the site of the abscess whether deep or superficial. Moist rales are heard as well as various kinds of crepitations if there is active inflammation around the cavity. Spoken whispered voice is intensified

At an early stage, X-rays will usually show a wedge-shaped area of opacity due to the consolidation or closed abscess formation. After it opens, and its contents are discharged, a cavity is seen with or without fluid level, surrounded by an area of opacity due to consolidation (Fig. 33).

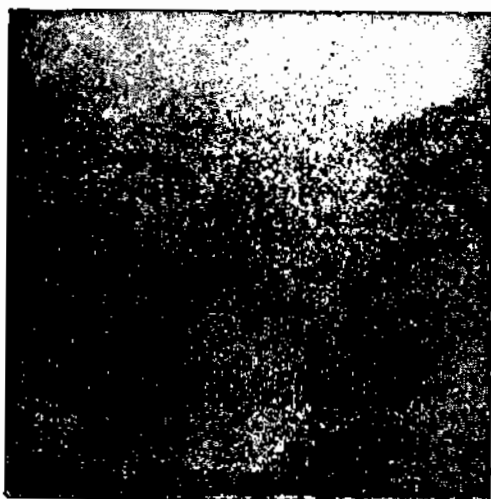


Fig. 33 : Lung Abscess.

Differential Diagnosis Refer to pneumonia and bronchopneumonia.

Trophylaxis : Local anaesthesia for tonsillectomy decreases but do not abolish the incidence of aspirating infected material. A prophylactic course of sulfonamides or penicillin is a practical and wise precaution. Early discovery and adequate treatment of pneumonia or any sepsis in the body is of prime importance.

Treatment :

- Help good drainage of the abscess cavity by proper postural drainage and may be bronchoscopic aspiration also
- Help liquification of the abscess contents by proteolytic enzymes.
- Try to combat the infecting agent by proper systemic antibiotic administration.
- Aspiration of the abscess and instillation of antibiotic solution is very helpful
- Open surgical drainage should be resorted to when medical treatment proves to be inadequate.
- Lobectomy is indicated in case of chronic rigid abscess and for residual bronchiectasis.

BRONCHIECTASIS

Bronchiectasis is a condition of chronic and progressive inflammation of the bronchi and their supporting tissues that induce an abundant formation of connective tissue in and around the bronchial walls. This results in dilatation of the bronchi and their fixation in such a stretched state. Stagnation of purulent exudate occurs leading to more weakening of the bronchial walls, more fibrosis, more dilatation and thus a vicious circle is established.

The infections of childhood that most commonly precede bronchiectasis are pneumonia, measles, pertussis, influenza, cystic fibrosis of the pancreas and sinobronchitis. Foreign body may initiate infection as well. Congenital anomalies of the bronchi may be responsible.

Pathology : At first, diffuse bronchial dilatation, later, fusiform or saccular dilatations with accumulation of secretions. There is mucosal atrophy, ulceration of the bronchial walls that often leads to stenosis. At times there is peribronchial abscess formation, interstitial inflammation with pulmonary fibrosis and pleural thickening. Other times, bronchopneumonic areas with compensatory emphysema of the healthy lobes occur. Such a varying pathology is the cause of the variable physical signs met with in this disease.

Once bronchiectasis is established, the lesions are irreversible and represent areas which are particularly susceptible to reinfection and superimposed infection, so that bronchiectasis requires management throughout the remainder of the patient's life.

Symptoms : Hacking cough with an abundant discharge or swallowing of sputum particularly in the morning. The cough is initiated by change of position and may be paroxysmal. The sputum is loose and purulent with offensive odour and may contain traces of blood and sometimes significant amounts of it. Low grade fever that sometimes shoots due to the repeated episodes of pneumonia.

Signs : Chest signs are variable. In mild cases there may be nothing or the signs are those of bronchitis. In severe cases, there is flattening and retraction of the chest over the affected area with lagging of respiratory movements. Vocal fremitus is increased over the affected lobe, if pleural thickening is not too great. There is impairment to dullness over the diseased part but at times a tympanic note over a saccular bronchus near the pleura. Auscultation over the affected lobe gives bronchovesicular to bronchial breath sounds which are distant or faint if the pleura is greatly thickened. If a large saccular

dilation lies close to the periphery, cavernous breathing is heard. Coarse crepitations, consonating and non-consonating (bubbling), varying from time to time are always heard. Bronchoscopy is essential to determine the etiology. In severe and long standing cases, retarded development, poor physique and clubbing of digits take place.

X-rays of the chest may show only increased bronchovascular markings extending toward the base of the involved lung. The lung may appear to contain many small air-filled cavities (Fig. 34).



Fig. 34 : Bronchiectasis.

Xrophylaxis : Because pneumonias are most common among children living in unfavourable conditions; therefore bad housing, overcrowding and poor nutrition should be combated. Exposure to influenza, measles, pertussis etc. should be avoided. Vaccination against such diseases and proper treatment if contracted will definitely lower the incidence of the disease.

Treatment : Fresh air, moderate warmth, oxygen inhalation when indicated and frequent drinks.

The child must be kept in bed when febrile and his position must be changed frequently. Search for and eliminate all foci of infection. Postural drainage and breathing exercises if done properly are very helpful. Aerosol inhalation with antibiotics chosen on sensitivity tests. Proteolytic enzymes may help. In some cases repeated bronchoscopic aspirations may be needed. The general health should be supported by good diet and tonics.

Initially 2 - 4 weeks course of systemic broad spectrum antibiotic is advisable to overcome infections. Later, whenever infection occurs it should be vigorously treated to avoid new areas of destruction. Approximately 10 - 20% of patients with bronchiectasis have associated sinusitis and this needs treatment. Expectorants as glyceryl guaiacolate may be helpful. Iodides were used to decrease the viscosity of secretions. Oxygen inhalation is needed when pulmonary insufficiency has resulted from extensive bronchiectasis and lung fibrosis.

Lobectomy in selected cases should be tried if medical treatment fails.

DISEASES OF THE PLEURA

PNEUMOTHORAX

Pneumothorax is an accumulation of air in the pleural cavity either free or localised by adhesions. It is uncommon during childhood.

Etiology : It may occur in the course of pneumonia, infarct, abscess or gangrene of the lung. It may be secondary to trauma or thoracic disease when we may get hemopneumothorax, hydropneumothorax or pyopneumothorax. It may also occur during the paroxysmal stage of pertussis or be due to spontaneous rupture of a cyst or an emphysematous bleb. In the neonatal life pneumothorax may be related to birth injury or faulty resuscitation technique. It is common in staphylococcal pneumonia in infancy.

Pathology : Spontaneous pneumothorax usually results from a ruptured subpleural bleb or originates interstitially. In late childhood, localised pneumothorax may be of tuberculous origin.

Symptoms : Onset is usually sudden and accompanied by pain, sense of tightness and breathlessness.

Signs : If small amount of air, no abnormality is detected. In large accumulations of air there is increased size of the chest with levelling or bulging of intercostal spaces and decreased respiratory movements of the affected side. The trachea is displaced to the opposite side.

Tactile fremitus is decreased in small amounts but absent in large accumulations of air. According to the degree of pneumothorax, percussion will reveal hyper-resonance to tympany, displacement of the heart to the opposite side and may be lowered diaphragm on the affected side. Breath sounds decreased to absent in proportion to the amount of air present, or distant amphoric breath in the presence of high pressure, coin test is positive. Succussion splash if fluid is also present can be elicited.

X-rays of the chest shows a translucient area around the sharply outlined lung which collapses toward the hilus. If the air is under tension, shift of the mediastinum, wide intercostal spaces and flat diaphragm appear. (Fig 35)

Prognosis : Depends on the cause and whether there is fistula or not.

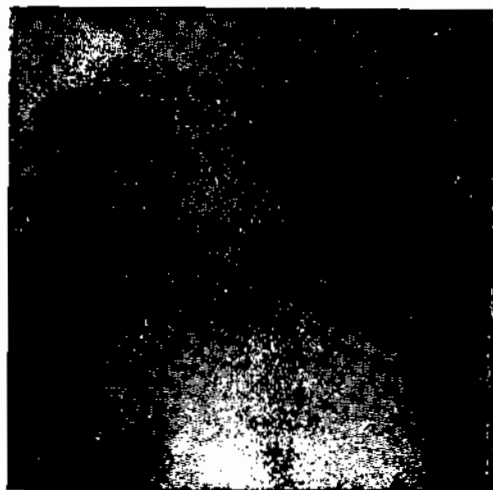


Fig. 35 : Right tension Pneumothorax.

Treatment : If there is no fistula and the amount of air is small, it is usually absorbed within a week or so. If there is bigger collection of air and the patient is becoming cyanosed with difficult hurried breathing, aspirate the chest through the second interspace in the mid-clavicular line with the infant in the semi-sitting position. Tension pneumothorax with fistula is best treated with closed aspiration using polythylene catheter taped to the chest wall and attached to a water-seal trap.

If this fails and in cases of post-pneumonic lung cysts leading to pyopneumothorax, surgical treatment to close the fistula will be necessary beside specific antimicrobial therapy and suitable supportive measures.

PLEURISY

Lesions of the pleura i.e. pleurisy or pleuritis, were commonly observed in infancy and childhood as secondary complications to pulmonary infections mainly pneumonia and tuberculosis. It is less frequent now because of the early treatment of bacterial pneumonia and decreased incidence of tuberculosis. Probably all cases of pleurisy begin as dry before many of them proceed to fluid or pus accumulation.

DRY PLEURISY

Dry or plastic pleurisy may occur in association with pneumonia especially the pneumococcal type as well as with tuberculosis. Occasionally it is a manifestation of rheumatic fever.

Pathology : The surface of the pleura becomes rough, dry and lusterless. Later it is covered with fibrin which may form a thick layer. In tuberculous cases tubercles are also found. In advanced conditions adhesions usually develop between the two layers of the pleura.

Symptoms and Signs : May be masked by those of the original disease. Older children complain of pain in one side of the chest, particularly when they cough, sneeze, strain or breath deeply. The pain may be referred to the shoulder and neck in cases of apical pleurisy and to the abdomen in diaphragmatic affections. The child usually lies on the affected side to minimize its painful movements. Local tenderness may be demonstrated.

Except in thickened pleura the note is normal. A characteristic friction rub is heard over the affected area. Breath sounds are normal but diminished in case of thickened pleura.

Differential Diagnosis : Epidemic pleurodynia, prodroma of herpes zoster, acute abdominal conditions (appendicitis, mesenteric adenitis) and meningism.

Treatment : Should be directed at the underlying problem, the control of which is followed by relief. In most children pleural pain can be relieved by simple measures as aspirin or other analgesics. In severer cases codeine in daily doses of 3 mg./Kg divided on 4 equal intervals is useful. The local application of heat or cold helps to relieve pain. Immobilizing the chest by strapping with adhesive plaster is rarely needed and it is contraindicated with pneumonia.

PLEURAL EFFUSION

Wet pleurisy is usually a reaction to diseases in the adjacent structures, although it may be a manifestation of a systemic process.

Etiology :

A) Pleural Exudate : Serous or sero-fibrinous pleurisy is rare in infancy and uncommon in young children. Tuberculosis is by far the commonest cause. It may be due to rheumatism. Little amounts may accompany pneumonia. Malignancy is a rare cause.

B) Pleural Transudate : As in cases of congestive heart failure, nephritis, nephrosis, and severe malnutrition.

Pathology : If it is exudate, usually it follows dry pleurisy. When fluid begins to accumulate in the pleural cavity, the lung, by virtue of its elasticity, retracts actively in order to maintain the negative pleural pressure which is necessary for normal respiration. If the fluid continues to be effused, the lung contracts to its full extent and the negative pressure on that side of the pleura is abolished. With more fluid, positive pressure is produced and the lung is compressed.

The lung owing to its hilar attachment, begins to retract upwards and medially allowing the fluid to accumulate at the base and in the axillary region where it reaches its highest level unless previously existing adhesions prevent it. In cases of massive effusion, the mediastinal contents including the heart are displaced away from the affected side; at first they are pulled towards the healthy side by its higher negative pressure and then they are further displaced by the positive pressure of the diseased side when the effusion becomes massive, and the pleural pressure becomes positive.

The exudate is absorbed with varying degrees of rapidity, but thickening of the pleura persists in long standing cases.

Symptoms : The initial symptoms of pleurisy with effusion are those of dry pleurisy i.e. shivering or rigor, fever, pain and dry cough. When effusion appears in the pleural cavity, pain and cough decrease while dyspnoea appears and may be cyanosis also if the effusion is poured out rapidly so that rapid collapse of the lung and mediastinal shift occur. Expectoration is not common unless there is underlying lung disease or hyperemia of the sound side.

Signs : Vary according to the amount and location of the fluid present. There is asymmetry of the chest, the affected side being more in size with bulging of its intercostal spaces in massive accumulation of fluid. Movements are decreased or absent on the affected side. Trachea may be deviated to the opposite side and is always so when the effusion becomes massive. Tactile fremitus decreased to absent over the effusion, while a friction rub may be felt at the upper level of the fluid. The note is dull to flat with increasing amount of fluid when displacement of the heart, liver and/or spleen can be detected. If the effusion is not massive, skodatic note due to relaxed lung tissue above the level of the effusion may be detected.

Auscultation reveals diminished to absent breath sounds and vocal resonance

over the effusion. At the level of effusion the voice sound has a nasal tone i.e. aegophony. If the effusion is massive and the lungs are completely collapsed bronchial breathing is transmitted to the stethoscope. The same occurs if there is consolidation of the underlying lung. Rales may be heard from the lung above the effusion.

The signs of non-inflammatory fluid, such as blood, chyle, serous effusion of congestive heart failure etc., are the same except for the friction rub.

Diagnosis :

(1) Clinically (i.e. symptoms and signs).

(2) X-ray shows diffuse clouding, the upper border of which is concave and extends up the lateral chest wall i.e. axilla (Fig. 36). If the effusion is massive, the trachea and mediastinum are seen to be displaced to the opposite side (Fig 37).

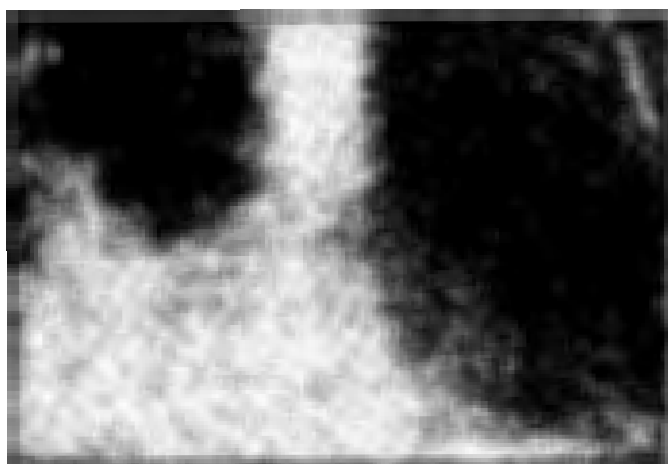


Fig. 36 : Right Pleural Effusion.

(3) Pleurocentesis and aspiration of fluid is imperative for diagnosis. The puncture could be done at the 6th space in the midaxillary line, 7th in the posterior axillary line or 8th space in the scapular line. The pleural fluid obtained is to be examined by the naked eye, microscopically, a culture may be done—and/or animal inoculation. Transudates are clear yellow fluids, do not coagulate, have specific gravity less than 1018, cells below 4/cml. and proteins less than 2 grams per cent. No organisms could be detected on stained film and

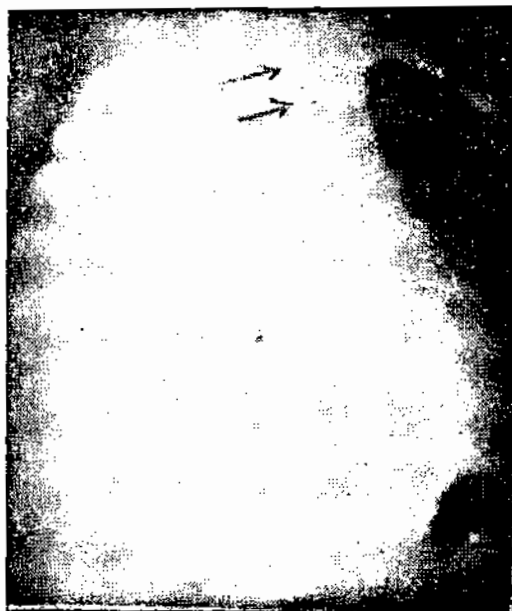


Fig. 37 : Right Massive Pleural Effusion.

they are sterile. Exudates are opalescent, may coagulate, of higher specific gravity, contain numerous cells/cml. and the proteins are more than 4 grams/100 mls.

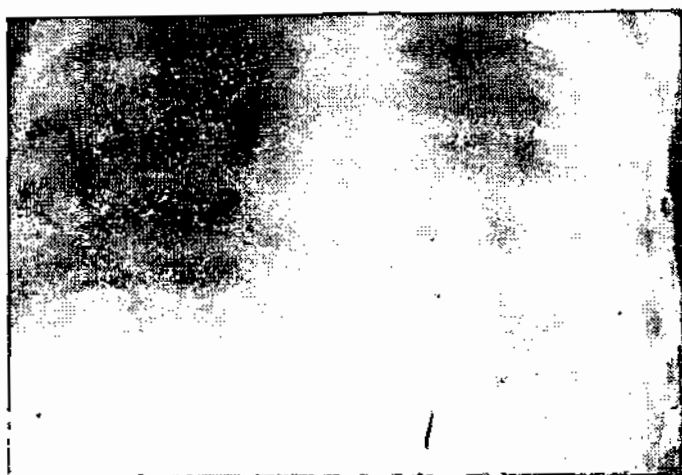


Fig. 38 : Left Pleural Thickening.

Differential diagnosis : Pneumonia especially the massive form, massive collapse, fibroid lung with thickened pleura, pressure on and obstruction of a main bronchus, large pericardial effusion, bronchiectasis and malignant disease of the lung, pleura or mediastinum.

Complications : Pleural thickening and adhesions, (Fig. 38), permanent collapse and carnification and interstitial fibrosis.

Treatment : The management is basically that of the primary disease. If there is respiratory distress, relief will promptly follow removal of the fluid. Occasionally the effusion reaccumulates and repeated aspirations are needed. In such cases a search for possible presence of intrathoracic malignancy or subdiaphragmatic abscess should be pursued. The rest of treatment is symptomatic and supportive similar to that of dry pleurisy. Corticosteroids may aid rapid absorption of the effusion.

EMPHYEMA

Purulent exudative pleurisy in children and particularly in infants, is chiefly a complication of acute or chronic pulmonary infections. Ninety per cent of the cases are due to pneumonia. The rest are secondary to trauma, necrosed rib, rupture of an abscess or as a metastasis from infection elsewhere. The causative agent is usually the pneumococcus but staphylococci, streptococci or H. influenza may be the cause especially early in the course of pneumonia in infancy and young children.

Pathology : Same as in pleural effusion. Syn-pneumonic empyema is common under the age of 2-3 years because the infection is generalised involving both the lungs and pleura. Blood culture at this age period is positive in about 40% of cases. Meta-pneumonic empyema occurs above 2 years and it develops either directly after a severe pneumonia or the pneumonia may be overlooked and the child is brought for general symptoms.

Symptoms and Signs : Symptoms are generally the same but more severe than those of sero-fibrinous effusion. Empyema may be missed in children because fever, cough and pain are all present in pneumonia also; therefore daily examination of cases of pneumonia is necessary for detecting empyema. Severe symptoms may indicate syn-pneumonic type. With the meta-pneumonic type, the fever may persist after the pneumonia or re-appear after the crises. There may be no fever due to development of immunity against the pneumococcus during the course of pneumonia. The general signs of anemia, anorexia, sweating, wasting and clubbing of fingers develop gradually. Diarrhea due to

toxemia may occur and nutritional edema may follow quickly. Physical signs are essentially the same as those of serous effusion.

Diagnosis :

- a) Clinically empyema is not very difficult to diagnose, but in cases of interlobar effusions where the pus has accumulated between the lobes of the lungs only, the diagnosis may become difficult (Fig. 39). The same may be said of mediastinal pleurisy when the exudate accumulates between the visceral pleura enveloping the lung and the pleura that lines the side of the mediastinum. Diaphragmatic pleurisy may cause such difficulty also.



Fig. 39 : Interlobar Effusion (Lateral view).

- b) X-ray gives great help in diagnosing the above mentioned localised empyemas.
- c) Pleural puncture may be difficult if the effusion is localised or the pus is so thick for aspirator. In long standing cases, fibrin deposits and the fluid becomes very thin. In such cases the pneumococcus may die and the fluid becomes sterile.
- d) Blood count usually shows marked leucocytosis.

Complications : Meningitis, arthritis and peritonitis. Neglected cases may rupture through the diaphragm or the chest wall (empyema necessitatis), or a bronchus leading to pyo-pneumothorax (Fig. 40).



Fig. 40 : Right Pyopneumothorax.

Prognosis The younger the child, the more severe the course and the poorer the prognosis. The type of the pathogenic agent influences the prognosis. Pneumococcal empyema has a more favourable termination than the streptococcal and staphylococcal types. Delaying aspiration makes the prognosis worse because it leads to non-expansion of the lung.

Treatment :

- a) Specific systemic antibiotic therapy should be given after culturing and doing sensitivity tests to the pleural fluid.
- b) Repeated aspiration of pus and instillation of the specific antibiotic into the pleural cavity. Fibrin solvents, as streptokinase and streptodornase, may be introduced also in chronic cases when the fluid contains lot of solid fibrinous material.
- c) General measures and supportive treatment is the same as in serous pleurisy.
- d) Surgical measures : Closed intercostal drainage may be necessary early in the course of the disease in infants, and when improvement does not occur after three or four weeks in older children.

In long standing and neglected cases extensive fibrinous deposit over the surface of the collapsed lung occurs and may require decortication.

A.S. ABBASSY

Chapter XIII

THE CARDIOVASCULAR SYSTEM

THE HEART

Normal Heart in Childhood :

It is worth noting that the normal heart of childhood differs in several important respects from that of an adult : —

1. The heart in childhood normally lies on a higher plane than in adults. The Point of Maximal Cardiac Impulse varies with age : —

- (a) Infants : 3rd or 4th interspace, just outside the nipple line.
- (b) 2 — 5 years : 4th interspace at the nipple line.
- (c) Over 5 years : 5th interspace at or within the nipple line.

2. The rate of the heart is more rapid in childhood, being (on an average) 130 per minute at birth, 110 at 2 years, 100 at 3 years, 90 at 8 years and 80 at 12 years of age.

3. Sinus arrhythmia or «juvenile irregularity of the heart», with its phasic respiratory variations of pulse rate, is physiological in childhood, being secondary to natural hypersensitivity of the vagus nerve mechanism.

4. The pulmonary second sound is relatively loud in children and may exceed in intensity the aortic second sound.

5. Either the first or second sound may be split in any valvular area without causing concern.

6. A third heart sound is present in about one-third of all children.

7. Cardio-respiratory and functional or innocent murmurs are very common in children. In fact, it is customary to expect a soft and transient systolic bruit in a child after exercise or emotional excitement.

8. Right axis deviation in the E.C.G. is a normal finding in infants and small children.

CONGENITAL ABNORMALITIES OF THE HEART

The etiological factors in congenital heart disease are only vaguely perceived at the present time. It is known that certain environmental factors operating in early pregnancy can result in malformation, e.g. rubella, irradiation, and drugs such as thalidomide. In most cases, however, no specific cause can be

detected. Although heredity cannot be completely ruled out as an etiological factor, it does not appear to be of great importance.

Cardiac malformations are well recognized to be the frequent accompaniment of several syndromes, e.g. mongolism, arachnodactyly, polydactyly, Turner's syndrome, . . . etc

Classification : The following classification of the more common anomalies will be used :

1. With no shunt :

- (a) Dextrocardia (as a part of situs inversus).
- (b) Endocardial fibroelastosis.
- (c) Aortic stenosis.
- (d) Pulmonary stenosis.
- (e) Coarctation of the aorta.

2. With left-to-right shunt (no cyanosis) :

- (a) Patent ductus arteriosus.
- (b) Ventricular septal defect.
- (c) Atrial septal defect.

3. With right-to-left shunt (with cyanosis) :

There is shunting of venous blood from the right to the left side of the heart, so that it passes into the systemic circulation without being oxygenated in the lung. This group is further subdivided into :

(A) With diminished pulmonary blood flow :

- 1. With right ventricular hypertrophy : (a) Fallot's tetralogy. (b) Fallot's triology. (c) Pseudo-truncus arteriosus.
- 2. With left ventricular hypertrophy : Tricuspid atresia.

(B) With increased pulmonary blood flow : (a) Complete transposition of the great vessels. (b) Eisenminger syndrome. (c) Truncus arteriosus.

DEXTROCARDIA WITH SITUS INVERSUS

Dextrocardia indicates that the heart is in the right hemithorax, the apex pointing to the right. This condition is frequently associated with situs inversus with abdominal and thoracic organs transposed to opposite side of the body. Bronchiectasis and paranasal sinusitis may complicate dextrocardia with situs inversus (Kartagener's syndrome). There is usually no cardiac defects.

Diagnosis : (1) Clinical Apex beat on the right side. Heart sounds louder on right side. Stomach (percussion) on right side. Liver on left side. (2) X-ray : Situs inversus. (3) E.C.G. Lead I is the mirror image of the normal tracing with inverted P and T waves
No treatment.

N.B. There is another type of dextrocardia which is called isolated dextrocardia in which the abdominal viscera are in their normal positions. In this, there are severe cardiac malformations; commonest are tricuspid atresia with transposition of the great vessels or single ventricle and transposition of the great vessels; Fallot's tetralogy is rare. The prognosis in this anomaly is poor and most patients succumb during infancy.

ENDOCARDIAL FIBROELASTOSIS

There is a fibro-elastic thickening which involves the endocardium and subendocardial tissues. This is most marked in the left atrium and left ventricle where the endocardium has a thickened and milky appearance. The disease may occur alone but is also seen in combination with anatomical abnormalities which involve the aortic valve and arch. The condition behaves functionally like constrictive pericarditis, causing impairment of left ventricular filling, diminished systolic ejection and narrowing of the pulse pressure.

Etiology is obscure. Recently the mumps virus is incriminated when it affects the pregnant woman in the first two months of pregnancy.

Clinical picture : The infant is normal at birth. The onset (between birth and six months of age) may be gradual or acute and is characterized by irritability and refusal of feeding, repeated episodes of vomiting and paroxysmal dyspnea. Slight cough may be noted, and shock and severe respiratory distress may be present in the later stages. Examination shows variable or no murmurs, cardiomegaly and cardiac failure. Expiratory wheezing is often heard. Fluoroscopy reveals an enlarged heart with poor pulsation.

Treatment : Apart from the treatment of cardiac failure, nothing can be done. Prognosis is very poor.

AORTIC STENOSIS

In most cases, there is fusion of the cusps of the aortic valve. Less commonly there is a fibrous ring around the left ventricular outflow tract (subaortic stenosis).

Clinical features : More common in boys. Most are symptomless, but few develop anginal pain on effort. Affected children are usually well grown. The heart is not commonly enlarged. A systolic thrill is palpable at the second right interspace and also along the carotid arteries and in the suprasternal notch. A harsh ejection systolic murmur is best heard in the aortic area. The pulse is anacrotic and of small volume. The pulse pressure is low. X-ray : Normal heart. E.C.G. Left ventricular hypertrophy.

Treatment : Most children with aortic stenosis are likely to live well into middle age. Surgery at the present time is only advised in the most severe cases with anginal symptoms.

PULMONARY STENOSIS

May be : —

- (a) Valvular (fusion or malformed semilunar cusps).
- (b) Infundibular (narrow infundibular chamber between the valve and right ventricle).

Clinical features : — Symptomless. — No cyanosis. — Powerful right ventricular thrust over the left parasternal area. — Systolic thrill at second left interspace. — Harsh ejection systolic murmur, maximum at second left interspace. — Second sound single because the low pressure in the pulmonary artery makes the valve closure inaudible.

X-ray : — Post-stenotic dilatation of pulmonary artery (in valvular stenosis). — Oligemic lung fields.

E.C.G. : Right ventricular hypertrophy. — P-pulmonale.

Cardiac catheter : — High right ventricular pressure. — Steep pressure gradient between ventricle and pulmonary artery. — Withdrawal tracings differentiate between valvular and infundibular stenosis.

Prognosis : *Mild degree* : Compatible with long life.

Severe degree : Heart failure before middle age.

Treatment : Surgical correction under direct vision in all cases where the pressure gradient across the pulmonary artery is more than 20 mm. mercury.

COARCTATION OF THE AORTA

A stenosis of a special type in the aorta. This is a relatively common anomaly and one so amenable to surgery that *palpation of the femoral arteries should form part of the physical examination of every patient of any age.* The common site of nar-

rowing of the aorta is just beyond the origin of the left subclavian artery and of the ligamentum arteriosum.

Clinical features : In a few cases coarctation of the aorta results in C.H.F. in early infancy. In the vast majority, the child is well developed and symptomless. The murmur, which is discovered during routine medical examination, is systolic in time. It is well heard at the aortic area, in the suprasternal notch and in the inter-scapular area. The apex beat is forcible due to left ventricular hypertrophy, but it may not be displaced for many years. Hypertension in upper limbs and very low pressure in lower limbs. Femoral pulse weak or absent. In adolescents, dilated and tortuous collateral vessels may be visible around the scapulae. Left ventricular hypertrophy.

Diagnosis : Reversed B.P. gradient in limbs at any age.

X-ray : No abnormality, or left ventricular hypertrophy. — Notch in the aortic shadow at site of coarctation and the aortic arch above the notch is dilated. — Rib notching (usually more than 10 years of age).

E.C.G. : Normal or left ventricular hypertrophy.

Right heart catheter : Excludes other lesions.

Aortogram : Shows coarctation precisely.

Left heart angio : Shows lesion well.

Right heart angio : Shows lesion poorly.

Differential diagnosis : Hypertension in the young, renal disease, renal artery stenosis, pheochromocytoma and al-dosteronism.

Treatment : Excision and anastomosis. Age : 4 — 7 years.

PATENT DUCTUS ARTERIOSUS

Persistence of fetal pathway through which blood leaving the right heart bypasses the lungs.

Clinical features : Physical retardation but no heart symptoms during infancy.

Murmur in 2nd left interspace appears in infancy. It may be systolic only but later most patients show diastolic component with machinery sound and thrill. Pulse pressure is high.

Flouroscopy : Increased pulmonary vascular shadow with marked arterial hilar dance due to shunt of blood from the aorta through the patent duct into the pulmonary artery. Heart may be of normal size or show left ventricular or combined hypertrophy.

E.C.G. : Normal or left ventricular hypertrophy.

Complications : Congestive heart failure. Subacute bacterial endocarditis.

Treatment : Surgical by ligation or division and ligation of the duct as soon as possible to avoid the complications and physical retardation and lead normal life.

VENTRICULAR SEPTAL DEFECT

Opening 1 — 15 mm. in diameter, most commonly found in the fibrous portion of the septum.

Clinical features :

- (a) *Small ventricular septal defect : Maladie de Roger* : The child is symptomless and development is normal. The heart is normal in size. A palpable systolic thrill and a harsh pansystolic murmur in the 4th interspace at the left sternal border. E.C.G. either normal or shows slight left ventricular hypertrophy.

Prognosis : Good.

Complications : Subacute bacterial endocarditis.

- (b) *Large V.S.D.* : The child is often underdeveloped. Dyspnea on exertion develops early. There is marked susceptibility to respiratory infections. Heart is enlarged with a forceful apex beat. Systolic thrill and pansystolic murmur at 4th interspace (left parasternal).

X-ray : Left or biventricular enlargement. Pulmonary artery dilated. Vascularity of lungs increased.

Complications : Pulmonary hypertension and reversal of shunt with development of cyanosis - Eisenminger syndrome. Pulmonary hypertension is due to increased ejectile force. There is proliferation of intima and later organic obstruction of arterioles. Thus, pulmonary hypertension here is irreversible. At this stage of reversal of shunt operation is contra-indicated.

Treatment : With open-heart surgery, V.S.D. can be repaired. The ideal candidate is the symptomatic patient over the age of 2 years who has moderate pulmonary hypertension and a large left to-right shunt (mortality 5%).

Infants with symptomatic V.S.D.; open heart surgery carries high mortality. In these, surgical production of pulmonary stenosis by pulmonary artery

banding should be considered. This procedure results in relief of C.H.F., and the number of intercurrent infections is reduced. In later years (5 — 6 years), surgical closure of V.S.D. and removal of the pulmonary artery band is carried out.

ATRIAL SEPTAL DEFECT

Two types :

I. Ostium secundum defect : More common. Defect is in the upper part of the septum. Shunt is from left to right (left auricle is in a higher position than the right).

Clinical features : Children are usually symptomless and underdeveloped (left output is diminished due to shunt). Increased susceptibility to respiratory infections. Females more than males. Right ventricle is enlarged. Soft ejection systolic murmur over 2nd or 3rd space (turbulent flow in pulmonary artery due to increased stroke volume). The second pulmonary heart sound is wide and fixedly split (prolongation of right ventricular systole, the ventricle being filled to its maximum from the left-to-right shunt). An apical mid-diastolic murmur may be heard (inflow murmur through the tricuspid).

X-ray : Large pulmonary conus.
Increased vascularity of lungs.

E.C.G. : Partial right bundle branch block.
May be prolongation of P-R interval.
May be right ventricular hypertrophy.

Catheter : Increased O₂ saturation in right atrium.
Catheter may pass through defect.

Prognosis : If defect is of large size, we get increasing cardiomegaly and increasing limitation of exercise tolerance. Pulmonary hypertension develops in 3rd or 4th decade. Increased susceptibility to rheumatic fever (Lutembacher syndrome).

Treatment : Surgical correction under hypothermia in every case in which there is cardiac enlargement. Mortality rate is very low.

2. Ostium primum defect : -- Less common but more serious. — Defect is in the lower part of septum. The base of the defect commonly involves the mitral valve. — Mitral incompetence due to bicuspid anterior valve.

Clinical features : Repeated respiratory infections. — Dyspnea and early fatiguability, eventually H.F. — Children are thin and underweight. — No cyanosis. — Precordial bulge. — Right precordial heave and apical heave. — Pansystolic of M.R. — Pulmonary 2nd sound accentuated and split. — *E.C.G.* : Characteristic : left axis deviation, partial right bundle branch block and right ventricular hypertrophy.

Treatment : Operation. Heart-lung bypass machine. Prognosis is poor.

CYANOTIC CONGENITAL HEART DISEASE

FALLOT'S TETRALOGY

The most common type of cyanotic congenital heart disease in children over the age of 1 year. The classical tetrad consists of :

1. *Pulmonary stenosis* : In most instances infundibular obstruction, sometimes valvular.
2. *V.S.D.* : Left to right shunt.
3. *Dextroposition of the aorta* : The aorta receives blood from both ventricles and this is the cause of cyanosis. The blood from right ventricle passes easier through aorta than through pulmonary artery. The pulmonary arterial tree is therefore hypoplastic.
4. *Right ventricular hypertrophy*.

Clinical features : 1. Cyanosis since birth. 2. Clubbing. 3. Stunted growth. 4. Effort intolerance and squatting. 5. Episodes of deep cyanosis, dyspnea, unconsciousness and may be convulsions (blue spells) mostly due to spasm of infundibulum so that no blood goes to the lungs (disappearance of the murmur of pulmonary stenosis). 6. Heart : Normal size. Right ventricular hypertrophy. Murmur of pulmonary stenosis. Murmur of V.S.D. 2nd pulmonary sound weak, absent or heard (aortic) but single. Never heart failure.

X-ray : — Small heart. — Concavity in region of pulmonary artery. — Apex raised above diaphragm. — Oligemic lungs. — Right aorta in 25% (important).

E.C.G. : Right ventricular hypertrophy.

Treatment : If effort intolerance is evident, the child is breathless after short walk, Taussig-Ballock operation is recommended in which the subclavian artery is anastomosed to the pulmonary artery. Later on, at the age of 6 years, total correction (open heart surgery using heart-lung machine).

FALLOT'S TRILOGY

Consists of : (1) Pulmonary stenosis, usually valvular. (2) Right ventricular hypertrophy. (3) A.S.D.

The degree of valvular stenosis is usually severe. The child has no cyanosis to start with. The degree of enlargement of right ventricle and right atrium is marked. Ultimately, the pressure in right atrium is raised and reversal of shunt at atrial level occurs with the development of cyanosis.

Clinically : (1) Cyanosis; starts later, may be at 1 — 2 years. (2) Mild clubbing. (3) Effort intolerance. (4) Venous engorgement in the neck with giant waves. (5) Heart size ++, right ventricular hypertrophy. (6) Signs of pulmonary stenosis i.e. systolic thrill and systolic ejection murmur.

X-ray : Heart is huge and looks like pericardial effusion. — Oligemic lungs. Post-stenotic dilatation.

E.C.G. : Right ventricular hypertrophy.

Catheter : Pulmonary stenosis.

Treatment : Pulmonary valvotomy.

PSEUDOTRUNCUS ARTERIOSUS

Consists of : (1) Pulmonary atresia. (2) V.S.D. (3) Dextroposed aorta. The aorta takes origin from both ventricles. The bronchial vessels form the sole means of pulmonary blood flow.

Clinical features : (1) Cyanosis — deep from birth. (2) Physical underdevelopment. (3) Clubbing of fingers. (4) Right ventricular hypertrophy. (5) Insignificant murmurs. Sometimes, machinery murmur over lungs (bronchial circulation). (6) 2nd pulmonary sound single and highly accentuated (Ringing).

X-ray : No pulmonary artery vasculature but bronchial only (Dotted).

E.C.G. : Right ventricular hypertrophy.

TRICUSPID ATRESIA

No communication between right atrium and right ventricle. All blood entering right atrium must cross an atrial septal defect to mix in the left atrium. There is usually a V.S.D. allowing some blood to enter the underdeveloped right ventricle. There may be pulmonary stenosis.

Clinical features : (1) Cyanosis : Marked from birth. (2) Dyspnea on feeding. (3) Failure to thrive. (4) Early clubbing of fingers. (5) Anoxic attacks of unconsciousness may occur. (6) Heart size : little enlargement. (7) Loud systolic murmur at left sternal border. (8) 2nd pulmonic sound quiet and single.

E.C.G. : Left axis deviation and L.V.H.

Prognosis : Few survive for more than 1 year. Cardiac failure occurs with progressive dyspnea, hepatomegaly and edema.

Treatment : All operations devised have the objective of improvement of blood flow : arterial shunts (Taussig-Blalock); enlargement of A.S.D.

COMPLETE TRANSPOSITION OF THE GREAT VESSELS

The aorta arises from the right ventricle and the pulmonary artery from the left. Other anomalies are usually present :

(1). Pulmonary stenosis : This if present is of good prognostic value.
(2). V.S.D. This if present is of good prognostic value. (3). A.S.D. (4) P.D.A.
Sometimes, there is over-riding pulmonary artery or over-riding aorta.

Clinical features : (1) Marked cyanosis since birth. (2) Failure to thrive.
(3) Dyspnea may be present at rest with subcostal recession and it is always obvious during feeds. (4) Early clubbing of fingers.
(5) Heart size is increased. (6) Insignificant murmurs.

X-ray : - Heart size ++ and egg shaped. — Narrow vascular pedicle in P.A. — Vascularity of lungs ++ Right axis deviation. — Right V.H. — P pulmonale.

Catheter and angio confirm the diagnosis.

Prognosis : Most infants die of H.F. in early months of life. Without surgical treatment, 85% die in the first 6 months of life.

Treatment : Begin with Blalock-Hanlon procedure : A.S.D. created or enlarged. At a later age : a patch of pericardium is inserted into the atria in order to direct the venous blood via the mitral valve and the arterial blood via the tricuspid valve (requires the use of heart/lung machine).

There are other types of cyanotic congenital heart disease, e.g. single ventricle, persistent truncus arteriosus, Ebstein's anomaly ... etc.

THE DIAGNOSIS OF CONGENITAL HEART DISEASE

Twenty years ago, the diagnosis of congenital heart disease was a subject of academic interest, but today, with the advances in cardiac surgery it is of great practical importance to all pediatricians. A reasonably correct diagnosis can be made in 80% of cases from the history, physical examination, plain x-ray and electrocardiogram. Nevertheless, a patient who is to undergo surgery requires other special investigations like cardiac catheterization, angiocardiology and aortography, not only to confirm the clinical diagnosis, but also to detect additional anomalies, the signs of which may be masked by the signs of the more obvious lesion.

History : 1. The antenatal history of rubella, any other virus infection, or bleeding in the first trimester of pregnancy may point to the possible cause of a congenital lesion.

2. Babies with congenital defects of a serious nature have a low birth weight, and many would fall within the weight limits of prematurity.

3. It is important to know the age of onset of symptoms and whether these were present from birth or were manifested later. An uncomplicated A.S.D. or a moderate coarctation of the aorta would not produce symptoms in infancy, whereas a large V.S.D., or transposition of the great vessels would go into C.H.F. as early as the first week of life.

4. If history of cyanosis is present, the time of its onset and progress should be obtained from the parents. A child with pseudotruncus arteriosus or an extreme tetralogy is markedly and visibly blue from birth. The milder form of tetralogy without marked dextroposition of the aorta may be so minimally cyanosed that parents would not notice it at all. Cyanosis that is decreasing spontaneously suggests the possibility of developing collaterals. Acute episodes of cyanosis associated with marked dyspnea with perhaps loss of consciousness are indicative of a condition in which there is marked pulmonary stenosis.

5. Feeding difficulties are often met with in these patients. Children who are dyspneic, naturally have difficulty in sucking, and have to stop often to recover their breath. The appetite of these children is on the whole poor.

6. The physical growth and development is retarded. The parents notice that the affected child looks much smaller and starts standing and walking later than did their other normal children. The degree of affection of growth depends upon the severity of the lesion. Cases of total anomalous pulmonary venous drainage are often severely marasmic.

7. A child with a cardiac lesion producing any degree of disability is

unhappy, irritable, constantly crying and sleeps poorly. It demands a good deal of the mother's attention.

8. Respiratory infections are common in children with congenital heart disease. Lower respiratory infections are particularly frequently seen when there is large left-to-right shunt.

9. Tachypnea, dyspnea and diminished exercise tolerance are signs of heart disease. The mother will have noticed that the patient is not able to run and play with other children of the same age, and will complain of fatigue or shortness of breath. A child with tetralogy will resort to squatting to regain his breath.

10. There is occasionally a familial incidence of congenital heart lesions. The same lesion in varying degrees of severity may be repeated in more than one child of the family and one or other parent might have a mild cardiac malformation.

Physical Examination : A general examination is done to note whether the child looks comfortable, or acutely or chronically ill. The height and weight should be taken at the initial examination and at each subsequent visit so that the patient's progress can be assessed.

The presence or absence of cyanosis should be noted, and if present its degree of severity and distribution, and whether it is associated with clubbing. It is most important to watch the respiration, noting not only the rate, but also the character. Children with a left-to-right shunt, have definite subcostal retraction with each inspiration. This observation alone gives a great deal of information. If the retraction is marked and has been present for sometime, a type of Harrison's sulcus develops. This type of retraction is not seen in cases where the pulmonary circulation is normal or diminished. Examination of the precordium gives information regarding the size of the heart, and whether the right or left or both ventricles are enlarged. The position of the apex impulse tells us the situation of the left border of the heart. The area of maximal cardiac impulse, that is the site at which the cardiac impulse is best felt, should also be noted. When the right ventricle is hypertrophied, the cardiac impulse is best felt along the lower left sternal border. When the area of maximal cardiac impulse is in the mid-clavicular line, it suggests left ventricular dominance.

The presence of a systolic thrill in the second left interspace, denotes either valvular pulmonary stenosis, or P.D.A., or an aorticopulmonary window. A systolic thrill in the 4th left interspace, along the sternal border is characteristic of a V.S.D. Infundibular pulmonary stenosis gives a systolic thrill best felt at the 3rd left interspace. A systolic thrill in the 2nd right interspace would be diagnostic of aortic stenosis. A systolic thrill at the apex would suggest mitral

insufficiency which in a patient with congenital heart disease, would be a part of an ostium primum defect.

A diastolic thrill at the 2nd left interspace would indicate a P.D.A. or an aortico-pulmonary shunt. A diastolic thrill at the apex is felt characteristically in mitral stenosis. A diastolic thrill at the 2nd right interspace is found in aortic regurgitation which, though rare, may be found with a V.S.D.

Auscultation of the heart is best carried out with bell-type stethoscope. The character of the heart sounds and the presence of murmurs are noted in all the areas.

Of the signs of C.H.F., it should be remembered that tachycardia, tachypnea and liver enlargement are the important ones in children. Edema of the feet is seldom seen in infants. Rapid enlargement of the liver is a notable feature in infants. The blood pressure should always be taken in the arm and the leg, when the patient is first seen. Coarctation of the aorta may be otherwise missed.

Plain X-rays and Fluoroscopy : Every patient with heart disease requires chest x-rays in 3 positions viz., antero-posterior, left anterior oblique and right anterior oblique. A thick paste of barium should be swallowed by the child while the plate is being exposed in order to outline the esophagus. In addition to the plates, fluoroscopy is also essential to observe pulsations of the different chambers and vessels, so that the heart may be carefully viewed from different angles as the patient is turned slowly from one side to another.

The A.P. View : 1. Size of the heart : If the maximal diameter of the heart is more than half of the diameter of the chest, enlargement is present.

2. If the lower half of the right border is more convex and seen beyond the sternum, we can conclude that the right atrium is dilated.

3. Displacement to the right of the upper right border of the sternum can be due to a dilated superior vena cava or a widened ascending aorta.

4. The arch of the aorta is the uppermost curve along the left border. If this shadow is narrow, it suggests the diagnosis of A.S.D. or V.S.D., since in these two lesions because of the large left-to-right shunt, the pulmonary circulation is much larger than the systemic circulation. A widened aorta with increased pulsations is seen in aortic stenosis, aortic regurgitation and in coarctation of the aorta. Widening of the ascending part and of the aorta is also seen in P.D.A.

5. The next convexity along the left border is formed by the main pulmonary artery. It is increased in size in all cases of large left-to-right shunt, when

the lung fields will also appear congested, and it is possible to see the large vessels at the hilum of the lung pulsating and radiating out to the periphery. Enlargement of the main pulmonary artery with diminution of pulmonary vascularity is found in cases with valvular pulmonic stenosis. If there is a concavity in the region of the main P.A. instead of its normal convexity, we may conclude that there is infundibular pulmonic stenosis, with narrowing of the pulmonary artery itself and the outflow tract of the right ventricle of the type seen in Fallot's tetralogy.

When neither aorta nor pulmonary artery can be distinguished separately, but a wide vessel is seen at the base of the heart, having the same diameter in all 3 views, a truncus arteriosus is probably present. When the vascular shadow is narrow at the base in the A.P. view and broader in the oblique views, the patient probably has a complete transposition of the great vessels.

Right ventricular enlargement is seen in the A.P. view when the left border is more rounded than usual and the apex of the heart is lifted up above the diaphragm. This is confirmed when a greater anterior convexity is seen in the left and right oblique views. In the R.A.O. view, when the anterior border of the heart is touching the chest wall, R.V. enlargement is definitely present.

Increase in size of the left ventricle is seen in the A.P. view, when the apex is displaced further downwards and outwards. In the L.A.O. view, the posterior border of the heart is seen to overlap the vertebral column. In some cases, it is difficult to decide which ventricle is enlarged or whether both are, and in such instance it is worth fluoroscoping the patient in the L.A.O. view to see the interventricular groove just above the diaphragm. Enlargement of the left auricle is seen in the A.P. view as a double density in the center within the main cardiac shadow. In R.A.O. view, an enlarged left auricle will push back the lower esophagus.

The position of the aortic arch is determined by noting the upper esophagus. A normal left aortic arch produces a convexity to the right in the A.P. view and convexity backwards in the R.A.O. view. A right aortic arch produces a convexity to left in the A.P. view and backwards in the L.A.O. In coarctation of the aorta, the esophagus has the characteristic E shape, where the upper convexity is formed by the proximal dilated portion and the lower curve by the poststenotic dilated segment.

Fluoroscopy helps one to distinguish a ventricle that is passively dilated from one that is actively pulsating. In Ebstein's anomaly, the right auricle may be tremendously dilated, but it can be seen that no vigorous pulsations are present. Sometimes a broad shadow at the base may be somewhat confusing, but the presence of pulsations points to the vascular origin. Patients with myocarditis have enlarged heart, but the pulsations are very feeble.

The Electrocardiogram : From the E.C.G. we note the presence or absence of ventricular hypertrophy, auricular enlargement, myocardial damages and/or any arrhythmias.

Cardiac Catheterization : The technique consists in passing a radio-opaque catheter into the long saphenus vein (infants) or the cubital vein (children) and guiding it with the aid of fluoroscopy into inferior or superior vena cava, R.A., R.V. and P.A. As the catheter is withdrawn, samples of blood are collected for oxygen estimation and the pressure tracings taken successfully from pulmonary A, R.V., R.A. and superior vena cava. A sample of blood from femoral artery is also taken simultaneously in order to note the arterial oxygen saturation.

Under normal circumstances, the oxygen content of the whole venous system should be about the same. An abrupt elevation of oxygen content in any chamber or vessel, is diagnostic of a left-to-right shunt. In some congenital cardiovascular abnormalities, the catheter may pass through intracardiac defects or into abnormally placed vessels.

Left heart catheterization is not often necessary in children and would be indicated only in cases of aortic stenosis and regurgitation. The method of choice is the insertion of a catheter up the femoral artery, retrograde into the aorta and left ventricle.

Venous Angiocardiography : Angiocardiography is particularly indicated in cyanotic heart lesions with a right-to-left shunt. It can be performed either by injecting the dye rapidly through the femoral or cubital vein, or when required, the dye may be injected directly into the right auricle or ventricle through a catheter placed there at the time of catheterization. A small child needs to be anaesthetised for this procedure. The dye should be injected at high speed so that a bolus of dye travels forwards undiluted with blood. As the heart rate in a child is usually fast, the film exposures also need to be fairly rapid, at least 6 exposures per second are required.

The course of the dye through the heart and lungs is followed. By this means one can get an idea of the size and shape of the different chambers and great vessels. Early filling of the aorta from the right side of the heart before the dye has circulated through the lungs, indicates a right-to-left shunt.

Two sets of films usually need to be taken, one set in the A.P. view and one in an oblique view. Machines which take both views simultaneously are of course preferable, as otherwise the dye has to be injected twice over. A cine-angio, though not always essential, affords a dynamic demonstration of an otherwise complicated or obscure lesion.

Retrograde aortography : In this investigation, as done in children, the dye is injected through a catheter introduced through the femoral artery, up into the aorta, up to whatever level the pathology is suspected. In pediatric practice it is particularly helpful in differentiating between a P.D.A. and an aortico-pulmonary window. The clinical picture in an infant can be the same with both conditions, and if the patient is in congestive failure or is not growing well, surgery may be required. A patent ductus division is an extra-cardiac procedure and no stoppage of the heart is necessary. It is a relatively simple procedure with a low mortality. The situation is different with an aorticopulmonary window, which is a more difficult matter and requires the use of a heart-lung machine.

Aortography is indicated also when coarctation of the aorta is present, particularly when multiple areas of constriction are suspected. It is also the diagnostic test to confirm the clinical impression of an aneurysm of the sinus of Valsalva or a coronary arterio-venous fistula.

All these special investigations require not only accurate instruments, but the work of an organized team that regularly studies such cases. The correct interpretation of hemodynamic data requires a knowledge of physics and biochemistry and a good grasp of the embryology and development of the cardiovascular system.

RHEUMATIC FEVER

Pathogenesis : Not yet known.

1. *Hypothesis of Allergy to Streptococci of Group A :* There is much evidence that the initial and subsequent recurrences of rheumatic fever follow scarlet fever or upper respiratory infection due to B-hemolytic streptococci group A. The attack of streptococcal pharyngitis may be extremely mild or moderately severe (Phase I). In most instances, the symptoms of upper respiratory infection subside quickly and are followed by a latent or «silent» period (Phase II) usually lasting one to three weeks, during which the patient is symptom-free. Phase II is followed by the onset of acute rheumatic fever (Phase III). If penicillin is given early within the first 9 days and in sufficient quantity over an adequate period of time, the patient escapes rheumatic fever. With such therapy, the hemolytic streptococci are eradicated from the throat in most instances.

The concept that rheumatic fever is an allergic process is based in part upon the following points :

(2) Recurrent attacks indicate absence of immunity.

- (b) The fibrinoid degeneration of collagen is considered characteristic of allergic reaction.
- (c) A period of 1 — 3 weeks commonly intervenes between the streptococcal infection and the onset of rheumatic fever. Such an interval is characteristic of known allergic diseases.
- (d) The acute phase of rheumatic fever has clinical signs and symptoms which are frequently indistinguishable from allergic diseases (e.g., serum sickness).

2. Hypothesis of Autoimmunity : The broad concept is as follows : in some way a cellular product of the streptococcus causes denaturation of the heart tissue antigen, this latter becomes auto-antigenic and stimulates the production of circulating auto-antibodies. Thus auto-immunization may be the underlying basis for the cardiac lesions.

It has been reported that serum from certain patients with rheumatic heart disease demonstrated marked reactivity with homologous or autologous heart tissue as revealed by immuno-fluorescence, complement fixation and agglutination tests.

Susceptibility : Besides infection, an important factor in the etiology of rheumatic fever, is individual susceptibility. The susceptibility in child population in general is between 0.2—1% The child who gets rheumatic fever is a susceptible one. If such a child gets streptococcal infection, he has a 50% chance of a recurrence. Susceptibility may be familial; if one child in a family has rheumatic fever approximately 10% of the children will develop it.

Age of onset : Usually between 5 — 10 years but in some cases it does begin at the age of 2, 3 or 4 years, however, this is not common.

Sex : In children, males and females are affected equally.

Manifestations : The classification of signs and symptoms proposed by Jones forms a convenient organization of a discussion of this complex disease.

MAJOR MANIFESTATIONS

I. Arthritis :

- Typical arthritis occurs in nearly half of the cases.
- The affected joints are swollen, tender and red.
- Several joints are commonly involved, sometimes together and sometimes one after another.
- Typically the large joints are affected as knees, wrists, ankles and elbows.

- As a rule there is prompt improvement under salicylates, but whether salicylates are given or not, it is rare for symptoms and signs to persist in any one joint longer than a week (a differentiating point from rheumatoid arthritis).

2. Heart disease :

(a) Pericarditis :

- There may be no audible or visible signs of pericarditis and the lesion appears in post-mortem.
- Mostly recognized by hearing friction rub as superficial scratchy noise which is heard over the precordium especially near the sternum, and which has to and fro character i.e. systolic and diastolic.
- It is accompanied by slight pain, fever, leukocytosis, and usually by abnormal S — T segment with inversion of T waves in precordial leads.
- In rheumatic fever, the rub lasts a few days to a week or two, whereas in pyemic infections it usually disappears in 2 — 3 days.
- When effusion forms, it produces an area of enlarged cardiac dullness and distant heart sounds. A rapid enlargement of cardiac shadow is due to pericardial effusion and not to myocarditis. Gross enlargement due to carditis takes 3 — 4 months to occur.

(b) Myocarditis & Endocarditis :

Mitral insufficiency : An apical systolic murmur is generally considered as evidence of mitral insufficiency when it occurs with other rheumatic stigmata. This type of murmur occurs in 70% of children with acute rheumatic fever. It is prolonged, filling most of the systole (pansystolic), is best heard at the apex, well transmitted to the axilla and does not change significantly with position and respiration.

First heart sound : In acute rheumatic fever, it is diminished in mitral regurgitation due to lengthened conduction time which facilitates early closure of the mitral valve and thus, diminishes the valvular component of the first sound.

Pulmonary second sound : May appear accentuated due to relative diminution of the first sound.

Third heart sound : Present in 30% of mitral insufficiency during active rheumatic fever, and in 8% when activity subsides.

Mitral diastolic murmur (Carey Coomb murmur; inflow murmur): A short diastolic murmur may be heard in children with mitral insufficiency. It usually occurs with an audible third heart sound. It is a short mid-or early diastolic

murmur. It is always associated with apical systolic murmur. It occurs in approximately $1/3$ — $1/2$ of children with mitral insufficiency during the acute stage, and in about $1/3$ of these, it disappears in the following year. It is an inflow murmur due to the gush of a big amount of blood from the left auricle to the left ventricle causing vibrations of the A - V ring. This murmur is to be differentiated from the murmur of mitral stenosis.

Mitral stenosis : of rheumatic origin does not occur in the acute phase.

The time from onset of the acute attack of carditis to the stage of significant stenosis is almost never less than two years, and most commonly is from 6 to 20 years. Mitral stenosis is thus relatively uncommon in the pediatric age and is found in only 5 to 6% of children with rheumatic heart disease. When present, it is likely to be associated with some degree of insufficiency. Yet, it is possible to get pure stenosis in some cases. Worthy of emphasis is the fact that the initial rheumatic episode is often subclinical in patients destined to develop dominant stenosis. The diagnosis of mitral stenosis is based on several characteristic features which are commonly but not invariably found. These include a mid-diastolic rumbling murmur, pre-systolic murmur, snappy first heart sound, accentuated pulmonary second sound, an opening snap of the mitral valve, a right ventricular heave of precordium, some degree of enlargement of the heart and the presence of right ventricular hypertrophy in the E.C.G.

Aortic regurgitation : May occur early in the first attack. Occasionally in the early stages of the disease, the aortic diastolic murmur will disappear, but commonly once it has been established for a few months, it will remain indefinitely.

Congestive heart failure (C.H.F.) : Almost any child with rheumatic heart disease who is in failure must have active carditis. Right-sided failure is characteristic of C.H.F. in rheumatic children. Pure left-sided failure is relatively rare. The accumulation of fluid in some of these children may be so marked that they have been known to be admitted to hospital as nephrotics.

3. Subcutaneous Nodules : These are shot-like hard bodies seen or felt over the extensor surfaces of certain joints particularly elbows, knees and wrists, in the occipital region or over the spinous processes of the thoracic and lumbar regions. At the end of 6 weeks, $2/3$ disappear and the majority at the end of 4 months. Presence of nodules is an indication that the heart is involved, both being proliferative lesions.

4. Erythema Marginatum : Circinate or annular rash, occurring on the arms, trunk and legs (never on face). It is usually faint with no elevations and has a dull purplish hue. If watched from hour to hour, it will be noted to change gradually. There is no itching or discomfort.

5. Chorea :

- (a) Purposeless involuntary movements, implicating many joints :
 - 1. may be mild or severe.
 - 2. may be unilateral (hermi-chorea) or bilateral.
- (b) Weakness of voluntary movements and hypotonia. May be severe as to amount to paralysis (chorea mollis).
- (c) Inco-ordination of voluntary movements.
- (d) Emotional instability, may be mild or severe amounting to mania.

MINOR MANIFESTATIONS

1. Fever : A significant rise in temperature is a common symptom, but because it occurs in so many illnesses it has little differential diagnostic value. Approximately half of the cases of children have fever. This fever is readily controlled by salicylates.

2. Arthralgia : Pain clearly located without objective findings is only a minor criterion for diagnosis. The pain must be in the joint and not in the muscles or other periarthritic tissues. It must be distinguished from the nocturnal pain in the extremities occurring in normal children.

Arthralgia must not be used as a minor criterion when polyarthritis is included as a major criterion.

3. Prolonged P-R interval in the E.C.G. : It cannot be used if carditis is already included as a major manifestation.

4. Increased E.S.R., leukocytosis or presence of C-reactive protein :

Elevation in one or more of these non-specific tests may be considered as a minor criterion.

5. Evidence of preceding B-hemolytic streptococcal infection. This must be documented by :

- (a) A history of scarlet fever, or of a typical clinical picture of other streptococcal infection. This should precede the onset of rheumatic fever by one week to one month. The nature of the infection must be confirmed by a

history of immediate contact with other individuals having typical streptococcal infection, or by positive culture of the nose or throat in which B-hemolytic streptococci predominate

(b) An elevated or rising A.S.O. titer.

6. Previous history of rheumatic fever or the presence of inactive rheumatic heart disease.

Other Manifestations: These include systemic manifestations such as loss of weight, easy fatigability, elevated sleeping pulse rate (more than 100), malaise, sweating, pallor, or anemia and local manifestations such as epistaxis, erythema nodosum, abdominal pain, headache and vomiting.

These, as well as a family history of rheumatic fever, provide additional evidence of the presence of rheumatic fever, but are not to be included as diagnostic.

Evidence of Acute Rheumatic Fever : Acute rheumatic fever is present when two major manifestations are present; or one major and two minors.

Natural Course : The natural course of an attack of carditis varies according to severity and is self-limited. Its duration may be a few weeks or months. The factors responsible for the termination of an attack are not understood. The inflammatory process subsides and is followed by a reparative proliferative phase. The duration of the latter depends upon the extent and severity of the irreversible damages sustained. Termination of an attack is indicated when there is no further progression of cardiac signs, when the child is afebrile, regains appetite, gains weight, is free from clinical symptoms and has a normal cardiac reserve.

The average duration of active carditis (from the day of onset of illness to the day the patient is ambulatory and free from clinical symptoms) :

Less than 2 months 20%, 2 - 4 months 30%, 4 months—1 year 50%.

Frequency of regression of murmurs during the natural course of acute carditis :

Mitral systolic :

70% of cases with murmurs on admission.

48% of cases with murmurs after one year.

Grade on admission :

I — 66% disappear in one year.

II 44% disappear in one year.

III 17% disappear in one year.

Early or Mid-diastolic Murmur :

27% of cases with murmur on admission

8% of cases with murmur after one year.

Third Sound :

30% on admission

8% after one year

Aortic Diastolic :

12% on admission.

11% after one year.

METHODS OF DETERMINING THE RHEUMATIC ACTIVITY (ACUTE PHASE REACTANTS)

I - C-Reactive Protein : Tends to disappear in the convalescent stage before E.S.R. - May not appear when a rebound occurs. Often absent in chorea and erythema marginatum. - Sometimes absent with long standing nodules. Remains positive when congestive heart failure complicates active carditis (unlike E.S.R.)

II - Serum mucopolysaccharides :

(a) Electro-phoresis for serum glycoproteins (glucidogram), reveals increase in the alpha-glycoproteins. The child should be treated as long as the glucidogram is abnormal.

(b) A purple color develops when the serum is treated with di-phenylamine reagent : most useful guide. The reaction remains high after C-Reactive Protein has disappeared. The color reaction is due to sialic acid, a constituent of mucoprotein.

III - Fibrinogen Polymerization Test : More fibrinogen is found in active rheumatic fever. This is a more sensitive test than E.S.R. & C.R.P.

IV Anti-Streptolysin O Titer : Rises in the second week, and increases to reach a maximum at the 4th to 6th week and then declines (titer reaches 250 or more), a low titer is observed in children below 6 years. Duration is short, rising titer is essential. However, 20% of children give negative results.

V — E.S.R. : Simplest and more reliable, though sometimes normal in heart failure, normal in simple chorea, normal in erythema marginatum, normal in old standing nodules, occasionally raised with no apparent reason and occasionally raised with penicillin.

VI — Strepto Antibyaluronidase : (N. about 135). Rises with active rheumatic fever, remains elevated during activity, diminishes with improvement and increases with exacerbations.

SUGGESTED SCHEME FOR THE MANAGEMENT OF ACUTE RHEUMATIC FEVER

Bed Rest : 1. All children may sit up in bed and feed themselves from the day of admission.

2. Patients whose illness is limited to polyarthrits and fever : Bed rest for two weeks, then gradual ambulation. If no signs of relapse, discharge and send to school.

3. Patients with minimal cardiac involvement (grade 1 to 2 systolic murmur) should be kept in bed long enough (3 weeks), to ascertain that there is no increase in cardiac involvement, after which ambulation is begun, and continued for three weeks i.e. full activities are resumed after 6 weeks from the onset.

4. Patients with a significant degree of myocarditis, valvulitis and/or pericarditis : Bed rest is indicated until :

- i — The intensity of their heart murmurs has diminished or has become stabilized.
- ii — Heart sounds are of good quality.
- iii — Sleeping pulse is normal.
- iv — C.R.P. is normal.
- v — E.S.R. is decreasing.

This entails 2 — 3 months of rest, and gradual ambulation for 3 months.

For Streptococcal Infection : The child should receive an intramuscular injection of 400,000 I.U. penicillin procaine, daily for 10 days, then either :

- i — 1,200,000 I.U. of long acting penicillin (Benzathine Penicillin), every month, or
- ii — One tablet of sulfadiazine (0.5 gm.), for those under 25 kg., daily.
Two tablets of sulfadiazine (1 gm.), for those above 25 kg., daily.

Suppressive Therapy :

1. Cases without cardiac involvement, are given aspirin only .
150 mg./kg./day, for the first two days, then
100 mg./kg./day, in four hourly divided doses (5 times/day), to maintain a
blood level of 25 -35 mg.%. The aspirin administered, should be continued
until the E.S.R. is normal for two weeks.

2. Cases with evidence of cardiac involvement :

(a) Give 300 mg./day of cortisone or one of its equivalents.

Steroid therapy is continued for 7 days. After which :

If no fever, no arthralgia, E.S.R. is dropping, pulse rate is dropping, no pericardial rub, and/or heart failure, stop the steroid therapy suddenly and begin aspirin, 150 mg./kg./day, for two days, and continue on 100 mg./kg./day until the E.S.R. is normal for 4 — 8 weeks.

(b) If there is no response to the corticosteroid therapy after the first seven days continue as such :

2nd	week	10 tablets Prednisone	} + Aspirin 150 mg/kg/day for the 1st 2days, then 100mg/kg/ day, until the E.S.R. is normal for 4—8 weeks.
3rd	week	8 tablets Prednisone	
4th	week	6 tablets Prednisone	
5th	week	4 tablets Prednisone	
6th	week	2 tablets Prednisone	

Anti-Congestive Measures : In congestive heart failure of rheumatic subjects, digitalis controversy exists : These children are extremely susceptible to digitalis toxicity, therefore smaller doses than normal must be given. Digitalis toxicity is liable to occur when potassium is depleted. If digitalis is administered, give potassium as well (K Cl 2.4 mg./day for those less than 27 kg., and 3.6 gm./day for those over 27 kg).

Diuretics : Mercurial Diuretics : (Ampoule of 2 ml.) give 0.5 ml. i.m./day, for 2 — 3 days, then twice a week.

Dichloride-K : 10 — 25 mg./kg./day.

PREVENTION OF RHEUMATIC FEVER THROUGH CONTROL OF STREPTOCOCCAL INFECTION

Rheumatic fever is a recurrent disease which frequently can be prevented. Infection with group A streptococcus precipitates both initial and recurrent attacks; therefore prevention of rheumatic fever and rheumatic heart disease depends upon the control of streptococcal infection. This may be accomplished by : (1) prevention and treatment of streptococcal infection in rheumatic subjects. (2) early and adequate treatment of streptococcal infections in all individuals.

I — Prevention and Treatment of Recurrences in Rheumatic Individuals

Continuous Prophylaxis :

Many streptococcal infections occur without producing clinical manifestations. For this reason, prevention of recurrent rheumatic fever must depend on continuous prophylaxis rather than recognition and treatment of acute attacks of streptococcal disease.

Who should be given prophylaxis ?

In general, all patients who have a well documented history of rheumatic fever or chorea, or who show definite evidence of rheumatic heart disease, should be given continuous prophylaxis.

When should prophylactic measures be initiated ?

Acute Rheumatic Fever : Prophylaxis should be initiated as soon as the diagnosis of rheumatic fever is made, or any time thereafter when the patient is first seen. The streptococcus should be eradicated with penicillin and following this the prophylactic regimen should be instituted.

Inactive Rheumatic Fever : Prophylaxis should be initiated when the patient is first seen.

How long should prophylaxis be continued ?

The risk of acquiring a streptococcal infection and the possibility of rheumatic fever recurrences continue throughout life. It is therefore suggested that the safest general procedure is to continue prophylaxis indefinitely, particularly if rheumatic heart disease is present.

Should prophylaxis be continued during the summer ?

YES, continuously. Streptococcal infection can occur at any season, although they are more prevalent in the winter.

Specific Prophylactic Methods : Several effective methods of continuous prophylaxis are available and the physician must decide which is most suitable for an individual patient.

Oral versus intramuscular route : Most failures occur in patients who forget to ingest the drug regularly. Patients who have proved unreliable in taking oral medication should receive long acting depot penicillin, given i.m. once a month.

Penicillin versus Sulfonamides : Sulfadiazine has the advantage of being easy to administer, inexpensive and effective. Although resistant streptococci have appeared during mass prophylaxis, this is rare.

Penicillin rarely produces toxic reactions. It has the further advantage of being bactericidal for group A streptococcus, and strains of group A streptococci resistant to penicillin have not been encountered.

- (a) *Benzathine-penicillin G*—i.m. : Dosage : 1,200,000 units once a month.
Toxic reactions : - - Urticaria and angioneurotic edema.

Reactions similar to serum sickness with fever and joint pains that may be mistaken for rheumatic fever.

A careful history of allergic reactions to penicillin should be obtained. It is safer not to use penicillin if the reaction has been severe and especially if angioneurotic edema has occurred.

- (b) *Sulfadiazine* — Oral : Dosage : from 0.5 — 1.0 Gm. once a day.
The smaller dose is to be used in children under 25 kg.
The chief toxic reactions are :

Skin eruptions : (a) Morbilliform — continue drug with caution.

- (b) Urticaria or scarlatiniform rash associated with sore throat or fever — discontinue drug.

Leukopenia : Discontinue drug if white blood count falls below 4000 and polymorphs fall below 35% because of possible agranulocytosis which is often associated with sore throat and a rash. Because of these reactions, weekly white blood counts are advisable for the first two months of prophylaxis. The occurrence of agranulocytosis after 8 weeks of continuous prophylaxis with sulfonamides is extremely rare.

II Combating Streptococcal Infection in the General Population :

During epidemics, and in certain population groups, it has been found that about 3% of untreated streptococcal infections are followed by rheumatic fever. Adequate and early penicillin, however, will eliminate streptococci from the throat and prevent most attacks of rheumatic fever.

A — Diagnosis of Streptococcal Infections: About half of the streptococcal infections which occur are likely to escape detection because they are asymptomatic or atypical. The other half can often be suspected by their clinical manifestations. However, in the absence of a scarlatinal rash, it is impossible to differentiate streptococcal infections with certainty on clinical grounds alone. Therefore, bacteriological support (by the throat culture) beside the clinical impression is highly desirable.

Symptoms of Streptococcal Pharyngitis : Sore throat — sudden onset and pain on swallowing. Headache is common. Fever is variable but generally 39–40C. Abdominal pain is more common in children. Nausea and vomiting are common in children.

Signs : Red throat usually with exudate. Lymphadenopathy (swollen, tender lymph glands at angle of jaw). Rash (scarlatiniform, usually diagnostic). Acute otitis media and acute sinusitis are frequently due to the streptococcus.

In the absence of the above symptoms and signs, occurrence of any of the following symptoms is usually not associated with a streptococcal infection : simple coryza, hoarseness of voice and cough.

Laboratory Findings :

Throat Culture : Hemolytic streptococci are almost invariably recovered on culture during acute streptococcal infection. A single well done culture is usually sufficient although hemolytic streptococci which are occasionally missed on initial culture may be detected in subsequent cultures.

White Blood Count : Generally over 12,000.

B — Treatment of Streptococcal Infections :

Penicillin is the drug of choice. Effective blood levels should be maintained for a period of 10 days to prevent rheumatic fever by eradicating the streptococci from the throat.

Recommended treatment schedule :

1. *I.M. Penicillin* Procaine Penicillin 400,000 units i.m. daily for 10 days.
2. *Broad-spectrum antibiotics*, such as erythromycin and the tetracyclines are useful in patients who are allergic to penicillin and must be given for 10 days.

N.B. : The sulfonamide drugs should not be used for the treatment of streptococcal infections. In an established infection, they will not eradicate the streptococcus and therefore will not prevent rheumatic fever. However, the sulfonamides are effective in preventing re-infection and recurrences when administered as continuous prophylaxis to rheumatic subjects.

DISORDERS OF CARDIAC RHYTHM

Sinus Arrhythmia : In this phenomenon, the heart rate increases towards the end of inspiration and slows towards the end of expiration. The cause is alternation in the vagal tone. Sinus arrhythmia is present to some degree in most children over four or five years.

Extra-systoles : Ectopic cardiac beats arise from impulses which have their origin outside the S.A. node, e.g. the atria, the A.V. node or the ventricles. They may occur in healthy children; here the extrasystoles are abolished by exercise. They may complicate organic heart disease; here the extrasystoles become more frequent after exercise. They may complicate digitalis therapy.

Treatment : Should be directed towards the underlying cardiac disease. In healthy children no treatment, but if producing anxiety give phenobarbital 0.03 gm. twice daily.

Paroxysmal Tachycardia : There is ectopic focus discharging at rapid rate. This may be located either in the atrium or in the ventricle. Thus we have two types :—

1. Paroxysmal supra-ventricular tachycardia.
2. Paroxysmal ventricular tachycardia.

The differentiation is usually made with the E.C.G. taken during an attack. The ventricular variety may show evidence of :

- An irregular rate.
- The atria beating independently of the ventricles, and at a slower rate.
- A widened QRS complex.

Paroxysmal ventricular tachycardia is rare in infants and children. The etiology of paroxysmal tachycardia is obscure in most of the cases. In about 10% of cases the condition is associated with the Wolff-Parkinson-White syndrome in which between the attacks of tachycardia, there is a short P-R interval and a wide QRS complex so that total P-S duration remains normal.

Clinical features : In older children attacks of paroxysmal atrial tachycardia are characterised by abrupt onset and cessation. The child is aware of the sudden onset, becomes quiet, does not wish to move about, may appear pale and anxious.

Attacks may last from few seconds to several weeks, but the average is few hours. The cardiac rate usually exceeds 180. If the attack is prolonged cardiac failure develops. The young infant with paroxysmal tachycardia develops cardiac failure early.

He looks ill with dyspnea, restlessness, subcostal recession, greyish cyanosis and refusal to feed. Cardiomegaly and hepatomegaly are marked. Crepitations over the lungs may be due solely to cardiac failure or in part to the respiratory infection which sometimes is the triggering mechanism. The heart rate rises to over 280 per minute. A systolic murmur may be heard which disappears after the attack is over.

Treatment :

Paroxysmal supraventricular :

(a) In infants :

Digoxin 0.1 mg./kg./day divided into 4 daily doses until the attack ceases. Maintenance 0.025 mg./kg./day divided into 2 equal parts and continued for 6 months to prevent recurrences which may be triggered by minor infections.

(b) In older children : — vagal stimulation.
— digitalis.

Paroxysmal ventricular tachycardia :

Procainamide i.m. 50 mg. at once and 50 mg. every 2 hours until the attack ceases. Hypotension is an indication for withdrawal of treatment.

CARDIAC FAILURE IN THE NEONATAL PERIOD AND INFANCY

Not uncommon. May be due to :

1. Congenital heart lesions : Most common :—

(a) Aortic atresia (birth — 1 week).	(b) Coarctation of the aorta.
(c) Transposition of the great vessels.	(d) Big V.S.D.
(e) Endocardial fibroelastosis.	

2. Paroxysmal tachycardia.

3. Virus myocarditis.

Clinical features Breathlessness on exertion takes the form of slowness with feeds. Dyspnea with subcostal recession.

— Sleeplessness, restlessness and weak cry. — Pallor or cyanosis. — Edema is a late sign. It appears first in the face of the young infant, then in the genitalia and lumbosacral region before the feet (because of the universal supine posture of the child). — Venous congestion; because of short neck and natural fat covering of the subcutaneous tissue, engorgement of veins is rarely visible. — The heart is normally grossly enlarged, tachycardia is present and there is often a loud murmur. — Lungs reveal fine to coarse rales and wheezing. — Hepatomegaly, the liver may touch the iliac crest and may be missed if palpation is not done carefully. The liver is quite soft and in a struggling child may be difficult to palpate. One should always make an attempt to feel the edge of the liver and it is a good practice to start feeling for it from left iliac and hypogastric quadrants in a direction towards right hypochondrium.

Management :

1. The infant is nursed with the head well raised above the feet.
2. Oxygen tent.
3. Digoxin : 0.1 mg./kg./day divided into four daily doses.
A maintenance dose 0.025 mg./kg./day in two equal doses.
4. If edema is marked, give chlorothiazide 25 mg./kg./day in four divided doses by mouth.

When diuretics are being given, the serum potassium level should be tested frequently. Hypokalemia should be treated with oral potassium chloride 0.5 gm. twice daily.

5. Corticosteroids are : only used when diagnosis of myocarditis or idiopathic cardiomegaly is established.

CARDIAC FAILURE IN OLDER CHILDREN

Pulmonary left heart failure : Uncommon in childhood but may occur in :—

- (a) Acute diffuse glomerulonephritis.
- (b) Coarctation of the aorta.

It is characterized by pulmonary edema and rales, gallop rhythm, cardiac asthma and pulsus alternans.

Pure right heart failure : More common and may be caused by ;

(a) Pulmonary stenosis. (b) A.S.D. (c) Transposition of great vessels. (d) Anomalies of pulmonary venous drainage.

Combined right and left heart failure : Most common form of C.H.F.

(a) Causes mentioned above.

(b) Myocarditis. (c) Paroxysmal tachycardia. (d) Pericarditis.

Myocarditis : This is the most important cause. The main causes of myocarditis in descending order of frequency are :—

(a) Rheumatic. (b) Acute glomerulonephritis.

(c) Isolated myocarditis. (d) Diphtheritic.

Isolated myocarditis . Usually seen between the age of birth and 5 years although all ages may be affected. Coxsackie B virus was established as a cause in some cases. However the etiology is still unknown in many cases.

Clinical features : Various forms of onset :

(a) There may be no preceding illness. The child may suddenly become dyspneic, cyanotic and dies in a few minutes or a few hours.

(b) A large proportion have a somewhat gradual onset. Many cases have a preceding upper respiratory infection or pneumonia.

In some babies there is failure to gain weight.

The symptoms of abdominal pain, fever, anorexia, dyspnea and cough develop suddenly in a young child who has previously been perfectly well. He quickly becomes seriously ill with pallor or cyanosis of the peripheral type.

The signs of C.H.F. which predominate are :

— Cardiac enlargement : (x-ray shows enlargement of a fairly marked degree).

— Tachycardia out of proportion to the temperature. — In most cases there is no murmur, but occasionally a soft systolic murmur at the apex. — A gallop rhythm is heard in the majority. — Crepitations over the lungs. — Hepatomegaly.

— Edema is often slight or absent.

— Sedimentation rate is usually elevated. The white blood cell count is slightly elevated.

The E.C.G. is an integral part of the diagnostic picture. It shows tachycardia and at times an abnormality of conduction with varying degrees of heart block. The most characteristic features are flattening or inversion of the S T segment and the T wave

Treatment : The prognosis is grave and many cases end fatally. Some, however show a marked response to the treatment.

- (a) Oxygen.
- (b) Digitalis; maintenance for 6 months after recovery.
- (c) Oral diuretics.
- (d) Broad-spectrum antibiotics to protect the very ill child from bacterial infection.
- (e) Corticosteroids.

M.K. BADR-EL-DIN.

Chapter XIV

NORMAL BLOOD VALUES AFTER BIRTH

Hemoglobin concentration : The cord blood hemoglobin ranges between 16 and 17 g./100 ml. Blood samples drawn from heel punctures show a higher concentration due to stasis in the peripheral blood of newborn macrocytic red cells. During the first week of life there is a slight decline in hemoglobin concentration. A physiologic anemia thereafter develops and the hemoglobin reaches its lowest level between 6 weeks and 2 months after birth. On an average it can be considered that during the first 2 years of life the hemoglobin concentration is 11 g./100 ml. After 2 years a gradual rise occurs and hemoglobin reaches the standard of 15 g./100 ml. at the age of 14 years.

Red cell count : At birth the red cell count is 5.5 millions/c.mm. and the cells are macrocytic. The count averages 4.6 millions/c.mm. at the end of the first year, 4.8 millions/c.mm. at the end of 12 years and 5 millions/c.mm. at the age of 14 years.

Hematocrit value : The hematocrit value (volume of packed red cells) averages 55% at birth, 30% by the 2nd month, 36% at one year, and 40% at 3 years. Normal adult values of 43% are usually reached at the age of 14 years. A transient elevation may, however be occasionally met with during adolescence.

Reticulocytes : Reticulocytes number 4 to 6% at birth. Their count drops rapidly between the 4th and 6th day after birth and then slowly till it reaches adult values of 0.5 to 1.5% in a few months.

Normoblasts : Normoblasts are frequently present at birth in a number reaching 3 to 10% of the white blood cells, and usually disappear during the first week. Their number is higher in prematures (10 to 20%).

White blood cells:

The average total leukocytic count at birth is 22000/c.mm. In the first week the count drops to 12000/c.mm. and remains at this value till

the end of the first year. Levels of 8000 to 10000/c mm are attained by about the 4th year. The total leukocytic count is lower in prematures than in full term babies.

Neutrophils average 60% at birth, 40% by the 10th day and 30% from the 4th month to the 4th year. The percentage then rises to 55-60% after 6 years of age.

Lymphocytes average 30% at birth and 60% at the age of 4 to 6 months. These values are maintained until the 4th year when they gradually drop to 40% at 6 years and 30% at 8 years.

The levels of monocytes, eosinophils and basophils are almost kept without variation at 6, 2 and 5% respectively through infancy and childhood. Monocytes, however may occasionally show a slight rise during the 2nd and 3rd months.

Platelets : The platelet count is slightly lower at birth than in the older infant, possibly due to the trauma of delivery. However, adult values of 250-350 thousands/c.mm. are reached at about 6 months after birth. This rise to normal adult levels is slower in prematures.

Blood volume : The blood volume of a full term infant at birth is 85 ml./kg. body weight, and that of a premature is 108 ml./kg. body weight, the difference being due to the excess of plasma in the premature circulation. Adult values of 75-80 ml./kg. body weight are attained after the 2nd month of life.

Life span of blood cells.

Red cells. The most recent methods for the estimation of the red cell life span are carried out with the use of red cells tagged with an isotope of iron (^{59}Fe) or chromium (^{51}Cr). The normal red cell has a life span in the circulation of about 120 days.

Leukocytes. The life span of leukocytes is divided into 3 phases :

- (1) The hemopoietic phase extending from the development of the primitive cell to its delivery into the circulation.
- (2) The intravascular phase i.e. within the circulation
- (3) The extravascular phase i.e. the time which the leukocytes spend in the viscera, and tissues, before their ultimate disintegration

One of the recent methods used in the estimation utilises the use of radioactive phosphorus ($\text{P } 32$)

Granulocytes enter the circulation from the bone marrow at the age of 6 days and survive in the circulation for about 9 days.

Lymphocytes were found to be of 2 types : one type has a life span in the circulation of less than 10 days, and the second type has a much longer one of 100-200 days.

The life span within the circulation of eosinophils and basophils is 8-12 days.

Platelets. Radioactive chromium (^{51}Cr) has been employed in the measurement of platelet life span. In normal subjects this is estimated as from 8 to 11 days.

THE ANEMIAS

Classification : The following is a classification based on the etiology :

I. Decreased or impaired production.

- A. *Deficiency of substances required for hemoglobin and red cell formation :* Iron, vitamin B₁₂, folic acid, ascorbic acid, protein.
- B. *Depression or inhibition of bone marrow :*
 - (1) Infection, chemical and physical agents, metabolic products.
 - (2) Idiopathic depression and aplasia with or without congenital anomalies.
- C. *Mechanical interference and replacement by abnormal cells :* Leukemia, malignancy.

II. Blood loss — Acute and chronic hemorrhage.

III. Excessive blood destruction.

- A. *Intracorpuseular defects.*
 - (1) Sick cell disease, thalassemia (hereditary hemoglobinopathies), hereditary spherocytosis.
 - (2) Elliptocytosis.
 - (3) Hemolytic anemia due to enzyme deficiencies.
 - (4) Paroxysmal nocturnal hemoglobinuria.
- B. *Extracorpuseular factors :*
 - (1) Factors due to antibodies and isoagglutinins.
 - (2) March hemoglobinuria, paroxysmal cold hemoglobinuria.
 - (3) Infection, chemical and physical agents, hypersplenism.

IRON DEFICIENCY ANEMIA

Etiology : Iron deficiency anemia is the commonest anemia in infants and children. The body of the newborn baby contains 0.5 g. of iron in contrast to the adult whose body contains 5 g. Accordingly an average full term infant requires 0.8 mg. of iron daily. In the first 6 months of life the infant is dependent upon the iron reserves he had accumulated during fetal life from his mother. After 6 months these are depleted and iron has to be supplied in the diet. As only about 10% of the dietary iron is absorbed, a diet containing 8 mg. of iron is necessary for optimal iron metabolism.

Iron deficiency anemia occurs most commonly between the ages of 6 and 24 months either due to an inadequate supply, impaired absorption, or excessive demand for iron. The major causes for iron deficiency anemia are as follows:

I. Inadequate supply of iron :

A. Inadequate iron stores at birth :

- (1) Premature, twin, or multiple births.
- (2) Severe iron deficiency in the mother during pregnancy.
- (3) Fetal blood loss at or before delivery.
 - a — Fetal hemorrhage into maternal circulation.
 - b — Retroplacental bleeding.
 - c — Injury or early clamping.

B. Inadequate intake — Deficient dietary iron.

II. Impaired absorption of iron :

A. Chronic diarrhea.

B. Celiac disease.

C. Gastrointestinal abnormalities.

III. Excessive demands for iron.

A. Blood loss during infancy :

- (1) Acute or chronic hemorrhage.
- (2) Parasitic infestation such as hookworm.

B. Failure to meet increased demands for growth :

- (1) In the premature infant.
- (2) During adolescence.

Inadequate supply of iron. Premature, twin and multiple births result in defective accumulation of iron in the body stores. Similarly, anemia of the mother during pregnancy will be reflected in the development of anemia in the infant during the first 6 months although it will not affect the level of hemoglobin and red cell count at the time of birth. Less frequently reduced stores will result from blood loss as when the fetus bleeds into the maternal circulation or into the circulation of a twin, from placenta previa, or from injury or early clamping of the cord. After the age of 6 months it is obvious that unless iron is supplied in the diet an iron deficiency anemia will develop.

Impaired absorption of iron. Iron deficiency anemia is observed in disorders of the alimentary tract in which absorption is impaired. Thus it may

be found in conditions of chronic diarrhea, celiac syndrome etc. Anemia is also present in most cases of hiatal hernia.

Excessive demands for iron. In addition to acute and chronic hemorrhage, blood loss is most commonly encountered after parasitic infestation with hook worms and bilharzia. Though such infestations are not common in infancy, they have to be considered in the older child. The severity of ankylostoma anemia will accordingly depend on the degree of iron stores of the body, the amount of iron in the diet, and the number of worms in the small intestines. It was estimated that a single worm can remove as much as 0.75 ml. of blood per day. Furthermore, worms move frequently and get stuck to new areas in the mucosa leaving oozing sites which add to the degree of blood loss. The anemia after bilharziasis is produced by loss of blood in the urine and stools. In the premature infant and during adolescence the amount of iron in the diet has to be increased to meet with the excessive demands for growth.

Clinical features : The history is usually suggestive. Pallor is the most important sign. It is waxy in type and often severe. In severe cases irritability, anorexia, and listlessness are present. The spleen may be slightly enlarged. A soft apical systolic murmur may be heard but the heart size is not usually enlarged. Changes in the epithelial structures seen in adults with iron deficiency such as atrophic glossitis, dysphagia, spoon shaped or concave nails do not occur in infants and may only be rarely seen in the older child.

• **Laboratory findings :**

Blood. The anemia is hypochromic and microcytic. Iron deficiency affects hemoglobin synthesis much more than red cell formation. Hemoglobin content is accordingly much diminished but the red cell count is only slightly below normal. The hematocrit levels are lower than normal. The following data are usually demonstrated . Red cell count of 3 to 5 millions/c.mm.; hemoglobin concentration below 9 g./100 ml., mean corpuscular hemoglobin (MCH) less than 27 micromicrograms, mean corpuscular hemoglobin concentration (MCHC) of less than 30% and mean corpuscular volume (MCV) of less than 78 cubic microns. The blood smear shows microcytes, poikilocytes and target

cells. The characteristic appearance of the blood smear is the presence of a majority of small red cells with marked central pallor and fine and poorly staining rims of hemoglobin. The reticulocytes are usually normal.

Plasma. The serum iron is reduced to 10-60 micrograms/100 ml. (normally about 120 micrograms/100 ml.) The latent iron binding capacity of the serum is increased to about 450 micrograms or more (normally 250 micrograms/100ml.)

Bone marrow. This shows erythroid hyperplasia with predominance of normoblasts and micronormoblasts. The cytoplasm is diminished. Hemosiderin is totally absent.

Diagnosis : Iron deficiency has to be differentiated from other hypochromic microcytic anemias. Lead poisoning leads to anemia of this type. However, coarse basophilic stippling of the red cells together with elevation of the blood and urinary content of lead are present. Also thalassemia produces a hypochromic microcytic anemia which does not respond to iron therapy. Even the radiological picture of "hair standing on end" characteristic for thalassemia, may rarely appear in chronic iron deficiency anemia and disappears with treatment. Rarely, pyridoxine deficiency may result in anemia of a hypochromic microcytic type.

Treatment : Therapy with iron salts is effective. However, a thorough investigation of the various possible etiologic factors must be undertaken. For infants, ferrous sulphate drops is the preparation of choice. For older children, ferrous sulphate or ferrous gluconate tablets are preferable.

The therapeutic dose must be calculated in terms of elemental iron. Ferrous sulphate is 20% and ferrous gluconate is 10-12% elemental iron by weight. A daily dose of 6 mg./Kg. body weight of elemental iron has to be given, in 3 divided doses. Iron therapy is better given between meals.

Parenteral iron therapy is indicated when a patient fails to respond to adequate oral dosage, because of gastrointestinal irritation, or rarely because of failure to absorb iron. An iron dextran mixture for intramuscular use is available and provides 50 mg. of elemental iron in each milliliter.

3-5 days after administration of iron peripheral reticulocytosis is seen and is followed by rise in hemoglobin level and red cell count.

Acute iron intoxication : The accidental ingestion of large doses of iron preparations has a mortality rate of about 50%. Early symptoms include vomiting, diarrhea, dehydration and the local effects due to the corrosive action of iron on the stomach and intestines. Later there is evidence of severe and often irreversible cardiovascular collapse, shock and coma. An associated marked increase in plasma iron is present. Postmortem examination reveals dilatation of the right heart, pulmonary congestion, hemorrhage and necrotising gastritis, cloudy swelling and areas of hemorrhage in the lungs, brain, kidneys and liver.

The treatment is symptomatic. Forced vomiting and gastric lavage with sodium bicarbonate are helpful. Blood and plasma transfusion, oxygen, and electrolyte correction are indicated.

MEGALOBlastic ANEMIAS

These are characterized by the predominance of megaloblasts in the bone marrow and evidence of macrocytosis in the peripheral blood. They are produced by deficiency of vitamin B₁₂ and folic acid. Both substances are necessary cofactors in the synthesis of nucleoproteins. Vitamin B₁₂ functions as the extrinsic factor and in the presence of the intrinsic factor secreted by the gastric mucosa it is absorbed into the small intestines and passes into the blood stream to the liver, where it is stored for use by the bone marrow.

Juvenile Pernicious Anemia

Pernicious anemia is very rare in children. Consanguinity is usually present in the parents and a mendelian recessive inheritance is suggested.

Etiology : The disease is due to an inherited inability of the stomach to secrete the intrinsic factor, resulting in deficient absorption of vitamin B₁₂. Recent studies, however suggest an autoimmune mechanism to be responsible. Intrinsic factor antibodies have been demonstrated in 20-30% of patients with the disease.

Clinical manifestations : The onset is insidious and not usually before the 9th month after birth. During this interval the stores of vitamin B₁₂ which had been accumulated during fetal life are exhausted. There is anemia, apathy, fatiguability, anorexia and may be diarrhea. The tongue is red with papillary atrophy and other manifestations or recurrent glossitis. Neurologic involvement is present in the form of ataxia, paresthesias, hyporeflexia, impaired vibratory perception, positive Babinski sign, clonus and may be coma. The liver and spleen are usually normal.

Laboratory findings : Macrocytes, many of them oval, with anisocytosis, poikilocytosis, polychromasia and occasionally nucleated red cells are characteristic. The hemoglobin is usually below 6 g./100 ml and the red cell count is comparatively lower than the hemoglobin level varying from 1 to 2.5 millions/c.mm. The anemia is macrocytic showing a high color index and an increase in the M.C.V. Leucopenia and thrombocytopenia due to depression of the myeloid and megakaryocytic series may be present.

The bone marrow is hyperplastic with nucleated red cells ranging up to 50% of the total count. Of these, megaloblasts in different stages of maturation and

hemoglobinization predominate. As peripheral anemia is present, this demonstrates a high degree of ineffective erythropoiesis.

Serum vitamin B₁₂, as measured by radioactive techniques or microbiological assays, is below 100 micromicrograms/ml. However, the concentration of serum folic acid is normal.

Absorption of vitamin B₁₂ is abnormally low. This can be assessed by the Schilling test by giving radioactive vitamin B₁₂ by mouth and then measuring its excretion in the urine.

In contrast to adults, children with juvenile pernicious anemia have free hydrochloric acid in the gastric juice and a normal mucosa.

Treatment : The response to liver extract and vitamin B₁₂ is rapid and specific. Vitamin B₁₂ has to be given parenterally. In children a remission of the disease is obtained with doses of 15 to 30 micrograms of vitamin B₁₂ every day or every other day for 2 to 4 weeks. A maintenance dose of the same amount is usually given every 2 to 4 weeks.

Megaloblastic Anemia of Infancy

Etiology : Megaloblastic anemia of infancy is due to deficiency of folic acid.

The normal daily requirements of folic acid are only about 20-50 micrograms per day, and the deficiency accordingly is encountered during periods of rapid growth or infection when the demands are increased. Premature babies are especially susceptible. Human and cow's milk contain adequate amounts of folic acid, whereas goat's milk is very poor. Ascorbic acid deficiency seems to play a role in the etiology.

Clinical picture : The onset is usually insidious at about the age of 7 months. There is anemia, anorexia, irritability, failure to gain weight and possibly an upper respiratory tract infection or diarrhea. Petichiae and ecchymotic patches may be present in severe cases. The liver and spleen may be slightly enlarged, but no neurological manifestations are described. Concomitant signs and symptoms of ascorbic acid deficiency may be present.

Laboratory data : The anemia is macrocytic and the red cells may in addition show poikilocytosis, and anisocytosis. Nucleated red cells demonstrating megaloblastic morphology are often seen in the peripheral circulation. Leucopenia and thrombocytopenia are usually present except

during infection when leucocytosis is demonstrated. The bone marrow shows erythroid hyperplasia with prominent megaloblastic changes.

Serum folic acid, measured by microbiological assays, is usually less than 3 millimicrograms/ml., but serum vitamin B₁₂ is normal. Formiminoglutamic acid (FIGLU) is excreted in the urine and its presence is a positive indicator of folic acid deficiency.

Treatment : Oral or parenteral administration of folic acid in a daily dose of 10-30 mg. for a period of about 2 or 3 weeks usually results in a complete and permanent cure. Ascorbic acid may sometimes be needed and antibiotic therapy is indicated when an infection is associated.

THE ANEMIA IN PROTEIN CALORIE MALNUTRITION

Protein calorie malnutrition which includes kwashiorkor and marasmus and the intermediate conditions in between them, is a syndrome of multiple deficiencies. Proteins, iron, folic acid and ascorbic acid, which are essential for normal erythropoiesis, are among the many defective factors. A hypochromic microcytic anemia due to iron deficiency or a megaloblastic anemia due to folic acid deficiency may accordingly be present either singly or in combination. The term dimorphic anemia is applied to the latter presentation when manifestations of both types of anemia coexist. Occasionally the anemia is aggravated by blood loss due to parasitic infestation, and in rare cases the severe protein deficiency in kwashiorkor results in inhibition of the bone marrow and the development of an aplastic type of anemia.

Laboratory findings : The red cell count and hemoglobin concentration are diminished. The anemia is microcytic hypochromic or macrocytic depending on the mechanism. In a good percentage of cases a combination exists, and the anemia is dimorphic manifesting laboratory findings of iron deficiency and folic acid deficiency. The prothrombin is diminished in most cases and about 15% show purpura and thrombocytopenia. The bone marrow is hypocellular and is either normoblastic or megaloblastic or both.

Treatment : The supply of protein and vitamin B complex is essential. The correction of anemia needs the administration of iron or folic acid or both.

HYPOPLASTIC AND APLASTIC ANEMIAS

The main feature in hypoplastic and aplastic anemias is hypofunction of the bone marrow to produce blood cells at a normal rate. In hypoplastic anemias it is mainly the formation of red cells and haemoglobin that is impaired with minimal or no involvement of white cells and platelets. Aplastic anemias on the other hand, are characterised by a simultaneous depression of the 3 cellular elements in the bone marrow and a resulting anemia, leukopenia and thrombocytopenia.

Pure Red Cell Anemia

(Congenital Hypoplastic Anemia; Erythrogenesis Imperfecta)

This is a congenital type of anemia with unknown etiology. The blood picture is usually normal at birth and profound anemia appears about the age between 2 and 6 months. An abnormality in tryptophan metabolism is sometimes present.

Clinical picture : Anemia is the main clinical finding. The spleen and liver are usually normal and they only enlarge after repeated blood transfusions when hemosiderosis develops. A benign thymoma may occasionally be present.

Laboratory findings : In the bone marrow there is evident absence of nucleated precursors of the red cells. Precursors of the white blood series and platelets are however normal, and the myeloid erythroid ratio is accordingly from 10 : 1 to 200 : 1. In the peripheral blood marked normocytic normochromic anemia is present with marked diminution or even complete absence of reticulocytes. The leukocytes and platelets are normal. Following repeated blood transfusions the level of serum iron is elevated.

Treatment : The disease is treated by the administration of corticosteroids in full dosage. Until a response occurs in about 3 to 4 weeks in fortunate cases, transfusion of whole blood or packed red cells should be repeated to maintain the level of hemoglobin above 6 g./100 ml. Splenectomy may sometimes be recommended.

Aplastic Anemia With Multiple Congenital Anomalies (Fanconi Type)

This is a congenital type of aplastic anemia which is inherited as an autosomal recessive character. Its main features are pancytopenia, bone marrow aplasia, and a number of congenital anomalies.

Clinical picture : The patient is usually born with congenital anomalies, the commonest of which are hypogenitalism, microcephaly, strabismus, ptosis of the eye lids, nystagmuous, anomalies of the ears, anomalies of the thumb, radii, syndactyli, congenital heart and kidney disease, and atrophy of the spleen. Some children have no serious anatomic anomalies but are short in stature and manifest a dark pigmentation of the skin due to deposition of melanin.

Pancytopenia is not usually present at birth or during infancy. Bruising is the first indication of a blood disorder and usually starts after the 3rd year. Anemia and leukopenia then follow, and when the latter is severe the child shows an increased tendency to infections

Laboratory findings : Pancytopenia is evident in the peripheral blood. The bone marrow is hypocellular with depression of all 3 types of cell precursors, and shows an increase in fatty tissue. Anomalies of the heart, kidneys, bones or other organs may be confirmed by specific laboratory investigations.

Treatment : This consists of supportive blood transfusions, androgens, adrenocortical hormones, antibiotics for infections and splenectomy in selected cases.

Acquired Aplastic Anemia

Etiology : Acquired aplastic anemia is of 2 types :

(1) *Secondary aplastic anemia.* Here a precipitating cause is present and may be :

a) Chemicals and chemotherapeutic agents. Some chemicals and drugs are known to be bone marrow depressants. Among these are : D.D.T., benzene, tridione, mesantoin, chloramphenicol, tetracyclines, some sulphonamides, and the antimetabolites used in the treatment of leukemias. Chloramphenicol is probably the commonest causative agent belonging to this group.

b) Radiation is a well known physical factor which causes bone marrow depression. Lymphocyte precursors are the first to be affected by radiation and are followed by those of granulocytes, platelets and lastly red cells.

c) Bone marrow replacement by leukemic or other malignant cells, and depression of the marrow by chronic infections, severe protein depletion as in kwashiorkor, chronic renal disease, hypothyroidism may be predisposing factors.

(2) *Primary or idiopathic aplastic anemia*. When no precipitating cause for bone marrow aplasia is present the disease is referred to as primary or idiopathic.

With the exception of those of the precipitating factor in cases of secondary aplastic anemias, the clinical manifestations and laboratory features of idiopathic and secondary aplastic anemias are the same. Patients with the secondary type, however, may have a slightly better prognosis.

Clinical picture : Cutaneous hemorrhages due to thrombocytopenia are usually early features. These are followed by anemia and then leukopenia. The latter may be associated with repeated infections which may be difficult to control. Intracranial haemorrhage is present in rare cases and may end fatally. Anorexia, weakness and dyspnea may complicate the anemia. The spleen and liver are normal except when haemochromatosis and hemosiderosis develop.

Laboratory findings . A normochromic normocytic anemia is present. Reticulocytes may be totally absent or as low as 1-2%. Thrombocytopenia and leukopenia are present. The bone marrow is hypoplastic and consists largely of fatty and fibrous tissue with only small clusters of hematopoietic cells. Lymphocytes, plasma cells and reticulum cells predominate in the marrow smear.

The level of serum iron is elevated due to a decrease in the rate of clearance of iron from the plasma. Hemochromatosis and hemosiderosis may be present following repeated blood transfusions.

Treatment : Removal of the causative agent is obviously the first item in the treatment of cases of secondary aplastic anemias. Thereafter, treatment of both types is the same. Blood transfusion is essential and is usually repeated. For stimulation of the bone marrow a combination of corticosteroids and androgens has proved helpful though the response is usually slow. This appears first on erythrocytes and hemoglobin then on leukocytes and only after many months on platelets. The treatment of infections even minor ones should be started early preferably by broad spectrum antibiotics and oral penicillin. Splenectomy has proved helpful in a few selected cases with hypersplenic functions

HEMOLYTIC ANEMIAS

A hemolytic anemia is one produced by excessive blood destruction.

Manifestations of increased hemolysis :

(1) *Hemoglobinemia, hemoglobinuria, and low haptoglobin concentration.*

The level of hemoglobin in the plasma is normally low (less than 5 mg./100 ml.), and is derived from destruction of red cells in the reticuloendothelial system. This is increased in hemolytic anemia.

If abnormal hemolysis occurs a substance called haptoglobin which is an alpha 2 mucoprotein normally present in the circulation, will combine with the liberated hemoglobin forming a hemoglobin - haptoglobin complex. This complex has a large molecular weight which prevents its passage into the urine. In this way hemoglobin is conserved to be later on utilised again by the bone marrow.

If the degree of hemolysis is severe, the amount of haptoglobin in the circulation will not be enough to combine with all the liberated hemoglobin. The excess hemoglobin will accordingly pass through the kidney resulting in hemoglobinuria. Accordingly, hemoglobinuria only occurs when all the available haptoglobin has combined with hemoglobin. Absent or very low haptoglobin concentrations can in these cases be demonstrated by laboratory tests.

(2) *Hyperbilirubinemia and jaundice.* When there is excessive red cell destruction plasma bilirubin increases. But, within limits, a normally functioning liver can remove the pigment from the plasma and excrete it in the bile. In other words, the absence of jaundice does not eliminate the diagnosis of hemolytic anemia.

(3) *Urobilinogen excretion.* Increased blood destruction is associated with excessive urobilinogen excretion in the stools and urine.

(4) *Reticulocytosis and nucleated cells in the blood.* In hemolytic anemias the peripheral reticulocytic count is increased which indicates an elevated activity of the bone marrow leading to premature delivery of red cells into the circulation. Nucleated red cells, like normoblasts may also similarly appear in the peripheral blood.

(5) *Abnormal cells in the blood.* Spherocytes are sometimes present in hemolytic anemias of varied etiology. In addition to hereditary spherocytosis,

they are common in hemolytic disease of the newborn due to A B O incompatibility. Heinz bodies, which are damaged red cells showing intracorpuseular particles, may also be seen in some hemolytic anemias.

(6) *Shortened red cell survival.* The red cell life span can be directly estimated by isotopic techniques. ^{51}Cr and ^{59}Fe are the isotopes most commonly used. A shortened red cell survival is the most accurate confirmation of the presence of abnormal hemolysis.

(7) *Additional tests for increased hemolysis.* Some additional tests can show abnormal hemolysis in a number of hemolytic anemias. Among these are the osmotic fragility test, the autohemolysis test etc.

Hemoglobinopathies

Hemoglobinopathies comprise genetically determined disorders in which synthesis of normal adult hemoglobin is partially or completely suppressed causing its replacement by a hemoglobin variant. All hemoglobinopathies show an increased rate of hemolysis.

Many abnormal hemoglobins have been identified by electrophoretic studies, and after giving the designation A to adult hemoglobin, F to fetal hemoglobin, and S to sickle cell hemoglobin (the first abnormal hemoglobin to be discovered), it was agreed to give consecutive letters of the alphabet to all newly identified ones. Of the important abnormal hemoglobins are hemoglobin C, hemoglobin D, and hemoglobin E.

Sickle Cell Disease

Etiology : Sickle cell disease is a term which includes disorders produced by the presence of sickle cell hemoglobin in the red cell. It is more prevalent in the negro race. Heterozygous occurrence of the sickle gene is associated with a benign clinical disorder called sickle cell trait. Here the red cells contain a mixture of hemoglobin A and hemoglobin S (25 to 45% as hemoglobin S) and sickling does not occur under normal conditions. Anemia is usually not present.

If the gene for sickling is present in the homozygous state as a result of its inheritance from both parents, sickle cell anemia results. Here 90% of the hemoglobin is in the S form and about 2 to 10% in the fetal form. Hemoglobin A₂ is present in its normal percentage but hemoglobin A is totally absent.

Possession of a sickle gene is believed to confer a degree of resistance to falciparum malaria.

Pathogenesis : The sickling phenomenon is a rapid and reversible one and is responsible for all the manifestations produced in the disease. The sickle cells, which are rigid and inflexible, due to their shape, get entangled with one another and lead to an increased viscosity of the whole blood. Sickling and increased blood viscosity combine to produce capillary stasis, plugs of impacted red cells, thrombi, hemorrhage, vascular occlusion, infarction and ischemic necrosis. Plasma viscosity is furthermore increased by infection.

The sickle shape of the red cells produces shortening of their life span with a resulting chronic hemolytic anemia.

Pathology : Manifestations are related to chronic hemolytic anemia and to interference of the blood supply of various tissues. The vascular lesions result from capillary obstruction. Infarcts may thus occur in many organs most commonly in the spleen, and less often in bones, the gastrointestinal tract, kidneys, lungs, heart and brain. Thrombosis may occasionally occur. Hemosiderosis may take place especially in the liver and spleen as a result of chronic hemolysis and as a complication of repeated blood transfusions. Gall stone production may take place in patients living to adulthood.

Clinical manifestations : Manifestations do not usually start until late infancy. Patients with sickle cell anemia experience episodes which are usually called crises. Four types of these are described :

1. The commonest variety is the painful or *thrombotic crisis* which results from occlusion of small blood vessels with distal ischemia and infarction. It may occur spontaneously but is more commonly precipitated by an infection. There may be pain in the extremities either muscular or osseous or localised to the joints which may even be hot and swollen. Severe abdominal pain and rigidity due to splenic infarction may be present and may simulate an attack of acute abdominal surgical emergency. Cerebral occlusion or pulmonary infarction are rare but serious complications.

2. *Sequestration crisis.* This is only seen in the younger patient and appears when large amounts of blood become, for no obvious reasons, sequestered in the liver and spleen. These organs suddenly increase markedly in size and there are manifestations of sudden circulatory collapse.

3. *Aplastic crisis.* Here a sudden attack of aplasia of the bone marrow develops. It lasts about 10 to 14 days and usually recovers spontaneously. It may be associated with an infection.

4. Hemolytic crisis. This is uncommon and may also be precipitated by an infection. A sudden increase in the rate of hemolysis develops.

In addition to the crisis there is anemia and subicterus. The abdomen is slightly enlarged due to an enlarged spleen and sometimes a liver. Gall stones may be seen in children as young as 3 years old. Cardiac enlargement with an apical systolic murmur may be present. Patients with sickle cell anemia are predisposed to salmonella osteomyelitis and pneumococcal septicemia. Chronic leg ulcers occur in the adolescent and adult but are very rare in children.

Laboratory findings: The red blood cells appear in a sickled shape if examined under conditions of low oxygen tension. Electrophoretic studies will reveal the presence of hemoglobin S, hemoglobin A₂ and hemoglobin F in sickle cell anemia, and hemoglobin S, hemoglobin A₂ and hemoglobin A in sickle cell trait.

There is diminution in the red cell count and hemoglobin level with a moderate degree of hypochromia. In rare instances a nutritional megaloblastic anemia due to excessive demands for folic acid and vitamin B₁₂ is present.

The reticulocytic count is raised. Leukocytosis appears especially during the crisis. The sedimentation rate is low even during a severe infection and the urine has a characteristic low specific gravity due to a tubular defect. The serum level of indirect bilirubin is high. Bone marrow aplasia will be present during an aplastic crisis.

X-ray examination of the skull and long bones of the hands and feet will show widening of the medullary spaces and thinning of the cortex. Infarctions of large areas of bones may lead to extensive changes similar to those of osteomyelitis.

Course and Prognosis : The crises tend to occur less frequently with increasing age. The prognosis however, must be guarded since fatal cerebral and cardiac accidents may suddenly occur. Gall stones may develop in the older child.

Diagnosis : The anemia has to be differentiated from other types of anemias. The disease has also to be differentiated from other conditions of painful bones and joints especially rheumatic fever and rheumatoid arthritis. Osteomyelitis is sometimes difficult to rule out. Sickle cell anemia has to be born in mind when examining a negro child with manifestations of an acute abdominal emergency. Disorders of the nervous system like poliomyelitis and hemiplegia may sometimes simulate the nervous complications associated with sickle cell anemia.

Treatment · Blood transfusion and protection against infection are the basis of treatment. Iron chelating agents which increase the urinary excretion of iron are helpful in diminishing the dangers of hemosiderosis and hemochromatosis. The treatment of painful crises involves relief of pain by sedatives like codeine or aspirin, and maintenance of hydration with water free of electrolytes. A coexisting infection should be treated by antibiotics.

Iron, liver extract and vitamins have no effect on the disease. Splenectomy should be considered if the size of the spleen is huge, producing pressure symptoms, if manifestations of secondary hypersplenism are present, or if repeated attacks of sequestration crises develop.

The Thalassemias

These are chronic hemolytic anemias characterised by hypochromia, microcytosis, poikilocytosis and immature erythrocytes in the peripheral blood.

Etiology : Two types of the disease are described :

(1) *Beta thalassemia*. This is more prevalent in Mediterranean countries. It results from marked decrease or total absence of beta chain synthesis and thus of hemoglobin A. Accordingly hemoglobin F and hemoglobin A₂ tend to increase in amount owing to a compensatory overproduction. Manifestations of this type of the disease are usually delayed till the age of 6 to 18 months when the switch from hemoglobin F to hemoglobin A normally takes place.

When this defect is homozygous, the disease is called thalassemia major in which the manifestations are usually severe. When heterozygous the defect is termed thalassemia minor which usually manifests mild or no symptoms. However, an intermediate clinical syndrome in which the severity lies between thalassemia major and thalassemia minor is sometimes described. It is given the designation thalassemia intermedia. This may be due to a homozygous or heterozygous defect, or rarely an interaction of thalassemia with another hemoglobinopathy.

(2) *Alpha thalassemia*. This is rare and more prevalent in Southeast Asia. It develops as a result of decreased synthesis of the alpha chain and thus hemoglobin A, hemoglobin F, and hemoglobin A₂. As a compensatory mechanism abnormal hemoglobins containing 4 nonalpha chains are produced. These abnormal hemoglobins have been designated hemoglobin H (beta), Bart's hemoglobin

(gamma) and delta hemoglobin. Alpha thalassemia is compatible with life only in the heterozygous state.

As in the case of sickle cell disease patients with thalassemia are more protected than usual against malaria.

Pathogenesis : Defective synthesis of normal hemoglobin with an increased percentage of the fetal type, impaired formation of circulating erythrocytes, and increased hemolysis of the defective cells are the cause of manifestations. However, the inadequacy of erythropoiesis to compensate for the increased rate of hemolysis is more marked in thalassemia than in sickle cell disease and other hemolytic anemias. This explains why thalassemics usually need more frequent blood transfusion than other patients with chronic hemolytic anemia.

Pathology : The skeletal structures contain abundant active red marrow.

The bony trabeculae are thinned and often the site of new bone formation. The spleen is enlarged, firm with marked extensive hematopoiesis chiefly of the red cell series and to a lesser extent other myeloid elements. The follicles are atrophied. Lymph nodes show pigmentation and are also the site of increased erythropoiesis. Hemosiderin deposits are marked in the liver, spleen and pancreas, and to a lesser extent in other organs like the thyroid, adrenals, kidney and heart etc. The heart may be dilated and hypertrophied.

Clinical features : In thalassemia minor there is only slight pallor and occasionally a slight enlargement of the spleen. Thalassemia intermedia manifests midway severity between thalassemia minor and thalassemia major.

In thalassemia major the anemia is usually severe and there is often mild jaundice. A characteristic facial appearance is usually present. This includes prominence of the frontal and parietal bones, enlargement of the head, protrusion of the maxillae and teeth, depression of the bridge of the nose and slanting of the eyes with an epicanthic fold. This facial characteristic in addition to the icteric tinge gives the child a mongolian appearance. Hemic murmurs and cardiac enlargement are common. The abdomen is usually protruded due to a huge spleen and an enlarged liver. After repeated transfusions for years hemosiderosis occurs with bronzing of the skin and further enlargement of the liver and spleen. Lymphadenopathy is occasionally noted. Growth retardation invariably occurs and secondary sexual characters almost never develop. Gall stones and chronic leg ulcers are rare. An aplastic crisis is also a rare finding.

X-ray and laboratory findings : An X-ray of the skull shows widening of the diploic spaces, with radiating bony trabeculae giving a "hair standing on end" appearance. Similar changes can be also seen in the vertebrae and bones of the hands and feet.

The blood shows anemia which is hypochromic and microcytic. Both the red cell count and hemoglobin concentration are diminished. The red cells show anisocytosis, poikilocytosis, and polychromatophilia. Target cells are present. The reticulocytic count is high and some nucleated erythrocyte precursors may be present. The leukocytes and platelets may be slightly increased in the early stages of the disease, but later when hypersplenism occurs they tend to diminish. The osmotic fragility is strikingly abnormal and the red cells are more resistant to hemolysis in hypotonic saline than normal. Serum indirect bilirubin is elevated and serum iron is increased with full saturation of the iron binding capacity. Aplasia of the bone marrow may be present during an aplastic crisis and a megaloblastic anemia due to folic acid deficiency is a rare complication. By electrophoresis the erythrocytes are found to contain increased amounts of hemoglobin F and hemoglobin A₂ in the more common beta thalassemia.

Differential diagnosis : The disease has to be mainly differentiated from iron deficiency anemia. Thalassemia should be always suggested when a hypochromic microcytic anemia thought to be due to iron deficiency does not respond to iron therapy.

Differentiation from other types of hemolytic anemias can be made from the facial features, blood picture, osmotic fragility and electrophoretic studies.

Prognosis : Due to repeated transfusions many patients acquire hemosiderosis and hemochromatosis which may be terminal complications. Cardiac failure is a constant threat to life.

Treatment : Thalassemia minor usually requires no treatment. For thalassemia major blood transfusion is an essential measure. It should be periodically repeated to keep the hemoglobin concentration above 6 g./100 ml. To diminish the development of hemosiderosis and hemochromatosis, iron chelating agents should be always combined. Splenectomy should be advised if the spleen is huge in size producing pressure symptoms, or if manifestations of hypersplenism become superadded.

Hereditary Spherocytosis

This is a genetically determined, chronic hemolytic disease characterised by spherocytosis, increased osmotic fragility of the red cells, and splenomegaly. The disease is inherited as a dominant character.

Etiology and pathogenesis : Normally the red cell membrane is relatively impermeable to the free movement of cations. However, a "pump activity" normally balances the pushing out of sodium which had entered the cell and the re-entrance of potassium which had leaked out. The energy necessary to provide for this metabolic activity is furnished by adenosine triphosphate.

The basic defect in hereditary spherocytosis is believed to be an abnormality of the red cell membrane which becomes unduly permeable to sodium. Spherocytosis is the morphologic result of this biochemical abnormality. The increased concentration of intracellular sodium leads to an extra utilisation of adenosine triphosphate to extrude this excess of sodium from the cell. This overwork increases the vulnerability of the red cell to destruction. When such cells are subjected to metabolic stress, as is believed to occur in the spleen, sodium irreversibly accumulates in them with ultimate hemolysis.

The spheroidal configuration is not present in the red cell precursors in the bone marrow but starts to appear in the reticulocytes. The abnormal shape furthermore accelerates sequestration of the red cells in the spleen.

Clinical picture : Jaundice, symptoms referable to anemia and splenomegaly constitute the most important clinical features. Manifestations may appear very early in the neonatal period when anemia, and jaundice are usually severe and may even be complicated by kernicterus and require exchange transfusion. In the older child there is a chronic type of anemia and a mild icteric tint which becomes more pronounced with advancing age. Jaundice is accompanied by dark pigmentation of the urine and stools. The anemia produces lassitude, fatigability and anorexia. The spleen is nearly always enlarged and the liver may be felt below the costal margin. The disease is characterised by the periodical development of an aplastic type of crisis which is associated with cessation of blood formation. The crisis is ushered in by fever, extreme pallor, shortness of breath, nausea, vomiting and extreme weakness. It may occur in several members of the same family almost simultaneously which may suggest its possible precipitation by an infection.

Gall stones may occur in older patients. A history of cholelithiasis in a parent justifies examination for spherocytosis in the off spring who is pale, easily fatigued

and without appetite. Leg ulcers may also appear in the older patient. Hemic murmurs may be heard over the heart. The disease does not usually affect growth of the child except when the anemia is severe.

Laboratory data : The red cell count and hemoglobin level are low. The anemia is normochromic and normocytic and the reticulocytic count is high. This may however be diminished during an aplastic crisis. The peripheral blood film shows anisocytosis and many of the red cells are spherocytic. The leukocytic and platelet counts are normal.

The osmotic fragility of the erythrocytes is typically increased. The auto hemolysis test reveals greater than normal lysis of the red cells. This abnormal autohemolysis can be corrected by the addition of small amounts of glucose to the blood before incubation. The serum level of indirect bilirubin may be elevated.

The bone marrow shows hyperplasia of the erythroid series except during the crisis when it becomes hypoplastic.

Differential diagnosis : The disease has to be differentiated from other types of chronic hemolytic anemia. The clinical picture and laboratory findings are helpful. Acquired spherocytosis is also present in autoimmune hemolytic anemia. Here the Coombs test is positive. It may be difficult to differentiate hereditary spherocytosis in the newborn from hemolytic disease due to A or B incompatibility, in which the red cells are spherocytic in shape. In the latter disease the Coombs test is usually positive but in some cases a period of observation may be necessary to clarify the diagnosis.

Treatment : Splenectomy completely alleviates the anemia and the accompanying symptoms. The blood picture improves strikingly and the crisis disappears. Spherocytosis and increased osmotic fragility however, persist after splenectomy. As splenectomy in early childhood may cause increased susceptibility to infection, the operation may be postponed until the patient is at least 5 years old. This may also prevent the development of gall stones which usually occurs after this age. Splenectomy however, may be performed at an earlier age if the anemia is severe enough to impair growth or if aplastic crises are frequent.

Hemolytic Anemia¹ Due To Enzyme Deficiency

Defective production of red cell enzymes may involve the major pathways of glucose catabolism, the anerobic Embden - Meyerhof pathway or the oxidative pentose phosphate shunt. Such enzymatic abnormalities may result in the development of a hemolytic anemia. The commonest deficiency encountered clinically is glucose 6 - phosphate dehydrogenase deficiency.

Glucose 6- Phosphate Dehydrogenase Deficiency

(Drug Induced Hemolytic Anemia; Primaquin Sensitivity)

Etiology : The genetic deficiency of the enzyme glucose 6 - phosphate dehydrogenase has been found to be the cause of an aquired type of hemolytic anemia. Hemolysis in such susceptible patients occurs after the administration of a number of factors of which primaquin was the first to be identified. Besides primaquin and some other antimalarial drugs, these factors include synthetic vitamin K, furadantin, some sulphonamides, paraaminosalicylic acid, phenacetin and some other antipyretics, naphthalene and an ingredient in the fava beans (*vicia faba*). The anemia developing after the intake of *vicia faba* has been termed favism. It may rarely occur after inhaling the pollen of the bean flower. Most of the above mentioned drugs, which are oxidant in nature, can produce hemolysis of normal red cells when they are given in doses larger than normal or to patients with impaired renal function. Favism however, occurs exclusively in enzyme deficient subjects. Accordingly the basic defect in the disease appears to be the production of an unstable enzyme which becomes inactive much more rapidly than normal.

The disease is inherited as a sex linked character with incomplete dominance and thus affects males more than females. It is more prevalent in negroes, and Mediterranean, Middle Eastern and African children.

Clinical picture : There is history of the development of anemia after the intake of one of the above mentioned drugs or fava beans. It may be mild and take about 3 days to develop, or severe and rapid especially in the case of favism. The hemolytic attack may be accompanied by nausea, vomiting and epigastric pain. If hemolysis is severe hemoglobinuria with red urine and jaundice follow. Even if administration of the responsible agent is continued, spontaneous recovery is usually the rule. The defect may be the cause of hyperbilirubinemia and kernicterus in the newborn infant. It should be remembered that the older cells in the circulation are more susceptible to hemolysis than the younger ones and the reticulocytes.

Laboratory findings : Sudden anemia is present with diminution in the number of red cells and hemoglobin level. Reticulocytes and young red cells predominate in the peripheral blood. The red cells show an increased tendency to form Heinz bodies. Hemoglobinemia, hemoglobinuria and very low or absent serum haptoglobin are demonstrated in severe cases. The diagnosis can be made certain by direct determination of the activity of the enzyme. As reticulocytes and young red cells have higher enzyme activity than older cells, therefore the result of testing may be within normal during an attack and may only show diminution after a few weeks.

Treatment : If the attack is mild it may be compensated within a few days by hyperactivity of the bone marrow. Removal of the offending agent and avoidance of its intake are essential. In severe cases blood transfusion is necessary.

HEMOLYTIC DISEASE OF THE NEWBORN

Hemolytic disease of the newborn includes a number of hemolytic processes occurring in the fetus and newborn infant. It can be caused by isoimmunization with respect to the RH factor. Less frequently it may be due to A or B isoimmunization. Very rarely it may be produced by incompatibility to rare blood groups such as the Kell-Cellano or MNS.

Hemolytic Disease due to RH Incompatibility (Erythroblastosis Fetalis)

The disease manifests itself in 3 main forms; hydrops fetalis, icterus gravis neonatorum and hemolytic anemia of the newborn. The 2nd and 3rd forms, however are always present in the same patient in various degrees.

Etiology and pathogenesis :

The RH factor: It is now clear that the cause of hemolytic disease of the newborn is the sensitization of the mother to some antigen contained in the fetal red cells and inherited from the father. The mother produces an antibody to this antigen which then passes through the placenta to the fetal circulation. Here it destroys the fetal red blood cells and attacks other fetal organs particularly the liver.

It was previously shown that if the red cells of the rhesus monkey were injected into a gineapig, antigens contained in the red cells of the monkey caused the production of antibodies which would agglutinate the red cells not only of the rhesus monkey but also of about 85% of white people. The 2 types of human red cells thus distinguished were described as follows :

RH positive (RH) = 85% agglutinated.

rh negative (rh) = 15% not agglutinated.

The RH characters of the individual obey the laws of inheritance. The RH factor is inherited as a dominant trait. As mentioned, persons having the factor in their blood are called RH positive and those lacking it are called rh

negative. RH positive persons may be homozygous for this trait (RH RH) or heterozygous (RH rh). RH negative persons are always homozygous (rh rh). Children of a homozygous RH positive father and an rh negative mother are always RH positive. In the case of the heterozygous RH positive father and an rh negative mother only half the children will be RH positive.

The RH antigen was further found to be more complex, and it was demonstrated that there are 6 RH antigens. These are called Cc, Dd, Ee. Each of these antigens can stimulate the production of its equivalent antibody. Each individual has 3 of these 6 antigens carried on the same chromosome. The most important is the D and its antibody the anti-D.

RH antibodies : Maternal antibodies to the RH factor are of 2 types :

(1) Complete antibodies which agglutinate red cells in saline media. These do not cross the placenta and are not involved in the causation of the disease.

(2) Incomplete antibodies which agglutinate RH positive red cells only in albumen or other colloidal media such as plasma or serum. These antibodies cross the placenta freely and are responsible for manifestations of the disease. They can be detected by the Coombs test.

Isoimmunization to the RH factor This can occur after 3 conditions :

(1) *Pregnancy*. Isoimmunization occurs when an rh negative mother carries an RH positive fetus. This depends on 3 factors.

- a) The number of previous stimuli. i.e. previous pregnancies with RH positive fetuses or as will be mentioned later previous blood transfusions or intramuscular injections of blood.
- b) An unknown factor, for some women become sensitized in their 2nd pregnancy whereas others become sensitized after repeated pregnancies and some never become sensitized at all.
- c) The fetal red cells must be able to enter the maternal circulation. Ordinarily, the placenta should be impervious to formed blood elements. It is presumed that the transfer is made through small breaks in the placenta. Transfer is also facilitated by the existence in man of a single syncytial cell layer separating the villi containing fetal blood cells and the maternal sinuses, and by thinning out of the expanding placental surfaces.

(2) *Repeated blood transfusions*. Blood transfusion is a much more potent stimulus to the production of RH antibodies than is pregnancy. But fortun-

ately repeated transfusions are relatively rare. There is evidence that the spacing of transfusions is important in determining the antibody response. Probably if they are spread over many months they are more likely to induce sensitization. The size of the transfusion is not important. Experimentally the injection of amounts of RH positive blood as small as .05 c.c. may be sufficient in some cases to produce an optimal antibody response.

(3) *Intramuscular injections of blood.* At present these are rarely done. But there are reports in the literature that sensitization followed repeated intramuscular injections of blood which were in the past used for the treatment of eczema.

Pathology : If jaundice is severe the entire brain is pigmented. More intense staining of the basal ganglia and other nuclei in the brain stem and medulla is present in kernicteric infants. Ganglion cells degenerate leaving empty spaces.

The bone marrow shows active hemopoiesis. The liver and spleen are always enlarged and histologically show wide spread areas of extramedullary hematopoiesis. Proliferation of normoblasts is seen in the liver sinusoids. Extramedullary hemopoiesis also appears in the pancreas, kidney, adrenals, lymph nodes, thymus and placenta.

Many of the hepatic cells are vacuolated and severely damaged livers show evidence of intrahepatic biliary obstruction. Hemosiderosis may be present in the liver and spleen. Hypertrophy and hyperplasia of the pancreatic islet cells are present.

In hydrops fetalis, extensive edema, maceration of the body, effusions into serous cavities and marked enlargement of the liver and spleen are demonstrated. The placenta is bulky and edematous.

Clinical picture :

Hydrops fetalis : This is the most severe form of hemolytic disease, and nearly all infants so affected are either stillborn or die shortly after birth. The fetus is grossly edematous and body cavities contain fluid. Occasionally the fetus can be recognized as hydropic by radiological examination in utero by its inability to flex the legs to the same extent as a normal fetus, or by a halo surrounding the skull. The massive edema is attributed to heart failure. Usually intrauterine death occurs. If the fetus dies and is retained in the uterus for some time after death, it may be delivered in a macerated condition with little edema.

Hemolytic disease is the commonest cause of hydrops or of a macerated fetus. It can also occur from congenital syphilis, and the diagnosis can be confirmed by serological tests.

Icterus gravis neonatorum This is the commonest form of the disease. The infant is usually born at term, occasionally jaundiced at birth but much more commonly jaundice comes on subsequently generally making its appearance within 24 hours of birth. In the untreated patient or the patient treated by simple transfusion jaundice usually fades in 3-4 weeks and as the jaundice fades anemia becomes obvious. Sometimes however, deep jaundice may persist for many weeks. The infant usually has a definitely enlarged spleen and in severe cases a palpable liver. Petichae, and in severe cases hemorrhages and edema due to heart failure may be present.

Brain damage (*kernicterus*) represents the most serious complication of *icterus gravis*. It is associated with high concentrations of indirect bilirubin. It can thus be regarded as a bilirubin encephalopathy. The affected children show involuntary movements, commonly of extension and sometimes repetitive in type, have neck rigidity, head retraction, or even opisthotonus, and alternating states of muscular rigidity and flaccidity. The respiration may be grunting. There is alteration of the Moro reflex. Most of these infants if not treated, die after 3 or 4 days. A small number however, recover and are nearly certain to show neurological complications later on. They may also show green pigmentation of the deciduous teeth. *Kernicterus* however, can be almost completely prevented by early treatment. It has been well documented that the likelihood of *kernicterus* develops when indirect bilirubin concentrations reach 20 mg.% and above.

Sometimes a child with *icterus gravis* has a slight neck rigidity only, without other neurological signs. In such a case spastic diplegia may develop later. Staining of the basal ganglia, not associated with isoimmunization has been described in connection with prematurity, in patients with spherocytosis, in newborn infants given large doses of vitamin K and even in newborn infants with severe physiologic jaundice.

Hemolytic anemia of the newborn : This is the mildest form of the disease. The jaundice may be very slight or not noticed at all. Usually the anemia becomes manifest after the jaundice if any, disappears. Infants with this type of the disease usually do not develop any neurological complications and respond dramatically to treatment.

Laboratory findings. The following can be performed during pregnancy:

(A) — *Estimation of the maternal anti RH titre.* Significant disease of the fetus is usually associated with a maternal titre of incomplete antibodies of 1 : 8 or more. Titres of more than 1 : 64 are usually suggestive of hydrops fetalis and still birth. Though the height of the maternal titre is not always

correlated with severity of the fetal affection, a rising one is always a serious finding.

(B) — *Amniocentesis*. Examination of the amniotic fluid during pregnancy gives more precise information than antibody titre estimation. The fluid can be obtained by direct puncture through the abdominal wall. Normally the amniotic fluid is clear and colourless. It turns yellow if the fetus suffers from hemolytic disease. This results from the excretion of bilirubin and related pigments into the amniotic sac. The optical density of the fluid can be measured by spectrophotometric methods and the severity of the disease can accordingly be predicted.

Findings in the newborn baby include the following :

1 — *Hyperbilirubinemia*. At birth the normal baby has a bilirubin level of 0.7-3.1 mg. per 100 cc. (average 1.6). This level rises to 10 mg./100 c.c. after 2-3 days. In prematures the level may reach 15 mg./100 c.c. after 3-4 days. This shows that no jaundice appears in the first 24 hours after birth.

In hemolytic disease the level at birth is 3-6 mg./100 c.c. and may rise up to 20 mg. or more after about 24 hours.

2 — *Anemia*. This is another important feature of the disease. It is best diagnosed in the cord blood. Hemoglobin values less than 13.6 g/100 c.c. can be taken as pathological.

3 — *Erythroblastemia*. The peripheral blood of the normal newborn infant sometimes contains a few nucleated red cells usually less than 5 per 100 white cells, and usually disappear after a day or two from birth. In hemolytic disease these are far more numerous and may even outnumber the white blood cells. They are erythroblasts and persist for many days after birth. But it must be born in mind that this erythroblastemia is not specific to hemolytic disease of the newborn as was first thought. It is a common feature in infants born to diabetic or prediabetic mothers.

4 — *Reticulocytosis*. Counts above 6% are suggestive of the condition.

5 — *Thrombocytopenia* is present in severe cases.

6 — *Positive Coombs test*. The Coombs test is a sensitive method for demonstrating the presence of incomplete antibodies. A positive Coombs test is also obtained in patients with hemolytic disease due to ABO incompatibility, anti-immune hemolytic anemia, acquired hemolytic anemia secondary to leu-

kernia, lymphosarcoma, disseminated lupus erythematosus, and thrombotic thrombocytopenic purpura.

Differential diagnosis : The disease has to be differentiated from hemolytic disease due to ABO incompatibility, and other rare blood group incompatibilities. It has also to be differentiated from other causes of neonatal jaundice. These mainly include physiologic jaundice, congenital biliary atresia, hereditary spherocytosis, hemolytic anemia due to glucose 6 - phosphate dehydrogenase deficiency, neonatal hepatitis, toxoplasmosis, cytomegalic inclusion disease and septicemia. Hydrops fetalis has to be differentiated from congenital syphilis.

Treatment : Once pregnancy has begun and there is reason to believe that the infant is going to be affected 4 lines of action have to be considered : —

1 — Induction of abortion.

2 — Intrauterine transfusion.

3 — Induction of premature labour.

4 — Allowing the pregnancy to proceed to term. In 2, 3 and 4, preparation must be made to exchange transfuse the infant shortly after delivery if necessary.

Induction of abortion. This is very rarely considered. Only in the case of a woman who has had 2 or more stillbirths due to isoimmunization to RH and the husband is homozygous. There is no need for the mother to undergo another fruitless labour.

Intrauterine transfusion. The aim of this line of treatment is to prevent hydrops fetalis and stillbirth. Estimation of maternal antibody titre and performance of repeated amniocentesis at weekly intervals will help to decide this line of treatment. Because it is a difficult and hazardous technique both to mother and fetus, it is only considered when fetal death is likely. However, it should not be done if x-ray signs of hydrops fetalis are already present. It should not be performed after the 34th week and may be repeated more than once. Transfusion is done into the fetal peritoneum using an rh negative blood.

Induction of premature labour. It was shown that most intrauterine deaths occur before the 37th week of gestation. It was also shown that in the infant with severe disease the chances of survival diminish with the period of gestation. Induction of labour accordingly has been recommended at or shortly after 37

weeks when conditions are obstetrically favourable and the fetus is of good size and is viable.

Treatment of the affected infant. The treatment of the infant with hemolytic disease has 3 major aims:

- 1 — The prevention or control of cardiac failure (the major cause of death within the first 24 hours),
- 2 — The prevention or control of hyperbilirubinemia in an effort to prevent the occurrence of kernicterus (the major cause of death after 48 hours).
- 3 — The control of anemia (this is almost automatically associated with the first 2 aims).

Once the infant is born 2 facts must be ascertained :

- 1 — Whether it is affected with hemolytic disease.
- 2 — Whether the degree calls for immediate exchange transfusion.

The criteria for immediate exchange stem from clinical and laboratory evidencies. Thus pallor, edema, poor respirations and hepatosplenomegaly constitute clinical indications for immediate treatment. Laboratory evidence of a severe hemolytic process includes the presence of anemia at birth, i.e. low hemoglobin level in the cord blood, elevation of cord bilirubin and a high degree of reticulocytosis.

If no criteria for immediate treatment are present the hemoglobin level and bilirubin content should be followed up as the need for exchange may arise few days after birth. It can be recommended that a hemoglobin level below 11-12 gm. per cent and a bilirubin level of 20 mg-% reached at any time are urgent indications for exchange transfusion.

— *Exchange transfusion.* Group specific ABO, rh negative blood is used. The amount of blood to be used equals twice the blood volume which is estimated on the basis of 85 ml./kg. body weight. One or more transfusions may be necessary. The umbilical vein may be used in the first 2 or 3 days after birth. Thereafter the saphenous or femoral veins are used.

— *Treatment of cardiac failure.* Here exchange transfusion must be done slowly and less than the calculated amount of blood is given (approximately 1-1.5 times the blood volume). Administration of digitalis is unnecessary. Antibiotics should not be administered through the umbilical vein for fear of an adverse reaction through a direct effect on the myocardium.

— *Miscellaneous treatment.* Administration of ACTH or corticosteroids to the mother during pregnancy and the infant after delivery has been tried without definite beneficial results.

Prevention of RH sensitization :

If an rh negative mother delivers a normal RH positive infant and is found to be still not sensitized, her further sensitization during a 2nd pregnancy can be prevented by the intramuscular injection of 300-400 microgram of human anti-D-gamma globulin within 72 hours after delivery.

Hemolytic Disease due to ABO Incompatibility

Etiology : Hemolytic disease of the newborn due to A or B incompatibility is a generally mild disorder. Usually the mother is group O and the fetus group A or B. Although such a combination is not uncommon, hemolytic disease due to A or B incompatibility is of a rare occurrence. This is because the antibodies produced are mainly of the complete type which does not cross the placenta and has no role in the production of the disease. High levels of incomplete antibodies which freely cross the placenta and which are responsible for the disease are however rarely produced against A or B antigens.

Clinical features : The first born is usually affected in contrast to RH incompatibility in which the disease starts to appear in the 2nd or 3rd child unless the mother had been previously immunized by an RH positive blood transfusion. Jaundice develops within the first 24 hours and is therefore sometimes termed icterus precox. Anemia at birth is rare and mild. Splenomegaly is slight or absent. Stillbirth and hydrops are rare, and the prognosis for succeeding pregnancies is excellent. Hyperbilirubinemia can occur and if not properly treated may result in kernicterus.

Laboratory findings : The hemoglobin level and red cell count are usually normal or slightly reduced. Reticulocytosis of about 5-7% may be present. The most characteristic finding is the presence of microspherocytosis which is best observed in the first days after birth. There is an associated increase in osmotic and mechanical fragility. The Coombs test is positive in 90% of cases.

Treatment : As in the case of RH incompatibility, the treatment is by exchange transfusion. But it must be emphasized that the indication for treatment in this case is the degree of hyperbilirubinemia and not

the anemia. To prevent the development of kernicterus, exchange transfusion should be performed and repeated if necessary to keep the level of indirect bilirubin below 20 mg/100 ml. The blood to be used should be fresh group O of appropriate RH type. It is also preferable if anti A and anti B antibodies are neutralised with group specific substances A and B. As for subsequent pregnancies there is no fear of increasing severity and they may be normal.

Autoimmune Hemolytic Anemia

This anemia is characterised by the presence of demonstrably abnormal antibodies in the blood which are produced by the body and cause hemolysis of its own blood cells.

Etiology :

(1) The cause may be unknown (idiopathic).

(2) The condition may be associated with another disorder e.g. chronic leukemia, Hodgkin's disease, lymphosarcoma, disseminated lupus erythematosus and other collagen diseases, neoplasms, liver diseases and some virus infections.

It is suggested that drugs, infections or other agents may in some way alter the red cell membrane so that it becomes "foreign" or antigenic to the host.

Clinical features : Anemia of a chronic course which is prone to severe exacerbations is usually present. There is jaundice and a mild fever. Hepatosplenomegaly and rarely mild lymphadenopathy are present. Purpura may be met with and is usually indicative of a secondary condition. Hemoglobinuria is unusual and is a sign of severe hemolysis. Manifestations of the underlying disease are usually prominent in secondary cases.

Laboratory findings : The red cell count and hemoglobin level are low. Persistent reticulocytosis is present. Spherocytosis and polychromasia are marked during the active phase of the disease. The platelet count is usually normal but may be low. The leukocytic count is usually elevated during exacerbations. The bone marrow is hyperplastic and aplastic crises are rare. Three different types of autoantibodies affect the red cells in autoimmune hemolytic anemia; autoagglutinins, autohemolysins, and incomplete antibodies which produce a positive Coombs test.

Treatment : The basis of treatment includes blood transfusion, adrenocortical steroids, cytotoxic drugs and splenectomy.

Steroids should be tried first, and cytotoxic agents which are capable of suppressing immune responses may be only used when steroids have failed. Of these, the most commonly used are 6 mercaptopurines and cyclophosphamide. Splenectomy should be considered in patients who fail to respond to hormone and drug therapy.

HYPERSPLENISM

One of the major functions of the spleen is the control of blood formation and the regulation of the delivery of blood cells from the bone marrow. If this function is greatly exaggerated, a condition termed hypersplenism is produced. This condition therefore represents a functional and not an anatomic change in the spleen. Hypersplenism, however, is usually associated with some degree of splenomegaly.

The blood disturbances dependent upon hypersplenism may be attributed to one of two mechanisms :

(1) Selective sequestration and increased destruction of formed blood cells in the spleen.

(2) Inhibition upon a normal or hyperactive bone marrow by a hormone secreted by the spleen. This inhibition may be through prevention of the growth and maturation of blood cells, or by a block to their delivery from the bone marrow.

Hypersplenism therefore is associated with :

(1) Neutropenia, thrombocytopenia and anemia either singly or in combination.

(2) Splenomegaly.

(3) Normal or hypercellular bone marrow.

Hypersplenism may be primary, when there is no obvious cause for the depletion of blood cells, as in patients with splenic panhematopenia or idiopathic thrombocytopenic purpura. It may be secondary in patients with splenomegaly in combination with well defined disorders such as Hodgkin's disease, chronic leukemia, lymphosarcoma, Gaucher's disease, thalassemia etc..

Two tests can sometimes help in the diagnosis of hypersplenism :

(1) The adrenalin test : Adrenalin is said to prompt the mobilization of sequestered cells into the peripheral blood.

(2) Infusion of the patient's own red blood cells tagged with radioactive chromium may indicate rapid destruction in the splenic area.

Splencetomy frequently restores a normal peripheral blood picture but obviously does not affect the underlying disorder.

LEUKEMIA

Leukemia is a disease characterised by widespread proliferation of the leucocytes and their precursors in the bone marrow and reticuloendothelial tissues.

Etiology : The etiology is not certain. The following theories are put forward :—

(1) Viral infection. The theory that a viral agent is responsible is strengthened by animal experimentation especially on mice. Leukemia can be transmitted by a viral agent in susceptible strains of mice.

(2) There is reason to believe that heredity plays an important role in the etiology. The incidence of the disease is higher in some families. Recent chromosomal studies have shown that in acute leukemia there is a high incidence of chromosomal abnormalities consisting of alterations in their number and structure. However, these abnormalities are not always constant. The only constant abnormality has been described in chronic myelocytic leukemia in which an abnormal chromosome termed the Philadelphia chromosome was demonstrated in hematopoietic cells.

(3) There is evidence that irradiation increases the incidence of leukemia. The disease was more prevalent among atomic bomb survivors in Hiroshima and Nagasaki.

Age incidence : In children, leukemia has a peak of onset at 3-4 years of age. Congenital leukemia (leukemia affecting the newly born infant) is very rare. Manifestations may appear at birth or more commonly some time later in the neonatal period. The myelocytic type is the commonest at this age period.

Classification : Leukemia can be classified into acute and chronic in relation to clinical severity. It may be also classified according to the predominant cell into the following types. The first two are the commonest in children :

(1) Acute stem cell leukemia. Here the predominant cell in the bone

marrow is a primitive cell without easy differentiation into myeloblastic, lymphoblastic, or other types.

- (2) Acute lymphoblastic leukemia. The predominant cell in the blood and bone marrow is the lymphoblast.
- (3) Granulocytic types : which include 3 varieties : —
 - a) Acute promyelocytic leukemia. This is the commonest of the granulocytic types. The predominant cell is the early myelocyte.
 - b) Acute myelocytic leukemia. Here the predominant cell is the more mature myelocyte.
 - c) Chronic myelocytic leukemia. This is the commonest chronic leukemia in children.
- (4) Monocytic leukemia. This may manifest itself in one of two forms :
 - a) When the blood picture is marked by the presence of both myelocytes and monocytes the disease is called the Naegeli type.
 - b) When the immature cells resemble monocytes and reticuloendothelial cells, the disease is called the Schilling type.
- (5) Less common types of leukemia. These include the following :
 - a) Eosinophilic leukemia. Here the majority of cells in the peripheral blood are eosinophils but in some cases these are accompanied by myeloblasts and myelocytes.
 - b) Basophilic leukemia. Here the predominating cells are basophilic.
 - c) Plasma cell leukemia. In this type plasma cells are found in the blood. Multiple myelomata are usually also present.

The term aleukemic leukemia (subleukemic leukemia) describes the disease when there is a diminution in the number of leukocytes in the peripheral blood. Immature elements are however, present.

Pathology : The lymph nodes, spleen, liver and kidneys are often enlarged due to proliferation of leukemic tissue. On section the normal splenic architecture is lost and the red pulp shows a homogeneous overgrowth of leukemic cells. Similarly the liver shows an excessive content of leukemic proliferation. In the kidneys leukemic infiltration extends along the medullary cords into the cortex. There is almost complete replacement of fatty marrow by greyish red leukemic marrow. Proliferation of leukemic tissue may also be

seen in the central nervous system. Changes in bone may be present and are due to osteoblastic and osteoclastic reactions and to destruction of bone by leukemic cells. Extensive hemorrhages may occur in parenchymal organs, the retroperitoneal space, the gastrointestinal tract and the central nervous system. Areas of ulcerations and secondary infection may be found in various sites.

Clinical manifestations : Result from anemia, diminution in the number of normal leukocytes, thrombocytopenia, and disturbances of the organs affected. The rapid growth and destruction associated with leukemic infiltration result in increased metabolism of the body manifested by fever, weight loss and fatigue.

Anemia is an early and severe finding. The skin has a waxy whiteness. The red cells are normocytic and normochromic. A hemic murmur may occasionally be present. The following mechanisms are responsible for the development of anemia :

- * Blood loss due to thrombocytopenia. This factor is more pronounced in acute than in chronic leukemia.

- * Mechanical overcrowding of the bone marrow and replacement by leukemic tissue. A myelophthisic type of anemia is produced.

- * It was proved by isotopic studies that in leukemia there is an increased rate of red cell destruction. This is occasionally produced by an autoimmune process.

Although leukemia is associated with an increased proliferation of white cells, these are abnormal and have extremely defective phagocytic functions. The normal leukocytes are diminished in number with resultant frequency of pyogenic infections in many sites such as the skin, lungs, and mucous membranes of the mouth and pharynx. The commonest organisms responsible are the streptococci, staph. aureus, E. coli and monilia.

Thrombocytopenia is a constant feature and purpuric spots or extensive bruises may be one of the earliest findings in the disease. Hemorrhagic manifestations may be also present in the form of hematuria, hemorrhagic diarrhea, renal hemorrhages or intracranial hemorrhage. In addition to thrombocytopenia these hemorrhages may be also accentuated by some coagulation defects which were reported in a big number of leukemic patients.

Infiltration of leukemic cells may produce lymphadenopathy, splenomegaly and hepatomegaly. Rarely enlargement of the kidneys and testes occurs. Leukemic infiltrations are occasionally seen in the lungs, skin and skeletal sys-

tem. Bone pain in these cases results and is due to destruction by leukemic infiltration or subperiosteal hemorrhage. The joints may also be affected leading to arthralgia. Involvement of the central nervous system is an important and serious finding. It may be affected by hemorrhage, thrombosis or leukemic infiltration. The latter will be manifested by vomiting, papilledema, separation of the cranial sutures, headache, stiff neck and the appearance of blast cells in the cerebrospinal fluid.

Chronic leukemia is uncommon in children. It is insidious in onset. Lymphadenopathy, splenomegaly, anemia, ulcerations of the mucous membranes and weakness are the commonest symptoms.

Laboratory findings : Anemia is a constant feature. Except in chronic myelocytic leukemia, thrombocytopenia is always present. Moderate to severe leukocytosis is usually present with a percentage of immature cells. This is much more important than the increase in number of white cells. Rarely the leukocytic count is low.

Bone marrow examination is an essential step before the diagnosis of leukemia. The marrow will show an abnormal overgrowth of leukopoietic tissue. The type of leukemia depends upon the predominant mother cells (blasts) present. The blast is a large cell with scanty blue cytoplasm which contains no granulations. The nuclear chromatin is dispersed in a finely stippled pattern. One or more nucleoli may be seen. Megakaryocytes and erythropoietic precursors are greatly diminished.

The blood levels of uric acid, glutathione, phosphorus and alkaline phosphatase are usually increased.

If leukemic infiltration of the central nervous system occurs the cerebrospinal fluid will be under tension and will contain a high percentage of lymphoblasts.

X-ray examination may be helpful to diagnose enlarged lymph nodes in the mediastinum or abdomen. It may also confirm the presence of effusions, liver, spleen and kidney enlargements and affections of bones.

Differential diagnosis : Leukemia should be included in the differential diagnosis of any blood disorder associated with depression of one or more blood elements. It should also be considered in the diagnosis of any condition in which the leukocytic count is abnormally increased. Complete hematological investigations including bone marrow studies are in these cases mandatory.

Diseases which may be confused with leukemia include idiopathic thrombocytopenic purpura, scurvy, rheumatic fever, aplastic anemia, sickle cell disease, osteomyelitis, infectious mononucleosis, infectious lymphocytosis and disseminated neuroblastoma.

Treatment : This includes supportive therapy and specific therapy.

Supportive therapy. Includes blood transfusion, when the anemia is severe. It also includes antibiotics to control infections and analgesic drugs if the pain is severe.

Specific therapy. The principal therapeutic agents for the treatment of leukemia in children are :

(1) Antimetabolites (Table 18)

— Folic acid antagonists .	— Purine antagonists.
— Amino acid antagonists.	

(2) Cytotoxic agents.

— Radiation therapy.	— Radioactive isotopes.
— Cytotoxic drugs (Table 19).	

a. Alkylating substances :

- * Nitrogen mustard
- * Triethylene melamine (TEM)
- * Triethylenephosphoramide (TEPA)
- * Cyclophosphamide
- * Myeleran.

b. Antimitotics :

- * Vincristine sulphate
- * Urethane
- * Fowler's solution

(3) Hormones (Table 20)

- ACTH.
- Cortisone, hydrocortisone, prednisone, prednisolone, methyl prednisolone, dexamethasone.

(4) Enzymes.

L asparaginase is the enzyme at present used.

Antimetabolites. This group includes :

1. *Folic acid antagonists* : which act by blocking the transformation of folic acid into folinic acid during the synthesis of purines and pyrimidines, thus

inhibiting cellular growth and multiplication. Aminopterin and methotrexate belong to this group. Toxic effects are varied and include anorexia, ulceration of the oral mucosa, diarrhoea, and alteration of the bone marrow with megaloblastosis.

2. *Purine antagonists* : which inhibit the synthesis of nucleic acid. The main compound is 6-mercaptopurine. Toxic effects are generally rare and are shown by anemia, leukopenia and thrombocytopenia.

3. *Amino acid antagonists* : These act by inhibiting the utilisation of formates and glycine in purine synthesis. The best known is asaserine. Vomiting, nausea, diarrhoea and leukopenia are the commonest toxic effects.

Cytotoxic agents. These include :

1. *Radiation therapy* : X-ray therapy is beneficial in relieving pressure symptoms and pain due to enlargement of infiltrated organs and localised leukemic masses. It is very effective in the treatment of central nervous affection.

Radium has the same effect.

2. *Radioactive isotopes* : The most effective for the therapy of leukemia is radiophosphorus (P 32). It has a physical half life of 14.3 days and is given by mouth or intravenously as an isotonic solution of sodium phosphate and is distributed in the body through the blood stream. Its dose is 0.1 millicurie/kg. once or twice a week. It is usually only suitable in chronic leukemia.

3. *Cytotoxic drugs* : these include the following :-

a) *Alkylating substances.* These inhibit the proliferation of neoplastic and rapidly reproducing cells (blood cells) by interfering with the synthesis of nucleoproteins. They have a toxic action on the bone marrow shown by leukopenia, thrombocytopenia and anemia. The most important are cyclophosphamide and myeleran.

b. *Antimitotics.* The most important of these is vincristine sulphate. Urethane and Fowler's solution (potassium arsenate) also belong to this group. They inhibit cellular growth and reproduction. The toxic effects of vincristine sulphate are peripheral neuropathy, weakness, fever, alopecia and marrow depression. Because of these serious side effects its main usefulness may be in inducing remissions after which another drug may be substituted. The drug is characterised by producing remissions rapidly.

Hormones. The commonest hormones used are ACTH, cortisone, prednisone, prednisolone and dexamethasone. The blood response after their administration is an increase in circulating neutrophils and a decrease in lym-

phocytes and eosinophils. The mechanism by which this is produced is not entirely understood. Moon face, electrolyte disturbances and other Cushing like manifestations are the main side effects.

Enzymes. Enzyme treatment of leukemia has been recently achieved by the use of L asparaginase. L asparagine is a nonessential amino acid which is vital for cell metabolism. Normal cells of the body can themselves form the amino acid. Leukemic and malignant cells however, do not possess this property and require the provision of the amino acid from extracellular sources eg. the intercellular spaces. Injection of the enzyme L asparaginase in these cases, will break down L asparagine present in the intercellular spaces into aspartic acid and ammonia. Eventually this deprivation of L asparagine will lead to destruction of leukemic and malignant cells. The enzyme will obviously produce no effect on normal cells.

L asparaginase is most effective against acute leukemias especially acute stem cell and acute lymphoblastic leukemias. It has the major advantage over other antileukemic agents in that it may be used to treat patients in whom the bone marrow is severely hypoplastic without producing further marrow depression.

It is given intravenously in a dose of 200 units/kg./day. The course is from 4 to 6 weeks. Toxic manifestations are usually not severe in the form of allergy, nausea, vomiting, lassitude, fever, hepatic dysfunction and changes in blood coagulation. The drug is contraindicated during pregnancy as it may lead to fetal congenital anomalies.

Table 18 : Antimetabolites.

Drug	Method of administration	Daily Dose	Cycle
Folic acid antagonists			
Aminopterin	oral	0.25 - 1 mg.	3 - 4 weeks
Methotrexate	oral	2.5 - 5 mg.	3 - 4 weeks
Pyrimidine antagonists			
6 - M.P.	oral	1.5 - 2.5 mg./kg.	3 - 8 weeks
Amino acid antagonists			
Azaserine	oral or i.v.	2.5 - 10 mg./kg.	1 - 5 weeks

Table 19 : Cytotoxic Drugs.

Drug	Method of administration	Daily Dose	Cycle
<i>Alkylating substances</i>			
Nitrogen mustard H N2	intravenous	0.4 mg./kg. in single or divided doses	administration may be repeated after one month.
T.E.M.	oral	1.5 - 5 mg.	2 - 3 times/week for one month or longer. Total dose 20 - 40 mg.
T.E.P.A.	intramuscular	0.2 mg./kg.	Total dose 1.5 - 2.5 mg./kg.
Myeleran	oral	2 - 6 mg.	Total dose 150 - 200 mg.
Cyclophosphamide (Cytoxan)	oral or intravenous	5 mg./kg. then reduced to 2 - 3 mg./kg.	
<i>Antimitotics</i>			
Vincristine sulfate	intravenous	0.05 - 0.15 mg./kg.	Single weekly dose
Urethane	oral, intramuscular or i.v.	2 - 4 gm.	Total dose 30 - 300 g/m.
Fowler's solution	oral	5 - 20 drops	

Table 20 : Steroid Hormones and A.C.T.H.

Drug	Method of administration	Daily Dose
Cortisone	oral and intramuscular	100 - 400 mg.
Hydrocortisone	oral, intramuscular or intravenous	50 - 200 mg.
Prednisone, Prednisolone	oral	1.5 - 2.5 mg./kg.
Dexamethasone	oral	0.15 - 0.25 mg./kg.
A.C.T.H.	intramuscular or intravenous	60 - 200 units 25 - 50 units

TREATMENT OF ACUTE LEUKEMIA :

Induction : This is carried out by giving two or more drugs known for their effect as remission producers till a remission is induced. The commonest combinations are corticosteroids and vincristine sulfate or corticosteroids and L asparaginase.

Treatment of the C.N.S. This should be done in every case as a completion of induction. The C.N.S. can be treated by deep X-rays on the skull and by intrathecal methotrexate.

Maintenance. After a remission is induced maintenance therapy is started. The commonest two drugs used for maintenance are 6- mercapto purine and methotrexate. They may be given in combination or in rotation.

Booster therapy : During the maintenance therapy and every 3 months a booster course is given. Two injections of vincristine and one week of corticosteroid therapy are given. Sometimes a booster course of intrathecal methotrexate may be also needed. During booster therapy maintenance drugs are temporarily stopped.

TREATMENT OF CHRONIC LEUKEMIA :

This is treated radiologically and by chemotherapy. The most effective chemotherapeutic agents are : myeleran, 6 mercaptopurines, cyclophosphamide, Fowler's solution, urethane and TEM. In cases resistant to all these nitrogen mustard is considered. Steroids are helpful when there is a tendency to hemorrhage.

Treatment of central nervous system involvement. The best response is obtained by methotrexate. Because of its poor penetration into the cerebrospinal fluid it should be given intrathecally. The dose is 0.2-0.3 mg./kg. body weight every 3-5 days until the cerebrospinal fluid is normal. Usually 3 doses are sufficient but sometimes more are required. During intrathecal therapy, oral methotrexate should be discontinued. Radiotherapy is also very effective.

CRITERIA OF A REMISSION :

The patient can be considered in remission when the following criteria are fulfilled : —

- (1) Disappearance of the clinical symptoms of leukemia.
- (2) Return to about normal of the peripheral blood picture including hemoglobin level, red cell, white cell and platelet counts, and disappearance of immature cells.
- (3) Normal erythropoietic, leukopoietic and thrombopoietic appearance of the bone marrow. Blast cells should not exceed 5% of the count.

BLEEDING AND COAGULATION DEFECTS

Patients who are prone to bleed excessively after minor injuries are not uncommon. It is important that the significance of this abnormality should be recognised since many deaths can result from subjecting these patients to operation. Excessive bleeding of this kind is usually due to a break down of the hemostatic system, and the causes can be subdivided into vascular factors, blood platelet abnormalities and defects of the blood clotting mechanism.

Vascular factors : If small venules and capillaries are injured, hemostasis is accomplished by direct adhesions of their endothelial surfaces. If the injury affects larger veins or arteries however, an immediate reflex vasoconstriction occurs. This vasoconstriction is less marked in veins than in arteries since the media of veins contains less muscle than that of arteries. Venous hemostasis therefore depends mainly on the accumulation of platelets at the edges of the vessel wall which eventually occlude the vessel. In small arteries and arterioles vasoconstriction is strong and permits adherence and subsequent clumping of platelets with a resulting sealing off of the injured area. Contraction of the vessels is further accelerated by the release of the powerful vasoconstrictor substance serotonin. The platelet mass is reinforced by fibrin derived from the process of blood coagulation which occurs during vasoconstriction. Platelets and precipitated fibrin threads then form a hemostatic plug which fills the lumen of the vessel. This clot subsequently retracts and is partially digested and organised and the vessel is in this way recanalised.

Hemorrhage from larger arteries however, is controlled with difficulty until the blood pressure drops within the vessel and allows a blood clot to form.

Vitamin C and vitamin P are additional factors which help in normal capillary functions.

Role of platelets : Platelets are known to have 3 major functions :

(1) Maintenance of vascular endothelium. Platelets tend to adhere to other platelets and to injured blood vessels, check the formation of petichiae, and extravasations of blood in spontaneous hemorrhage. It was found that this platelet adhesiveness is essential in the process of their clumping and that it is induced by a heat stable extract from the red cells called factor R. When a vessel is injured red cells come into contact with the wound surface and liberate factor R which makes the platelets adhesive and leads to formation of the platelet plug.

(2) Participation in blood coagulation.

(3) Transport of various chemical substances. The platelet can be simulated to a sponge which adsorbs coagulation factors and possibly vascular factors on its surface and carries them through the circulation to the site of vessel wall injury.

Blood coagulation : The coagulation system is a complex one involving a chain of reactions between many factors which at present are known to be 13 in number. These are sometimes described under numerous synonyms and abbreviations as follows : —

Factor I	Fibrinogen.
Factor II	Prothrombin.
Factor III	Thromboplastin, prothrombinase, tissue thromboplastin.
Factor IV	Calcium.
Factor V	Proaccelerin, labile factor.
Factor VI	No longer differentiated from factor V.
Factor VII	Proconvertin, stable factor.
Factor VIII	Antihemophilic globulin (A.H.G.), antihemophilic factor (A.H.F.).
Factor IX	Plasma thromboplastin component (P.T.C.), Christmas factor.
Factor X	Stuart - Prower factor.
Factor XI	Plasma thromboplastin antecedent (P.T.A.).
Factor XII	Hageman factor (H.F.).
Factor XIII	Fibrin stabilising factor (F.S.F.).

The process of coagulation can be divided into 3 phases :

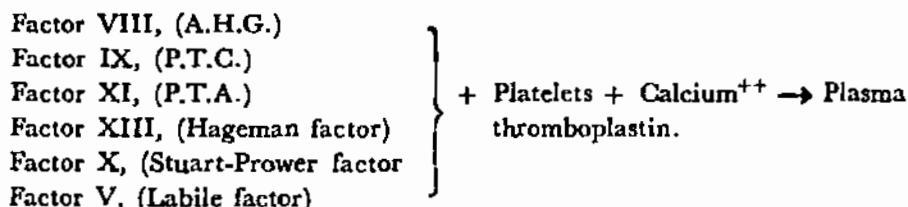
(1) The first phase is concerned with the elaboration of thromboplastin.
 (2) The second phase is concerned with the conversion of prothrombin to thrombin.

(3) In the third phase fibrinogen is converted to fibrin through the action of thrombin liberated in the second phase.

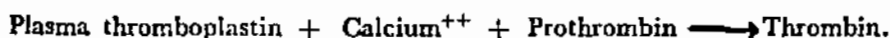
Thromboplastin originates from 2 sources, the tissues and the platelets and as is shown in the schematic representation, the various factors needed for the 3 phases of coagulation are outlined.

Plasma Thromboplastin System

Phase I.



Phase II.

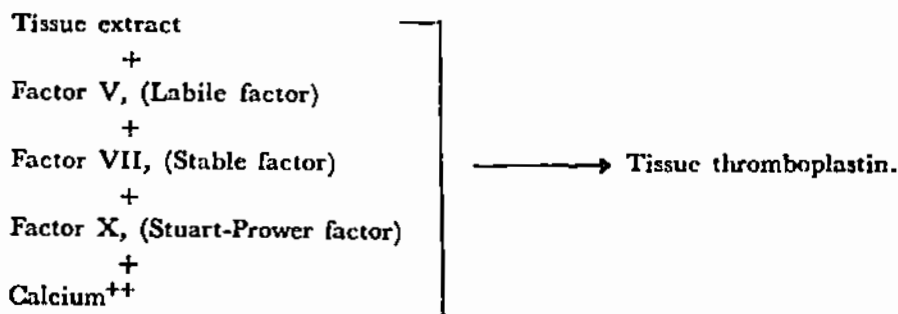


Phase III.

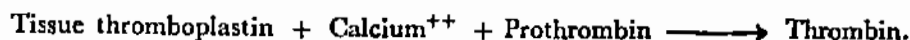


Tissue Thromboplastin System

Phase I.



Phase II.



Phase III.



Clinical Diagnosis : The patient or his family usually consult a doctor because of excessive bleeding from small injuries, epistaxis, oozing from the gums, gastrointestinal hemorrhage, hematuria etc. There may be a history of undue bleeding after tooth extraction, tonsillectomy or other operations. The patient may complain of symptoms not connected with abnormal hemorrhage such as deep tissue swellings and painful or swollen joints. The clinician must then determine whether or not these manifestations indicate a generalised hemorrhagic state.

Points which tend to confirm the existence of such a state are hemorrhage affecting different parts of the body, a long history of a similar condition in one or more relatives. Points somewhat against the diagnosis of a hemorrhagic state would be the limitation of bleeding to some particular site and the presence of symptoms suggesting an organic disease for hemorrhage. But it must be stressed that a hemorrhagic diathesis can start by being localised and then acquire the generalised typical character.

Since many of these conditions are hereditary, a detailed family history is essential. Attention should be always paid to the presence of consanguinity between the parents.

Differentiation of Clotting defects from Bleeding tendencies. Some separation can be made on clinical findings. In general, spontaneous bleeding such as oozing from mucous membranes, and the occurrence of petichae or ecchymosis in the skin suggests the group of bleeding rather than coagulation defects. Abnormal hemorrhage due to defective coagulation on the other hand is not limited to the skin and mucous membranes and is usually related to trauma or tissue damage. When this damage affects a body surface, obvious hemorrhage occurs, usually in the form of a slow and persistent oozing which may continue for days or even weeks. If there is no break in the surface, persistent bleeding into the tissues may produce hematomata sometimes of enormous extent. A characteristic site for such internal bleeding is the joint cavities. Hemarthrosis, which may initially be related to a blow or strain becomes more and more easily produced as the affected joint becomes progressively disorganised until hemorrhage appears to be spontaneous. Hematuria is another form of bleeding which is often apparently unrelated to trauma or infection.

Diagnosis of the Coagulation disorder : After the diagnosis of a coagulation defect is made, attention should be directed towards its etiology. Nearly no help can be obtained from the signs and symptoms since all of them produce the same clinical picture. Even the occurrence of hemarthrosis, once thought to be pathognomonic of hemo-

philia is not specific. If the patient is a male and male members of the family but not females are affected, then the condition is very probably either hemophilia or Christmas disease. If there is no family history and the condition has arisen in late childhood or in adult life it is unlikely to be hereditary and an attempt should be made to discover an immediate cause. Factor V deficiency may occur as a complication of severe infections or liver disease and fibrinogen deficiency may occur if there is severe liver damage.

Laboratory investigations : The first step in differentiation is to determine whether a patient with an abnormal bleeding tendency has a coagulation defect or a capillary abnormality with or without thrombocytopenia. Preliminary investigations usually include a platelet count, bleeding time, tourniquet test and a whole blood coagulation time. If the first 3 investigations give normal results, the general capillary function is probably normal. If the blood clotting time is prolonged, the patient most probably has a coagulation defect. After these preliminary investigations the problem is one of distinguishing between the different types of coagulation defects. This can be achieved by specific laboratory procedures.

These procedures include in the first place, assesment of the 3 phases of coagulation. The adequacy of phase III should be ascertained first, followed by that of phase II and finally of phase I.

Phase III can be evaluated by the thrombin time which is the time required for plasma to clot after the addition of bovine thrombin. The normal thrombin time is 15-20 seconds. Prolongation usually indicates hypofibrinogenemia.

Phase II can be evaluated by the prothrombin time, which is the time taken for plasma to clot after the addition of thromboplastin and calcium. The normal prothrombin time is 12-14 seconds. Its prolongation indicates deficiency involving factor II, V, VII, and X either alone or in combination. Assays of these factors can then be made to identify the specific defective one.

Phase I can be evaluated by the partial thromboplastin time which is the time required for plasma to clot when calcium and platelets are added to plasma. The normal time is 60-90 seconds and its prolongation indicates deficiency of factor XII, XI, IX, and VIII. Other sensitive tests for evaluation of phase I are the prothrombin consumption time and the thromboplastin generation test. As in the case of phase II, tests are available to determine the specific defective factor.

FACTOR VIII DEFICIENCY

(Classic Hemophilia; Hemophilia A)

This is a severe disorder of coagulation caused by a congenital deficiency of the antihemophilic globulin. In severe cases the antihemophilic globulin ranges from 1-3% of the normal. The disease is inherited as a sex linked recessive character. Only males are affected and females act as carriers but do not show clinical, and in most cases laboratory manifestations of the disease. If a male hemophiliac marries a female carrier there is the possibility of giving birth to the extremely rare female hemophiliac. In the absence of a family history sporadic cases may represent new mutations.

Clinical picture : There are recurrent episodes of bleeding from various parts of the body, occurring either spontaneously or following slight traumata. Factor VIII does not cross the placenta and the bleeding tendency may start in the neonatal period. However, hemorrhages usually occur almost invariably in the first year of life with the onset of walking or after minor operations like circumcision. Petichae are rare, but hemorrhages under the skin or into the muscles are common. Bleeding into the pleural or peritoneal cavities, the gastrointestinal tract, nervous system, or genitourinary system may occur. Hemorrhage into the retroperitoneal region, the mesentery or iliopsoas may give rise to clinical manifestations similar to acute appendicitis. The most characteristic site of hemorrhage is the joint cavities. The mostly affected joints are the ankles, knees, and elbows. Acute hemarthrosis occurs suddenly with severe pain, swelling, heat, tenderness and limitation of motion. Recurrence of the bleeding eventually leads to extensive damage and thickening of the synovial membranes, destruction of articular surfaces and erosion of bone.

If the level of factor VIII is greater than 5% of the normal a mild type of the disease results with absence of spontaneous hemorrhage and development of bleeding only after surgery or tooth extraction.

Laboratory findings : There is anemia and prolongation of the coagulation time. The bleeding time, clot retraction, tourniquet test and platelet count are normal. The partial thromboplastin time is prolonged to greater than 120 seconds. The prothrombin consumption is impaired and the thromboplastin generation test is abnormal. Factor VIII is either diminished or totally absent.

X-rays of bones and joints show defects of the epiphysis and erosions of joint margins.

Treatment :

— *Local measures.* These consist in the application of a coagulant and local pressure at the bleeding site if possible. A mixture of adrenalin and thrombin is a suitable coagulant. Cauterisation and suturing of wounds are always contraindicated.

Hemarthrosis should be treated promptly. Bed rest, elevation with slight flexion of the joint and surrounding it by ice packs constitute the initial local treatment. After the control of bleeding, cautious active motion and massage should be gradually instituted. If bleeding into the joint is extensive, aspiration of the blood may be helpful.

— *General treatment.* This includes transfusion of whole blood or plasma. For the patient who has suffered extensive blood loss, immediate transfusion with whole blood or packed cells is necessary. The treatment if anemia is not severe is by transfusion of fresh or frozen plasma or by plasma concentrates. A level of factor VIII between 10 and 25% of normal is achieved by administering plasma in a dose of 10 ml./kg. body weight initially, and 5 ml./kg. body weight every 4-6 hours. To avoid the danger of circulating overload no more than 30 ml./kg. body weight should be given in 24 hours. The minimal hemostatic level of factor VIII is from 10 to 20% of the normal.

Several factor VIII concentrates are available. The commonest of these is cryoprecipitate which is prepared from fresh plasma. An initial dose of 1 unit/5kg. body weight followed by a dose of 1 unit/10 kg. body weight every 12 hours raise the level of plasma factor VIII to 25-50%. Corticosteroid therapy is used by some people as an adjuvant to transfusion or replacement therapy.

Treatment when major surgery is performed. A dose of fresh frozen plasma 10-20 ml./kg. body weight is given half an hour before the operation. Blood and plasma are also replaced during the operation. After operation 5 ml./kg. body weight are given every 4 hours for 48 hours, and every 6-8 hours for 48 more hours. After that a dose of 10 ml./kg. body weight is given every 12 hours for 5-10 days depending on the operation.

Factor VIII inhibitors :

Few patients become refractory to factor VIII therapy due to the deve-

lopment of circulating inhibitors or antibodies which are Ig G globulins. If such patients bleed, massive doses of factor VIII concentrates should be given or an exchange transfusion with fresh blood performed.

FACTOR II, VII, and X DEFICIENCY

(Hemorrhagic Disease of the Newborn)

This is a self limited hemorrhagic disorder which usually occurs between the second and fifth day after birth. It is caused by a marked deficiency of the vitamin K dependent clotting factors, i. e. factor II, factor VII and factor X. Their level is normal at birth, drops between the second and fifth day and there after returns to normal. Several factors may contribute to this physiological deficiency of vitamin K dependent coagulation factors : —

- (1) The infant's intestinal tract at birth is free from bacteria which are necessary for vitamin K synthesis. Intestinal flora start to be established with the ingestion of food.
- (2) Liver immaturity at birth is partially responsible.
- (3) Lack of reserve supply of the vitamin.

In some instances there is an associated deficiency of factor IX.

Clinical picture : Hemorrhage usually becomes evident on the 2nd or 3rd day after birth. Melena, bleeding from the umbilical stump or hematuria are the most frequent types of hemorrhage. The most serious however, is intracranial hemorrhage.

Laboratory findings : A prolonged prothrombin time is diagnostic. If factor IX deficiency is associated abnormal phase I tests are also demonstrated.

Treatment : Vitamin K administered to the newborn infant arrests the fall of vitamin K dependent clotting factors and is therefore the agent of choice both for prophylaxis and treatment. Excessive doses of vitamin K are to be avoided because of their known hemolytic action and tendency to cause hyperbilirubinemia especially in the premature infant. Natural vitamin K preparations act more rapidly than synthetic ones. Doses of 1-2 mg. are usually sufficient. In cases of intracranial or other serious hemorrhages blood or plasma transfusion may be necessary.

THE PURPURAS

Purpuras are a group of blood disorders characterised by skin hemorrhages, with or without bleeding into mucus membranes and into other sites and internal organs. They may be classified into 2 groups according to the platelet count : —

- (1) Thrombocytopenic purpuras in which the platelet count is reduced below 40000 per c.mm. The commonest is idiopathic thrombocytopenic purpura.
- (2) Nonthrombocytopenic purpuras in which the platelet count is normal but bleeding results from defects in small blood vessels or from defective platelet function. The commonest is allergic purpura.

Idiopathic Thrombocytopenic Purpura

Etiology and pathogenesis : The etiology is not settled. Many theories have been suggested : —

(1) It is suggested that an immunologic reaction is involved. The observation that infants born to mothers with this disease were often purpuric was ascribed to the transmission of an immune body across the placenta. It is accordingly thought that the disease is due to a platelet autoimmune antibody. In more than 50% of cases the disease is preceded by an infection either viral or bacterial, and the precise manner in which these infections affect the platelets is not clear. It is however suggested that these infectious agents combine with platelets to render them antigenic.

(2) The enlarged spleen seems to have a role in the etiology of the disease.

- a. It may produce a substance which affects capillary permeability.
- b. It may be the site where the antiplatelet antibodies are formed.
- c. It may be an active site for removal of platelets from the circulation.

(3) Thrombopoietin deficiency : This is a factor present in normal plasma which stimulates megakaryocyte maturation and platelet production. Its diminution leads to thrombocytopenic purpura.

Clinical manifestations : The disease appears in 2 forms, an acute self limited form mostly in children, and a chronic protracted form with occasional remissions in adults.

The acute form has a sudden onset frequently after a bacterial infection, mostly respiratory, or viral. Measles, rubella, chicken pox, mumps, and infectious mononucleosis are the commonest viral affections described. The chief complaint is easy bruising either spontaneous or after a minor trauma. Nose bleeds, bleeding from the gums, oral mucous membranes, gastrointestinal tract, kidneys and vagina frequently accompany the purpura. Large echymotic areas may appear. Intracranial hemorrhage is uncommon in children and constitutes the most serious complication of the disease. The spleen is not regularly palpable and is never greatly enlarged.

Approximately 10 to 15% of the cases in children are of the chronic variety. Here the onset is insidious and the condition may be only first recognised after a tooth extraction or a small operation. Physical signs are usually more extensive than in the acute form.

Laboratory findings.

Blood findings : The platelet count is low (frequently below 20,000). The platelets in the film are usually single, large and abnormal in shape. The bleeding time is prolonged, the tourniquet test is positive, and the clot retraction is poor or absent. The whole blood clotting time is normal. Anemia and reticulocytosis may occur if the bleeding is severe.

Bone marrow findings . The megakaryocytes are normal or even increased in number and show reduced platelet formation. Degenerated and immature forms of megakaryocytes with deep basophilic cytoplasm are present. Platelet budding may be scanty.

Course and prognosis : A spontaneous remission occurs in 75% of infants and children affected. The majority of children recover completely within 3 months. Sometimes recurrences occur before complete recovery and about 10% of children develop the chronic form. In chronic cases a search must be always made for an underlying disease particularly aplastic anemia.

Differential diagnosis : It is important initially to distinguish between thrombocytopenic and nonthrombocytopenic purpura. Thrombocytopenic purpura has then to be differentiated from aplastic anemia and leukemia. Bone marrow examination will be essential for this differen-

tation Since the bone marrow picture is not very specific in thrombocytopenic purpura it can be stressed that bone marrow examination is more important to exclude aplastic anemia and leukemia When the spleen is greatly enlarged other conditions like Gaucher's disease or reticuloendotheliosis must be considered Also it is important to remember that petichae may be early manifestations of disseminated lupus erythematosus and an examination for L.E. cells is always recommended as a routine test before arriving at a diagnosis

Treatment

- (1) Transfusion of fresh blood, platelet rich plasma, or platelet concentrates is of great help in the treatment
- (2) Adrenocortical steroids and ACTH are effective in the relief of bleeding symptoms, by an early hemostatic effect on the blood vessel wall, and by a later rise in platelets
- (3) Splenectomy is indicated if with adequate therapy with corticosteroids thrombocytopenia persists for 6 months or longer. The finding of a few or no megakaryocytes in the bone marrow is a contraindication to splenectomy and warrants a search for an underlying condition.

Allergic Purpura

(Henoch - Schonlein's Purpura)

This is a nonthrombocytopenic purpura accompanied by a pleomorphic urticaria like and purpuric type of cutaneous eruption in combination with gastrointestinal symptoms, painful swelling of the joints, and a tendency towards renal involvement These symptoms may occur individually, in combination, or in sequence

Etiology: The etiology is not known. Allergy or drug sensitivity seems to play a role in some cases. The disease often follows an upper respiratory tract infection sometimes with beta hemolytic streptococci. A large variety of foods have also been implicated. Eggs, milk, chocolate and beans have been suspected as the commonest responsible of these. Antibiotics and sulphonamides are among the commonest drugs implicated.

The disease is more common in children than in adults, occurring mostly in the age range from 2 to 8 years. Males are more affected than females.

Clinical manifestations : These involve the skin, abdomen, joints, urinary tract and nervous system.

Skin : Recurrent attacks of urticarial and maculopapular lesions occur. Petichial and purpuric eruptions appear. Skin lesions usually appear in crops and are rarely pruritic. Erythema multiforme and erythema nodosum are sometimes present. Angioneurotic edema is common and may be extensive.

Abdominal manifestations : Recurrent colicky pain referred to the umbilicus is common. It is usually associated with vomiting, and may occasionally be mistaken for an acute abdominal emergency. Stools show gross or occult blood. Haematemesis may rarely occur.

Joint involvement. Recurrent attacks of pain and swelling of the joints, occasionally accompanied by hotness may be present. The knees and ankles are the commonest to be affected. Effusions may be present and the joint fluid is serous and not hemorrhagic. Joint symptoms usually resolve after a few days without residual deformity or articular damage. Recurrences are common.¹

Renal complications. These are the most serious manifestations of the disease. Acute glomerulonephritis which may proceed to the chronic stage are the commonest to be met with.

Neurologic complications. These are rare and may include subarachnoid or cerebral hemorrhage.

The prognosis is excellent in the absence of severe renal disease. The course is usually from a few days to a few weeks in severe cases.

Laboratory findings: The sedimentation rate is elevated and acute phase reactants appear in the serum. Leukocytosis with eosinophilia may be present. Platelet count, bleeding time, coagulation time, clot retraction and tourniquet test are normal.

When renal involvement is present the disease can be differentiated from acute glomerulonephritis by finding an elevated serum complement titre. Serum complement titre is low in acute glomerulonephritis.

Treatment : This is essentially symptomatic. Antibiotics are of value when infection is present. Antihistaminics and elimination of the offending agent, if detected may be of value. ACTH and adrenocortical steroids are commonly used with fair results.

Disseminated Intravascular Coagulation

(Consumption Coagulopathy)

Disseminated intravascular coagulation has been incriminated as the pathologic mechanism in many disease processes. Among these are incompatible blood transfusion, thrombotic thrombocytopenic purpura, purpura fulminans, Waterhouse — Friderichsen syndrome and others. The primary abnormality leading to intravascular coagulation may be :

- (1) Intravascular hemolysis. (2) Diffuse vasculitis.

The process is usually followed by depletion of the consumable coagulation factors of the blood, i. e. factors I, II, V, and VIII. The platelet count is usually low.

Some of the clinical and pathological features in disorders produced by intravascular coagulation are similar to those of the generalised Shwartzman reaction in experimental animals.

Fibrinolytic States

Fibrinolysis is the physiological process for dissolution of a blood clot. It is mainly initiated by an enzyme, plasmin and its inactive form plasminogen, both present in normal plasma.

A hemorrhagic disorder may be produced by an increased fibrinolytic activity of the plasma. Trauma, hemorrhage and shock are recognised as potential initiators of excessive fibrinolysis. The lungs and uterus, especially in the older child and adult, are the commonest sites for bleeding disorders due to fibrinolysis. It may also produce hemorrhage in patients with leukemia, cyanotic congenital heart disease and malignant neoplasms. In contrast to disseminated intravascular coagulation, fibrinolytic states are accompanied by a normal platelet count and a normal level of consumable coagulation factors.

MOSTAFA KHALIL

Chapter XV

THE URINARY SYSTEM

ACUTE GLOMERULONEPHRITIS

Acute nephritis, a fairly common disease in childhood, is characterized chiefly by edema, hypertension, hematuria and various degrees of renal functional impairment.

Etiology : Acute nephritis is almost invariably a sequel to group A beta-hemolytic streptococcal infection and is regarded as a manifestation of hypersensitivity to extracellular antigens of the streptococci. Certain types of these organisms have remarkable predilection to produce acute nephritis (nephritogenic streptococci). In most instances type 12 is the etiologic agent, with types 4 and 25 being less frequently involved. Most cases of acute nephritis are secondary to streptococcal throat infection, but the disease may stem from streptococcal skin infection.

Nephritis usually occurs within one to three weeks after the antecedent streptococcal infection. During this period, the antistreptolysin O titer increases in almost all patients, being a manifestation of the body's reaction to the streptococci and in this instance is accompanied by the development of tissue hypersensitivity.

Age incidence : Its peak incidence is in the group 5 to 10 years of age. Although it may occur in infancy, it appears infrequently in children less than 3 years of age.

Case incidence : Since acute nephritis may be so mild that it causes no symptoms, and therefore the urine is not examined, it is impossible to state its true incidence. However, it is known that many more cases occur than are clinically detected.

Clinical manifestations : The three cardinal manifestations are urinary abnormalities, edema and hypertension.

Onset : This may be insidious or abrupt. Many cases of acute nephritis are asymptomatic and discovered only because their urine was examined for another reason or because they have been in contact with a case. At the other end of the spectrum are those in whom the onset is sudden and severe followed

quickly by threatening complications. However, the majority of children whose nephritic symptoms attract medical attention have the disease in a mild or moderate form.

Clinical evidence of the causative infection may have disappeared or may still be present.⁴ Fever is usually present and may persist for weeks. Other nonspecific symptoms include headache, anorexia and vomiting. However, many children mildly affected have few or no systemic manifestations.

Urinary changes : Hematuria is usually the first abnormality noted. Urine may be bloody, smoky or brown in colour. Gross hematuria usually lasts about two weeks and is followed by a microscopical one ending in six weeks. In a minority of patients, only microscopic hematuria occurs. The majority of patients have oliguria and very few have anuria. In some cases, urine volume remains normal.

Edema : It is the second most common presenting symptom. It is generally minimal or moderate in degree and is noted as puffiness around the eyes and of the face, often associated with slight edema of the extremities. Severe edema is usually not seen in acute glomerulonephritis except when fluids have been forced in the presence of oliguria, and during cardiac failure.

Hypertension : This is present in about 60 — 70% of patients. It may appear at any time during the acute phase. Systolic pressure may reach 200 mm. of mercury, with diastolic pressures of 100 — 120 and even more. Severe hypertension may develop rapidly over a period of few hours so that a child with minimal hypertension in the morning may be severely hypertensive in the afternoon. Therefore, frequent measurements of the blood pressure must be made in the first few days of the disease. Usually the hypertension returns to normal towards the end of the first week. Hypertension in nephritis is due to widespread arteriolar spasm secondary to vasopressor substances liberated by the ischemic kidney.

Laboratory Findings :

(1) *Urine :* Freshly passed urine should be examined for both red blood cells and casts, since both may disappear when alkaline or dilute urine is allowed to stand :

a — Specific gravity is usually high.

b — Gross hematuria is usually seen. In a minority the red cells are seen only on microscopical examination.

c — Mild to moderate proteinuria is present.

d — Microscopically, in addition to the RBCs., there are hyaline, granular and red blood casts. White blood cells are increased in number; occasionally so many are present as to suggest pyelonephritis.

(2) *Blood* :

a — Blood urea is usually raised and renal function tests show impairment in half of the cases.

b — Blood sedimentation rate is elevated.

c — A.S.O. titer is usually elevated.

Complications : (1) *Cardiac decompensation* : It is the most common cause of death in acute nephritis. It results from : (a) hypertension secondary to peripheral vasospasm, (b) myocardial ischemia due to coronary vasospasm, and (c) hypervolemia secondary to the retention of sodium and water.

Cardiac decompensation is manifested by dyspnea, orthopnea, dependent edema, venous engorgement, enlargement of the heart, systolic blowing apical murmur due to dilatation, gallop rhythm, pulmonary edema and enlargement of the liver.

(2) *Hypertensive encephalopathy* : It is the easiest of the three major complications to prevent or treat. It is associated with hypertension, usually of high degree. Cerebral hypoxia secondary to arteriolar spasm is the cause in almost every case. Edema of the brain is a rare causative factor of encephalopathy, it does occur in some instances particularly in the child with severe cardiac decompensation. The symptoms of hypertensive encephalopathy include irritability, headache, vomiting, double vision, dimness of vision, temporary blindness, drowsiness, stupor and generalized convulsions that may prove fatal. When the blood pressure is being determined at frequent intervals, one may anticipate the onset of encephalopathy if the pressure steadily mounts to high levels. Usually hypertension can be reduced in time to avert danger.

(3) *Uremia* : Fortunately severe renal failure is the least common of the three major complications, for it is the most difficult to treat. Renal failure may occur without hypertension, encephalopathy or decompensation. In such events, the child may appear surprisingly well for several days if maintained in good water and electrolyte balance and there may be a resumption of urine flow within a week. If urine flow is not re-established, renal acidosis becomes evident, vomiting and diarrhea may occur, anemia develops and the child drifts into drowsiness, stupor, coma, twitchings and convulsions.

This initially "quiet" uremia, is in contrast to what might be called "stormy" uremia in which the patient also has hypertension, decompensation and perhaps encephalopathy.

- Differential Diagnosis :** (1) *Focal nonsuppurative glomerulonephritis* may occur at the height of a variety of infections. The proteinuria in these conditions is usually transient. Transient mild hematuria has also been observed on the second or third day of 5-10% of patients with acute streptococcal infections and occasionally with non-streptococcal infections.
- (2) *Embolic nephritis* may occur during bacteremia such as that of subacute bacterial endocarditis; it is transient and disappears when the blood stream is free of bacteria.
- (3) Transient hematuria during *acute pyelonephritis* may be a diagnostic problem. Large numbers of pus cells in the urine, the presence of bacteruria and normal blood pressure aid in the differentiation from glomerulonephritis.
- (4) *Sulfonamide crystals* may give hematuria, decreased urinary output and occasional azotemia. The disappearance of these signs within a day or two after withdrawal of the drug is strong evidence against glomerulonephritis.
- (5) *From other causes of hematuria.*
- (6) *Anaphylactoid purpura.*
- (7) *The nephrotic syndrome* may have an onset with gross hematuria.

Course : In two to three weeks edema, gross hematuria and hypertension disappear. Abnormal urinary findings last for about six weeks. The erythrocyte sedimentation rate becomes normal in about three months and the Addis count in about 4-8 months (In normal children the twelve-hour collection of urine will contain up to one million R.B.C., one million W.B.C., 10,000 casts and 40 mg. of protein).

Prognosis : 85-90% of the cases make a complete recovery. Up to 5% die in the acute stage from one of the complications and less than 5% develop chronic nephritis and may survive a few months only or many years.

Second attacks of glomerulonephritis are extremely rare. Recurrence of the disease before healing is complete, however, is not uncommon in association with fresh respiratory infections.

Treatment : I — Rest: The child should be confined to bed until he is free from edema and hypertension, and naked-eye hematuria disappears. Thus, on the average 2 - 3 weeks in bed are sufficient. The child is then permitted to resume activities gradually. During this period of resumption of activities, the clinical condition should be observed closely and the urine examined frequently. Children are back to school when the E.S.R. has returned to normal, this varies from 4 - 8 weeks but exhausting competitive activities are prohibited until the Addis count returns to normal.

II — Antibiotic therapy : To treat any streptococcal infection, to prevent its transmission and to lessen the chances of upper respiratory tract infections which might initiate an exacerbation of the nephritis, penicillin therapy should be instituted. Procain penicillin 200,000 units I.M. daily for young children (below 15 kgs.) and 400,000 units I.M. daily for older ones, for 3 days to be followed by benzathine penicillin 1,200,000 units I.M. every 20 days, for the rest of hospital stay and for 3 months after recovery from the acute phase.

III — Fluid intake and diet : Free fluid intake is permitted unless :

- Blood pressure is extremely high.
- Decompensation is impending or present.
- The patient is markedly oliguric or anuric.

In markedly oliguric or anuric child, fluid intake should equal insensible losses plus urine output in the previous day. In the absence of fever, vomiting or diarrhea, the insensible loss will approximate $700 \text{ ml./m}^2 \text{ /day}$. If fever, vomiting or diarrhea are present, additional fluid should be given to compensate for these losses. Daily weighing of patients is the best guide.

In the usual uncomplicated case of acute nephritis the diet in the first few days of the disease should be a liquid one of sweetened fluids and milk. As the acute phase subsides, the child is given a soft diet and soon a regular diet.

Salt should be restricted if edema is marked, hypertension is severe or cardiac decompensation is present. It is advisable not to add salt to cooked food in the acute stage without decompensation.

Protein restriction is unnecessary except in patients who are markedly oliguric or anuric. Proteins should be withheld from such patients because of their potassium content and to less extent because they add to the nitrogenous load.

IV — Management of hypertension : The blood pressure should be followed carefully during the acute phase of the disease. Determinations should be made at least every 4 hours. As a general rule, if diastolic pressure is less than 90 mm. Hg. and systolic pressure is less than 140 mm. Hg. no hypotensive measures are required. Bed rest and sedatives (phenobarbital) are generally sufficient. Treatment of hypertension is definitely indicated if there is evidence of : —

- Hypertensive encephalopathy.
- Signs of circulatory congestion, pulmonary edema, with hypertension.
- Diastolic pressure over 90 mm. Hg.

In case of hypertensive encephalopathy :

- Drug of choice is diazoxide (hyperstate) - 5-10 mg/kg. I.V. rapidly, or methyldopa (aldomet) - 10-20 mg/kg. - I.V.'

In less urgent situations :

- Hydralazine (aprisoline) : 0.1-0.7 mg/kg and reserpine : 0.07 mg/kg. (maximal dose 2 mg).

Both are given I.M. and if there is no fall of blood pressure within 2-3 hours-doses are repeated.

Maintenance therapy : will be started when blood pressure falls below 140/90 :

- as oral methyldopa (20-40 mg/kg/day) on 4 divided doses, or as combination of a hydrochlorothiazide (esidrex) 2.5 mg/kg/day and Hydralazine 2-4 mg/kg/day in 3 divided doses.

Magnesium sulfate may be used if the above is not available or ineffective. It has got undesirable side effects in the form of local irritation and pain at the site of injection, precipitous fall in blood pressure to hypotensive levels, respiratory depression and a direct action on cardiac muscle. Its antidote is calcium gluconate given intravenously 5-10 cc. of a 10% solution. The dose of magnesium sulfate is 0.2 ml./kg. I.M. of 50% solution. This can be repeated, if necessary, after 4 hours.

V - - Treatment of complications :

- (1) *Hypertensive encephalopathy :* This complication is prevented and treated by reduction of hypertension as previously indicated. The relaxation of vasospasm offers relief from cerebral hypoxia.

Certain agents as phenobarbital may be employed. If convulsions occur,

phenobarbital I.M. 3 mg./kg. and oxygen should be administered. The patient should be protected from injury. If convulsions are severe and repeated they can be controlled by intravenous diazepam, 2-10 mg, according to response.

- (2) *Cardiac decompensation* : We have to reduce the blood pressure by relief of vasospasm, thus diminishing peripheral arteriolar resistance and offering more oxygen to myocardium and other tissues. Venesection and the withdrawal of 300 ml. of blood is often very effective.

Rapid digitalization : Digoxin 0.06 mg./kg. digitalizing dose for those under 5 years and 0.05 mg. / kg. for those over 5 years. The calculated digitalizing dose is administered orally in 3 divided doses; half the total dose is given initially, the other half is divided in two equal doses given every 8 hours. The heart usually becomes compensated after this rapid digitalization. However, if not, a maintenance daily dose of digoxin equal to 20 - 30% of the digitalizing doses should be given orally once daily. Salt and fluid intake should be restricted.

Symptomatic measures for heart failure include placing the child in the orthopneic position, administration of oxygen and the use of morphine.

- (3) *Uremia* : (For detailed information refer to renal failure).

Base line biochemical determinations should be done. E.C.G. should be obtained, and if possible correlated with serum potassium. Fluid intake should not exceed fluid loss. Protein should be withheld in order to avoid increasing hyperkalemia and nitrogen retention. Carbohydrate and fat are safe.

VI — Supervision of convalescence : When the acute phase of the disease has passed, gradual resumption of physical activity is permitted. The child is seen at frequent intervals (1 - 4 weeks) for one year. During this period, serial follow-ups and the general condition of the child should be evaluated. The blood pressure should be determined and the urine should be examined.

THE NEPHROTIC SYNDROME

"NEPHROSIS"

Nephrotic syndrome is a renal disease mostly of a primary origin and involving mainly the glomerulus. It is characterised by gross edema, heavy proteinuria, marked hypoproteinemia, hypercholesterolemia, a chronic course with remissions and relapses over a period of several years and a tendency to develop severe bacterial infections.

Etiology: There is a strong tendency at least among pediatricians to consider nephrotic syndrome as a separate primary renal disease (Idiopathic nephrotic syndrome). However, there are other conditions that may lead to the clinical picture and laboratory findings of the nephrotic syndrome. Among these secondary causes are : —

- 1 — Systemic diseases as amyloidosis, diabetes mellitus, systemic lupus erythematosus and syphilis.
- 2 — Renal disease as nephrotic stage of glomerulonephritis, renal vein thrombosis and thrombosis or obstruction of the inferior vena cava.
- 3 — Chemical agents as trimethadiones, paradiones, penicillamine, gold salts, bee stings, poison oak and mercury.

In the idiopathic nephrotic syndrome - that forms most instances of the disease in children - there appears to be no constant relationship to antecedent infection.

Currently, many observers think that the nephrotic syndrome is an autoimmune disease. Decreased complement activity in the serum during the active phases of the disease, and increased globulin in glomerular structure provides suggestive evidences favouring an autoimmune reaction. It is now generally held that the nephrotic syndrome is not related to acute glomerulonephritis.

Incidence : Nephrotic syndrome of idiopathic origin occurs most commonly between the ages of 2-6 years. It rarely occurs within the first days or months of life (Congenital and infantile nephrosis).

Pathology : Normally, the renal glomerulus has got three distinct components :

— The endothelial cells.

The basement membrane proper which is relatively dense centrally

The epithelial cells : Their cytoplasm branches into a number of primary processes which in turn form numerous secondary foot processes which insert upon the outer aspect of the basement membrane

The histological changes in the nephrotic syndrome have been intensively studied in renal biopsy material during recent years, using the techniques of both light and electron microscopy

Even when cases of nephrotic syndrome which are secondary to systemic lupus erythematosus, amyloidosis, diabetes mellitus, etc. are excluded the histological changes in the idiopathic cases show a wide variety. They had been classified into 3 main groups

- 1 - *Minimal changes* The glomeruli appear normal on light microscopy. Electron microscopy shows fusion of epithelial cells foot processes. This group is seen much more commonly in children than in adults and has a very much better prognosis.
- 2 *Membranous type* All glomeruli show diffuse capillary wall thickening without cellular proliferation. This is not very common in children, the prognosis is unfavourable.
- 3 — *Proliferative type* : There is marked swelling of endothelial cytoplasm, proliferation of mesangial cells and occasional crescent formation. The prognosis is not good.

Pathogenesis :

- 1 — *Proteinuria* : Results from the abnormal glomerular leakage of serum proteins.
- 2 — *Hypoalbuminemia* : Results from urinary loss of albumin and increased catabolism of this protein during the active phase without evidence of increased synthesis.
- 3 *Hyperlipemia* Its cause is still in doubt. It may be a consequence of decreased rate of removal of lipoproteins from the plasma.
- 4 *Edema* In nephrosis there is rapid lowering of plasma proteins due to proteinuria. The resulting decrease in plasma colloid pressure sets up a continuing shift of fluid from the plasma to interstitial space resulting in diminution in plasma volume. This in turn will provoke elaboration of antidiuretic hormone which promotes renal retention of water to augment the body water content, but with dilution of all solutes contained

in the body fluids. The hypovolemia and the solute dilution will stimulate elaboration of the salt retaining hormone (aldosterone) resulting in renal retention of sodium and water and the production of clinical edema.

Clinical Picture : The onset of the disease is usually insidious with periorbital puffiness and swelling of the ankles. Edema is the most striking feature of nephrotic syndrome. It often progresses rapidly, even to a massive degree. It collects in pleural and peritoneal cavities and marked ascites is a common event. When edema is maximal; vomiting and diarrhea may occur, presumably due to indigestion secondary to edema of the intestinal wall. Massive edema results in discomfort from many sources and the child may be markedly irritable. Ascites may be of such a degree that abdominal pain is present. It also handicaps respirations by forcing the diaphragm upwards. Respirations may also be impaired by the presence of hydrothorax. Because of the presence of ascitic fluid, umbilical or inguinal hernia may appear.

When it would be impossible for any more edema to be formed, diuresis occurs either : a) Spontaneously, b) Following an intercurrent infection as measles or c) Because of hormonal therapy.

Nephrotic patients are liable to intercurrent infections probably because of : a) Loss of gamma globulins in the urine, b) Low resistance of edematous tissues, c) General debility.

The common infections to which these children are liable are :

- a) Repeated upper respiratory tract infections,
- b) Cellulitis and erysipelas of the skin,
- c) Peritonitis : Formerly pneumococci were almost the sole offenders but now other organisms have entered the picture.

The child becomes acutely ill, may develop fever, and has abdominal pain; local signs may not be distinctive.

These various infections may seriously threaten the nephrotic child or even be fatal, but strangely enough may also suddenly result in diuresis that occurs as the infection wanes. Measles is particularly known to do this. It seems probable that stress of infection elicits an adrenal steroid response and corticosteroids spontaneously produced by the patient exert the same effect as if given therapeutically. As the edema recedes, it becomes evident how greatly malnourished the child is.

The blood pressure is usually normal. Transient elevations may occur. Persistent hypertension accompanies advanced renal insufficiency. In such cases, there is also azotemia.

With progression of the disease, there is tendency of persistence of the edema with minor fluctuations and the urine volume tends to be small. In the last stages the patient becomes relatively free of edema.

In children whose nephrotic syndrome is secondary to the systemic diseases already mentioned, clinical manifestations of these diseases may be superimposed upon the findings of nephrotic syndrome.

Laboratory Findings :

a) Urine :

- Oliguria during phases of edema formation.
- Proteinuria (up to 10-15 gm./day).
- Microscopically there are large numbers of hyaline, granular, and cellular casts, many containing lipid droplets. There may be some increase in leukocytes.
- Hematuria may be present in a mild degree. When it persists for more than a month it suggests progression towards chronic renal insufficiency.

In recent years the value of differential protein clearance tests on the urine in assessing the probable response to treatment has been increasingly appreciated. These are based upon the fact that in the nephrotic patient the low molecular weight proteins such as albumin and α_2 globulins escape through the glomerular filter more readily than high molecular weight proteins (selective proteinuria). As the glomerular leak becomes more severe proteins of higher molecular weight begin to appear also such as B-globulin (non-selective proteinuria).

A selective pattern of differential protein clearance is associated with a good response to the lines of treatment described below. Indeed this relates closely to minimal glomerular changes and obviates the need for renal biopsy. On the other hand a poorly selective or non-selective pattern of protein clearance makes a good response to treatment extremely unlikely although it cannot distinguish the various types of severe glomerular changes. In this situation renal biopsy is of diagnostic value.

b) Renal function tests : Unless the child has entered the stage of renal insufficiency, they are generally normal. Transient nitrogenous retention may occur.

c) Blood : The most characteristic changes in the blood are :

- Gross reduction in the total serum proteins (normal 6.5-8.0 g./100ml.)
- Disproportionate reduction in serum albumin (normal 3.5-4.5 g./100ml.) with inversion of the albumin/globulin ratio.

- Reduction in gammaglobulin (normal 12% of total serum proteins).
- High serum cholesterol (normal 180-250 mg/100ml.).
- Erythrocyte sedimentation rate is increased when the nephrotic process is active.

Diagnosis and Differential Diagnosis :

- 1 — One must determine whether the disease is idiopathic or secondary to one of the diseases previously mentioned.
- 2 — Hypoproteinemia due to protein losing enteropathy; a condition characterized by generalized edema, absence of proteinuria, normal blood cholesterol and reduction of total plasma proteins equally shared by both albumin and globulin components. The hypoproteinemia appears to be due to the large protein loss in the loose and voluminous stools.
- 3 — Nutritional edema.
- 4 — Acute glomerulonephritis associated with a mild transient picture of nephrotic syndrome. In such case, the nephrotic symptoms do not persist more than 10 days. The cholesterol is not highly elevated, and the plasma proteins are not much reduced. The diagnosis of acute glomerulonephritis in these cases is established by the typical short duration of the disease, and the elevated antistreptolysin O-titer.
- 5 — During periods of transient depression of renal function with azotemia, hematuria and hypertension, it is possible to confuse the nephrotic syndrome with acute or chronic nephritis, but comprehensive laboratory evaluation and observation of the patient usually readily clarify the diagnosis.

Prognosis : The course of nephrosis is variable, but in general is characterized by recurrent episodes of edema of varying duration. The main causes of death are intercurrent infections and renal failure. Antibacterial therapy has greatly reduced the death rate from infection.

Long term therapy with steroids has reduced the mortality to certain extent. Complete recovery is only likely in those children with a highly selective pattern of differential protein clearance and minimal glomerular changes. Children with membranous or proliferative nephropathy are almost certain to progress to renal failure although a very few may ultimately heal.

Management :

- 1 - *Rest* : The child should be kept in bed only during periods of severe edema or when other constitutional symptoms are present; otherwise the child should be out of bed and active. Activity does improve the morale of the child, and reduces the accumulation of fluid in the abdomen and chest.
- 2 — *Prevention and treatment of infections*: Prophylactic administration of penicillin is recommended. Benzathine penicillin 1,200,000 units I.M. every 20 days should be administered for the whole period of steroid therapy. Acute infections should be treated promptly with appropriate antibacterial therapy.
- 3 — *Diet* : The child should be offered a diet appropriate for a normal child of his age. An ample intake of proteins is desirable, salt should not be restricted except temporarily during periods of increasing or marked edema. This can be achieved through avoiding the use of salt in cooking and through having no additional salt or salty foods available at the table. Prolonged salt restriction may cause hyponatremia particularly when diuresis occurs, or when diarrhea develops. Water restriction to limit the accumulation of edema fluid is of no value and may be harmful.
- 4 - *Supporting measures to treat edema* : The patient's principal clinical problem is edema. When edema is very massive, diuretics are indicated as hydrochlorothiazide and the spironolactones. Salt-poor human albumin is also used to initiate diuresis when serum albumin levels are grossly deficient. Albumin provides a source of metabolically available protein, but its major effect is to increase plasma volume and improve circulation to the kidney. Paracentesis is a useful measure when patients are in extreme discomfort because of large accumulations of fluid in the peritoneal cavity.
- 5 — *Steroid therapy* : ACTH and corticosteroids are extremely potent in altering the course of the disorder. Steroid therapy should be started as soon as the diagnosis of nephrosis is established provided that there is no contra-indication. Infection should be treated adequately before steroid therapy is initiated. Electrolyte imbalance of severe degree should be corrected, and if hypertension is of more than minimal degree, steroids should not be introduced until the hypertension is under control. Advanced renal insufficiency is a contra-indication to hormone therapy. A tuberculin test is carried out when the patient is first seen. Those with positive reaction or those who have active tuberculous infection are treated with isoniazid in full dosage and continued throughout the time that steroids are administered.

The corticosteroid of first choice and least side effects is prednisolone. A suitable scheme of dosage is : --

Prednisolone 15 mg. four times daily for 10 days,
 10 mg. four times daily for 10 days,
 5 mg. four times daily for 10 days,
 5 mg. twice daily maintenance dose.

Treatment is withdrawn after 6 - 10 weeks because longer courses increase the risks of serious side effects such as arrest of growth, osteoporosis, peptic ulcer, diabetes mellitus and convulsions with or without hypertension. The remission as shown by sudden diuresis, rapid loss of proteinuria, reversal towards normal of blood chemistry and fall of E.S.R., commences between 10 and 14 days after start of treatment. If relapse does occur it should be treated by the same intensive course of prednisolone but this should be followed by intermittent treatment for a minimum of 6 months; prednisolone 10 - 40 mg. once in the morning on alternate days.

In some cases the child recovers after one or two relapses in the first year or two. In others, repeated and frequent relapses have lead to repeated courses of steroids or to continuous therapy with consequent severe side effect.

The introduction of immunosuppressive drugs such as cyclophosphamide has provided an alternative line of treatment for these frequent relapses, and also the few children who are intolerant to high doses of steroids. Toxicity of cyclophosphamide is in the form of temporary alopecia, hemorrhagic cystitis, marrow depression and sterility in adults of both sexes. At first the child is brought into remission with prednisolone and this drug is continued in a daily dose of 10 - 20 mg. A good urinary output is essential. Cyclophosphamide is then given in a daily dose of 3 mg. per kg. for eight weeks. If the total white cell count in the blood falls below 2,500 per/cmm³ the cyclophosphamide should be withdrawn until the marrow recovers and then re-started in a dose of 2.5 mg. per kg. per day. The prednisolone is slowly withdrawn after completion of the 8 weeks course of cyclophosphamide. It should be stressed that cyclophosphamide is only likely to prove beneficial in nephrotic children who show minimal glomerular changes in renal biopsy material and a highly selective pattern of differential protein clearance. The remissions that follow cyclophosphamide are often of many months duration.

In the case of the child whose nephrotic syndrome is unresponsive to or unsuitable for treatment with steroids or cyclophosphamide a diuretic regimen accompanied by a low sodium diet and restricted fluid intake can greatly reduce edema and improve the patient's comfort.

URINARY TRACT INFECTIONS

(Pyelonephritis)

Infections of the urinary tract represent one of the major problems in infectious diseases due to bacteria today. Urinary infections have often been classified according to their anatomic location into cystitis, pyelitis and pyelonephritis. However, in the absence of reliable means for distinguishing local involvement, all patients with urinary infection should be regarded as having pyelonephritis. The term pyelitis has no place, since the renal parenchyma is involved with the pelvic inflammation within the first few hours leading to pyelonephritis.

Pyelonephritis deserves attention not only because of the symptoms and signs it produces, but also because it often results in progressive and irreversible impairment of kidney function.

Etiology and Pathogenesis : The disease is uncommon in the newborn period, occurs most often in children under three years of age, but may appear at any age. In the neonatal period, the disease is distributed equally between the two sexes. In children less than two years old, it occurs six times more frequently in girls than in boys, and afterwards three times more in girls. This predilection to affect the female is attributed to the relatively short urethra and the ease with which fecal contamination of the urethral orifice may occur leading to ascending infection of the bladder, ureters and finally the kidneys themselves.

Routes of invasion :

- 1 — Ascending route : Ascending infection is by far the most common way in which pyelonephritis occurs. Gram negative organisms are the usual offenders in this route. Vesico-ureteral reflux is the mechanism by which infected urine in the bladder reaches the kidney even in the absence of bladder neck obstruction.
- 2 — Hematogenous route : This is much less common than the first route. Gram positive organisms are the usual offenders.

Organisms being borne to the kidney from a variety of external foci, the most common of which are infections of the respiratory tract, boils, carbuncles and osteomyelitis. The organisms reach the kidney via the blood stream and settle in the interstitial and glomerular vessels and in-

initiate the destructive process. Subsequently, they reach other parts of the kidney and distal parts of urinary tract by way of blood vessels, lymphatics, urine or by direct extension.

- 3 — Via lymphatics : Renal involvement via lymphatic channels apparently is rare. In most instances it is a lymphohematogenous extension from infected pelvic or genital structure to regional lymph nodes, and thence to thoracic duct, and then general circulation reaching the kidney by way of the blood.
- 4 — Very rarely a perinephric or appendiceal abscess ruptures into the urinary tract and causes pyelonephritis.

Causative bacteria : Pyelonephritis may be caused by a variety of bacteria either singly or in combination. The colon bacillus group accounts for the great majority of acute infections. Less commonly, pyelonephritis may be caused by staphylococci, hemolytic streptococcus fecalis, proteus, pseudomonas and salmonella. Mixed infections are more common in chronic than acute pyelonephritis and resistant organisms occur far more often owing to repeated courses of antibiotic therapy that foster emergence of resistant strains. Proteus, pseudomonas and aerobacter are the most common bacterial invaders in chronic pyelonephritis.

Under appropriate therapy, the acute pyelonephritis process generally disappears within few weeks and the patient is apparently cured. In some cases however, the clinical manifestations and/or urinary abnormalities will show themselves again, or the child will continue to show those findings suggestive of pyelonephritis.

Causes of recurrent or chronic infection of urinary tract :

- Administration of the antibacterial agents for a short period of time.
- Resistance on the part of the organism to the drugs used.
- Calculus disease of the urinary tract.
- Unsuspected urinary tuberculosis.
- Neoplasms of the urinary tract.
- Most important is obstructive uropathy.

Causes of urinary tract obstruction are :

- Urethral causes : Phimosis, stenosis of urethral meatus, urethral stricture, stone, diverticulum and congenital valve of the posterior urethra.
- Bladder causes : Contracted bladder neck, mucosal fold at bladder neck and bladder, diverticulum

Ureteral causes : Stricture of ureteral meatus at ureterovesical junction, ureteral obstruction by outside compression, ureteral diverticulum, stone, stricture, ureteral kink and tumours.

- Renal causes : Ureteropelvic junction stricture, aberrant vessel, pelvic stone and tumours.
- Neuromuscular disease of the urinary tract that interferes with normal drainage leading to urinary stasis

Pathologic Findings : Pyelonephritis produces inflammatory changes in the renal pelvis, in the substance of the kidney and in the submucosa of the ureters and bladder. Infection of the interstitial tissue of the kidney constitutes the most important aspect of the pathologic picture. Polymorphonuclear leukocytes are present in the interstitial tissue and tubules. In severe cases, multiple small abscesses form in the interstitial tissue. This diffuse infection leads to extensive irregular scarring and destruction of functioning nephrons. In chronic infection, arteriosclerosis and arteriolosclerosis may also occur. The pathological changes may be unilateral, especially in cases complicating unilateral obstructive kidney disease.

Symptomatology : Pyelonephritis begins usually as an *acute* process, but may, however, be asymptomatic or atypical. The age of the patient, the nature of the predisposing factors, the severity and extent of the inflammatory process and the nature of any associated illness are principal factors in determining the clinical patterns observed with acute pyelonephritis. It has been greatly documented that atypical cases far outnumber those with acute signs and symptoms.

In infancy, the onset of acute pyelonephritis is usually sudden and severe. There is high fever, prostration, vomiting, anorexia and may be diarrhea. The infant is irritable, and meningismus and even convulsions may occur. There are rarely any signs in the infant to localize the infection to the urinary tract except for frequency of micturition which is difficult to evaluate in this age group.

In older children, the manifestations may be more suggestive of urinary tract involvement. The onset is usually abrupt with fever which may reach high levels fluctuating rapidly from time to time, the child appearing ill and prostrated. The so-called classic symptoms, predominantly bladder symptoms, are common and they are urgency, frequency of urination and dysuria. Flank dull aching pain and tenderness may be present. In most untreated cases, the fever persists for 7 — 10 days, but the urinary changes last about three weeks if

they disappear at all. Rarely, acute pyelonephritis may be fulminating in nature and may attack the kidneys so rapidly that death may occur within a week or two. It cannot be over emphasized that at any age pyelonephritis may be asymptomatic and occurs as a smouldering chronic infection in which the diagnosis is often overlooked until advanced renal damage has been established.

In chronic pyelonephritis, the symptomatology includes :

- 1 — Manifestations due to persistent urinary tract infection : Fever, indigestion, malaise, nausea, vomiting, constipation, diarrhea, anemia and growth failure. Toxic nervous symptoms are headache, nervousness and even convulsions. Hypertension may be a complication.
- 2 — Local symptoms : Pain, renal tenderness, frequency and feeling of a mass due to obstruction, either unilateral or bilateral kidney enlargement, with or without enlarged bladder depending upon the site of obstructions and its severity. Occasionally we get hematuria, dribbling and enuresis.
- 3 — Renal insufficiency : This may develop on any one of the following ways in a child with pyelonephritis :
 - a) Rarely as the result of a rapidly progressive infection in the kidney substance.
 - b) More commonly as a result of low grade continuing smouldering infection that progressively destroys renal substance.
 - c) During periods of rapid growth such as during puberty, renal function may fail in a child with chronic active or inactive pyelonephritis.

Diagnosis : This depends on awareness of its frequency, knowledge of its various symptomatology and in particular the more unusual clinical manifestations, and a rational understanding of the laboratory procedures which are diagnostically useful.

I — Laboratory Findings of Urine Examination: This includes proper collection of urine specimen, bacteriologic examination both quantitative and qualitative, examination for pyuria and other pathological findings.

- 1 — Collection of urine specimens: This is so often done in a most haphazard and inaccurate manner that frequently erroneous conclusions are drawn from the examination of inadequately obtained sample, and errors are made both ways i.e. urinary tract infection is diagnosed when it does not exist and is missed when it is really present. It is thus essential whether in boys or girls that : —

- a) Proper cleaning of the parts should be carried out at first with soap and water, then washed with an antiseptic solution. This is done to obviate contamination with pus cells and bacteria.
 - b) The first part of the stream is discarded if there is voluntary control of micturition.
 - c) Urine should be collected in a clean sterile container.
 - d) The container should be immediately delivered to the laboratory or kept in a refrigerator until it is taken to the laboratory. At room temperature, bacteria multiply very rapidly in the urine. Besides, a change to alkaline pH may occur and this, combined with the delay itself, may lead to dissolution of cells giving a false low reading. Urine may be stored at room temperature for one hour or at refrigerator temperature for 48 hours without significant change in the bacterial population or pus cells.
 - e) If the child is not co-operative or if he is acutely ill and it is important to obtain a reliable sample as soon as possible, one should not hesitate to catheterize him.
- 2 — Bacteriologic examination of the urine : This is performed whenever urinary tract infection is suspected even if pus cells are not found in the urine.
- a) Determination of the number of organisms in the urine : Urine of patients with clinically overt untreated urinary tract infection almost always has counts of 100,000 or greater/c. mm. On the other hand, specimens contaminated during collection generally contain less than 10,000/c. mm. Counts between 10,000 and 100,000 are unusual and indicate the need to repeat the study. When there is bacteria from an extrarenal focus of infection as in the upper respiratory tract, bacteria may be filtered through the kidneys and appear in the urine in abundance but without concomitant pyuria. Thus, the presence of bacteria of marked degree does not always indicate true infection of the urinary tract.
 - b) The species of micro-organism present in the urine should be identified and in vitro antimicrobial sensitivity studies carried out.
 - c) Microscopic examination of a Gram stained smear of freshly collected and un sedimented urine is frequently helpful in differentiation of contamination from infection, since organisms are readily found in stained specimens of urine when about 100,000 bacteria or more per c.mm. are present.

3 — Examination of urine to determine the presence of pyuria : Methods of measuring pyuria are :

- a) The counting chamber method : The procedure is simple. The uncentrifuged urine is well mixed and a drop put in the counting chamber. This method seems preferable than others as it allows small amounts of pyuria to be detected and comparison to be made between one specimen and another.
- b) High power field method : This may vary by over 100% according to the size of the drop put on the microscope slide and amount of urine centrifuged.

Pyuria means the presence of an increased amount of W.B.Cs. in the urine. The presence of 5 or more W.B.Cs. /high power field in a centrifuged specimen of urine is considered pathological. Pyuria may also be defined as 10 or more leukocytes/c.mm. in an uncentrifuged sample of urine.

Differentiation between pus in the urine and phosphaturia : A parent sometimes observes that a child's urine is thick. Most often the cloudiness is due to phosphate deposits in the urine when it cools; but sometimes at the time it is passed, the urine is cloudy with phosphates. In a normal urinary tract, this phosphaturia is unimportant. It indicates a lack of water intake and alkalinity. Turbidity which persists when the urine is warmed and acidified must lead to microscopic examination.

Pyuria was often relied upon as the chief index of the presence of urinary infection. However, urinary tract infection may be present in the absence of pyuria. Thus, it is readily apparent that pyuria is of diagnostic value only when it is present. On the other hand, pyuria may arise from any site in the urinary and genital tracts, as well as extrarenal sources and therefore, it is not always diagnostic of intrarenal inflammation.

4 — Other pathological findings in the urine : Red blood cells are present in varying amounts, sometimes as much as to give frank hematuria. There is also albumin and various types of casts.

II — Detection of Foci of Infection that may be responsible for a hematogenous type of urinary tract infection.

III — Urologic Studies : Done whenever urinary tract infection persists or recurs inspite of adequate therapy. This includes : —

- a) Excretory urogram.
- b) Catheterization after voiding for residual urine.
- c) Voiding cystogram that may show ureteral reflux, bladder diverticulae and/or dilatation of the posterior urethra from urethral valves
- d) Cystoscopic examination and retrograde urography.

Differential Diagnosis : Misdiagnosis of pyelonephritis is common especially in infancy. The incidence of incorrect clinical diagnosis may be as high as 85%. The three main reasons why the disease is infrequently recognized in the pediatric age group are that the symptoms are frequently gastrointestinal, physical signs are often scanty and one or two urine specimens may not disclose pyuria. This intermittency of pyuria is striking and the diagnosis of pyelonephritis should not be excluded if one or two urine specimens contain no pus cells.

In infancy, the disease may simulate pyloric stenosis, meningitis and gastroenteritis. In the older child, the disease may simulate acute appendicitis.

If sufficient kidney tissue has been destroyed to cause chronic renal insufficiency, differentiation from chronic nephritis is to be considered but may prove difficult. Pyelonephritis must be considered in the differential diagnosis of the various conditions that give rise to hypertension.

Treatment :

- 1 — Bed rest till temperature is normal and for few days more.
- 2 — Liberal intake of fluids, liquid or soft diet.
- 3 — Measures to control fever and irritability.
- 4 — Specific treatment : Since pyelonephritis is a bacterial infection of the kidney, the goal of treatment should be the complete eradication of infection before significant renal scarring has occurred.

In a controlled study of children with acute pyelonephritis, a relapse rate of 60% was found after two weeks treatment, 40% after 4 weeks, and 25% after 6 weeks. In persistent infection, there is proved effectiveness in reducing recurrences from giving continued treatment for 6 months. Thus recently, prolonged therapy has replaced short courses in the treatment of this disease.

A variety of antimicrobial agents effective against bacteria which commonly are responsible for pyelonephritis are available. After taking urine sample for identification of the causative agent and its sensitivity, immediately a

sulfa drug is given. This is usually effective against most of the etiologic agents. Dose is 0.15 gm./kg./day on three divided doses.

The use of sulfa should be associated with a good fluid intake and an alkaline diuretic such as sodium bicarbonate or citrate. When the result of the sensitivity tests are available, treatment is modified as indicated. This often consists of prescribing an antibiotic to which the organism is sensitive so that the patient now receives a sulfonamide and an antibiotic. Among the most useful for oral use are nitrofurantoin (8 mg./kg/day), ampicillin (50 mg/kg/day) and nalidixic acid (60 mg/kg/day). Mandelamine (50 mg/kg/day) is sometimes valuable in chronic infections because bacteria do not readily develop resistance to it. Intramuscular administration of an antibiotic is indicated when the child is severely ill and toxic. The choice of drug should be based on the bacterial sensitivities but the available drugs in addition to ampicillin are streptomycin (40 mg/kg/day), colistin (150,000 units/kg/day), and cephaloridine (50 mg/kg/day).

In very young infants, who may have a Gram-negative septicemia, kanamycin (15 mg/kg/day) or gentamicin (5 mg/kg/day) are particularly useful. Pseudomonas infections, which usually infect an abnormal renal tract, can be combated with intramuscular colistin or gentamicin.

Drugs are given in full therapeutic dosages until :

- a) No clinical manifestations.
- b) Patient is afebrile.
- c) Pyuria disappears.
- d) Urine culture is sterile.

In view of the dangers of continued low-grade pyelonephritis it is advisable to continue the appropriate drug in half the above dosage for six months after the acute infection has been dealt with. The patient is thereafter kept under observation with periodic urine tests for another six months.

If the urine is not sterile after appropriate therapy for 2-3 weeks, a complete urologic examination is indicated. It is in such cases and also in chronic and recurrent pyuria that a thorough and detailed urologic investigation is needed. Remediable renal abnormalities should be treated surgically. When the developmental anomaly is not amenable to surgery, continuous or cyclical antibacterial treatment will greatly reduce the risk of relapses and re-infections.

RENAL FAILURE

Renal failure is a syndrome that results from reduction in or cessation of renal function. It is characterised by anuria or oliguria, acid-base disturbances, electrolyte disturbances and impaired excretion of waste products.

Etiology and Pathogenesis :

PRE-RENAL CAUSES :

The common pre-renal causes are :

- 1 — Blood loss in acute hemorrhage.
- 2 — Plasma loss as in burns.
- 3 — Fluid loss as in diarrhea, vomiting, and diabetic ketosis.
- 4 — Neurogenic shock from sepsis, trauma . . . etc.
- 5 — Acute heart failure.

They all result in renal circulatory insufficiency, leading to renal functional impairment which may be reversible when correction of the cause is attained before a permanent damage has taken place.

RENAL CAUSES : There is direct damage to the nephron, either the glomerulus or the tubule or both :

a) Acute glomerular lesions:

- Acute diffuse glomerulonephritis.
- Schonlein - Henoch syndrome.
- Nephropathy with hemolytic anemia and thrombocytopenia (Hemolytic-Uremic Syndrome).

b) Acute tubular necrosis :

- Nephrotoxicity : — certain sulfonamides, potassium bichromate, mercuric chloride and carbon tetrachloride produce uniform necrosis of tubular epithelium with minimal damage of the basement membrane except in severe cases.
- Renal ischemia : when the pre-renal causes of uremia are severe and prolonged, tubular epithelial necrosis with basement membrane disin-

tigation occurs. Restitution of the tubular wall seldom results because of the damaged basement membrane, but since not all the nephrons are affected in severely damaged kidney, restitution of function is possible. In severe cases, large number of nephrons are totally destroyed leading to cortical necrosis.

— Renal anoxia : in association with severe acute haemolysis.

c) **Chronic renal disease :**

Here renal failure may represent irreversible gradual deterioration of function. The chronic renal disorders are :

- Chronic glomerulonephritis - Chronic pyelonephritis.
- Hypoplastic and polycystic kidney - Vascular lesions of the kidney.
- Hereditary tubular defects e.g. Fanconi and Lightwood - Albright syndromes.

POSTRENAL CAUSES : In children, obstructive uropathy can lead to progressive renal atrophy and chronic renal failure. Obstructive uropathy in children may be due to : —

- Congenital anomalies : bilateral ureteric anomalies, bladder neck or infra-vesical obstruction.
- Neuromuscular disorders : Congenital and acquired.
- Bilateral stones.

Chronic renal diseases, as well as postrenal causes when complicated by intercurrent problems such as dehydration, volume contraction, and infection may present as acute renal failure.

Pathophysiology : Renal failure will include the following criteria :

1 — Oliguria.	4 — Acid-base disturbances.
2 — Hyperkalemia.	5 — Hypertension if present.
3 — Sodium and water retention.	6 — Miscellaneous.

1 — *Oliguria* : By oliguria it is meant urine flow less than 180 ml/m² /day. Oliguria may be :

Prerenal, renal or post renal.

i — Prerenal oliguria : It occurs in cases of diminished effective renal

plasma flow, when the underlying cause is corrected urine volume will increase.

ii — Renal oliguria (intrinsic) : It includes 2 types, glomerular, and tubular. As regard the glomerular type, diminution of glomerular filtration rate may be assumed as a cause of oliguria. While in the tubular type the following explanations will lead to oliguria :

- a) Obstruction of the tubular lumina by epithelial debris and casts.
- b) Interstitial edema.
- c) Back diffusion of the filtrate through the damaged tubular epithelium.

The tubular type is classically divided into three stages : anuric or oliguric phase, diuretic and convalescent phase. In pediatric practice this classic sequence does not occur.

iii — Postrenal oliguria : Release of the obstructing cause will result in re-establishment of urine flow unless there is permanent damage and the condition presents as one of the types of renal (intrinsic) oliguria.

2 — *Hyperpotassemia (Hyperkalemia)* : By hyperkalemia we mean increase in the potassium concentration in the serum exceeding its normal range with respect to age (infant serum K 4.1 — 5.3 mEq/L. and child serum K 3.5 — 4.7 mEq/L.). Hyperpotassemia results from diminution of renal excretion of K in conjunction with cellular release of K as a result of trauma, anoxia, hemolysis, and metabolic acidosis.

3 — *Sodium and water retention* : Overload with sodium and water with reduced excretion of urine will lead to interstitial edema, hypertension and circulatory congestion.

In spite of sodium retention there is hyponatremia. It results from dilution of body fluids as a consequence of excessive intake of water relative to that of sodium.

4 — *Acid-base balance disturbances* : Moderate to severe metabolic acidosis results from impaired elimination of hydrogen ions by the diseased kidney in contrast to continuous and even increased production of hydrogen ions by the body.

5 — *Hypertension* : If present it could be due to :

- Excess renin release.
- Sodium and water retention.

6 — *Miscellaneous* : Urea, plasma creatinine, and uric acid concentration increase because of diminished excretion.

- Blood changes in the form of anemia, thrombocytopenia and leukocytosis.
- Hyperphosphatemia and hypocalcemia.

Clinical Manifestations : The clinical pattern of renal failure is often overshadowed by the manifestations of the precipitating cause.

Clinical picture related to the cause: e.g.: shock, trauma, hemolysis, dehydration, congestive heart failure, and sepsis.

Clinical picture related to the renal failure :

- General : irritability or drowsiness, pallor and asthenia.
- Skin : Dryness, itching and in advanced cases vascular purpura.
- Hypertension or hypotension according to the cause of renal failure.
- Respiratory : hiccough, air hunger and in late cases Cheyne-Stokes breathing.
- Cardiac : arrhythmias and in terminal cases pericardial rub. The E.C.G. reflects the electrolyte status.
- Gastrointestinal : anorexia, nausea, vomiting, diarrhea, stomatitis, and bleeding.
- Neuromuscular: irritability, tremors, convulsions, drowsiness, confusion and coma (Hypocalcaemia and retention of phenolic compounds).

Laboratory Data :

Serum :

- Hyperkalemia — raised urea level
- Hyponatremia — hypocalcemia — anemia
- Metabolic acidosis — Increased phosphate, uric acid, and creatinine.

Urine :

- Marked oliguria.
- R.B.C. — casts — proteins — aminoacids.
- Sodium is low in prerenal and glomerular type of renal failure. However sodium is increased in tubular disorder.

E.C.G.

Findings of hyperkalemia

X-ray :

e.g. : Cardiomegaly — pulmonary congestion — radioopaque stones or shrunken kidney.

Diagnosis : Diagnosis of renal failure will involve the following steps :

- i — Simply it is based on oliguria (urine volume less than 180 ml/m^2 /24h.) or anuria. It is also suspected from the clinical feature and verified by the characteristic laboratory findings.
- ii — Diagnosis of the type of oliguria as will be explained in the treatment.
- iii — Diagnosis of the cause : this is essential for the therapeutic and prognostic purposes. It is attained through a thorough history, detailed clinical examination and special laboratory and radiological investigations directed to the suggested cause.

Prognosis : The majority of patients with acute renal failure when properly managed recover renal function spontaneously. Even after weeks of severe oliguria, recovery is possible if the biochemical status of the patient is maintained with reasonable adequacy, and if treatment is guided by physiologic principles.

Management :

- I — Base line and serial determinations of blood urea, serum sodium and potassium, body weight, urine volume and E.C.G.
- II - Treatment of the cause :
 - a) Correction of any blood loss.
 - b) Correction of fluid and electrolyte disturbances :
 - Urgent correction of hypovolemia irrespective of the nature of the loss whether it is plasma, blood, or water : 20 ml/kg body weight (450 ml/m^2) in the form of plasma or Ringer's lactate. It must be rapidly infused within 15-45 minutes.
 - Reassessment of the state of the kidney must be clarified after infusion; if the oliguria is pre-renal diuresis will occur. If there is no increase in the urinary output, the diagnosis of intrinsic renal touch is established. So, a test dose of 20% mannitol, 200 mg/kg body weight within 10-20 minutes with or without diuretics (furosemide) are given intravenously. If diuresis occurs, the condition is considered to be reversible intrinsic renal touch, if not, it will be considered irreversible intrinsic type.

N.B. : Mannitol is contraindicated in cases of congestive heart failure, while furosemide is contraindicated in cases of hypovolaemia.

- c) Treatment of infection : The proper antibiotic is used in sub-optimal doses to avoid accumulation toxicity. Kanamycin and polymyxin should be avoided.
- d) Nephrostomy or cystostomy : To bypass the obstruction if present.

III Management of the biochemical alterations :

- 1 — *Water balance* : Detailed sheet of intake and output of all fluids and electrolytes is performed. The amount of fluid should be equal to previous day urinary output + the insensible water loss ($300 - 400 \text{ ml/m}^2/\text{day}$), which will be increased in the presence of fever by $75 \text{ ml/m}^2/\text{degree centigrade}$. The most important guide to fluid administration is weight change.
- 2 — *Elevated nonprotein nitrogen* : Proteins should be eliminated from the diet. Carbohydrates owing to their protein sparing action tend to decrease tissue breakdown and should be given orally or as intravenous hypertonic glucose 10-30%. Whenever there is vomiting or coma, at least $400 \text{ ml/m}^2/\text{day}$ in the form of carbohydrates are given I. V, to minimize endogenous tissue catabolism. Infants need 12.5 g. sugar/kg/day, older children require 100-150 g/day. Vitamins should be given in generous amount. Anabolics may be given.
- 3 — *Hyperkalemia* : Ingestion of potassium by any route is to be avoided. Citrous fruits are high in K- content. A simple effective measure for removing excess potassium is by the administration of cation exchange resin, (sodium polystyrene sulfonate) at dose of 1 g/kg body weight, which will lower serum K concentration approximately 1 mEq/L. The desired amount of resin can be administered orally or rectally as 20-30% suspension. If needed a repeated dose is administered 12 hours later. When the potassium level falls below 4 mEq/L., resin should no longer be given. In situations of severe hyperkalemia, temporary measures can be used until more definite treatment can be instituted. These forms of treatment can include the infusion of calcium gluconate (100-200 mg/kg body weight) or insulin and glucose (1 unit of insulin to 3 g. of glucose).

Persistent hyperkalemia unresponsive to previous measures is a clear indication of hemodialysis. Recent experience with intermittent peritoneal dialysis indicates that it is a relatively simple, safe and practical procedure effective in carrying patients through the period of acute renal failure.

- 4 — *Hyponatremia* : Fluids have to be restricted : Intravenous sodium chlo-

ride has to be given only if the hyponatremia is severe or if there is diarrhea and vomiting.

5 — *Hyperphosphatemia and hypocalcemia* : Aluminium hydroxide gel may be used to diminish phosphate absorption. Calcium has to be given I.V.

6 — *Metabolic acidosis* : Two lines are followed :

a) General : Correction of the catabolic state through:

- Treatment of shock.
- Treatment of infection and hypoxia.
- Adequate caloric intake not less than 300 cal./m²/day as carbohydrate or fat.
- During oliguric or anuric phase 10-30% glucose I.V.
- With improvement high quality of essential aminoacids and IV glucose may speed recovery helping to maintain an anabolic state.

b) Specific : Metabolic acidosis can be combated by adding 40 ml. of molar sodium lactate to each 500 ml. of IV fluids.

7 — *Hypertension* : If present it will be managed as in case of acute diffuse glomerulonephritis.

N.B. : Dialysis is used to bypass the critical period in acute renal failure, when the conservative measures outlined above are no longer effective. The principal problems that lead to consideration of this line of treatment are :

- i — Hyperpotassemia : resistant or severe i.e. more than 8 mEq/L.
- ii — Severe acidosis.
- iii — Phosphate more than 11 mg/dl.
- iv — Blood urea more than 300 mg/dl.
- v — Circulatory congestion.

In chronic renal failure dialysis should be considered as a means for sustaining the child during the time before transplantation.

The indications for transplantation during the course of chronic renal failure are :

- Growth arrest.
- Severe renal osteodystrophy.
- Malnutrition and inadequate caloric intake.
- Inability to carry out normal activities which are essential for emotional well being and development.

ENURESIS

Enuresis is defined as repeated involuntary voiding of urine after the fourth year of life. A few children achieve voluntary control as early as one year of age. The majority do not begin to gain control before fifteen to eighteen months of age, and nocturnal control is usually not established until two to three years of age. In most instances, enuresis is a continuation of bed wetting from birth (*primary enuresis*). It may commence however, after a period in which bladder control had been gained (*secondary enuresis*).

The term enuresis alone, is commonly used to indicate night wetting only i.e. *nocturnal enuresis*; *diurnal enuresis* refers to involuntary voiding during both day and night. These terms should be restricted to persistent wetting and not used for transient wetting which is seen frequently even in older children during excitement or sometimes with temporary psychologic stress.

Enuresis has to be distinguished from urinary incontinence in which bladder control is completely lost. The enuretic subject is aware of bladder distension and can control its emptying but with greater difficulty than normal individuals.

Incidence : Age : Figures on the incidence of enuresis vary widely. In some reports 12% of 4.5 year-old children and 7.5% of 7.5 year-old children still wet the bed.

Sex : In most reports boys predominate.

Socio-economic status : The incidence is lowest among upper social classes where children are usually properly trained, the fluid intake before bed time is regulated and they are picked up during the night to void.

Family incidence : It is possible to obtain a history of enuresis in parents, siblings and near relatives in more than half of the children with enuresis.

Etiology : The etiology of enuresis is still not fully understood. The suggested factors are :

- 1 — **Developmental disorder :** The most popular concept is that the primary fault in enuresis is failure or delay in the development of inhibitory control on the bladder reflex. This may be due to :
 - a) Delay or defect in the functional or structural maturation of the neuromuscular pathways subserving bladder control. This is largely determined by hereditary factors.

b) Inadequate toilet training — An age between 12 and 14 months is the usual one for training (age of physiologic readiness). The response of the youngster to training will depend on the age at which training begins, the personality of the child and the attitude of the mother. Parent-child conflicts centering about toilet training raise the child's negativism and may delay the establishment of regular toilet habits.

2 — *Psychological disturbances* : Secondary enuresis is usually psychological in origin and related to stress and insecurity, e.g. emotional deprivation. It may represent a desire to regress. A common situation, out of which enuresis may develop, together with other more infantile habits such as a desire to take milk from the bottle and to be fed, is the birth of a younger brother or sister. A similar reversion may take place after a serious or distressing physical illness. The enuresis may be continued as a means of security for attention previously given. In primary enuretics, the incidence of behavioural symptoms is higher than in normal subjects; but it has to be determined whether the emotional disturbance is the cause or the result of enuresis.

3 — *Organic causes* : a) Mental retardation. b) Congenital extradural fibrous bands that constrict the cauda equina with or without spina bifida. c) Urinary tract infections (irritable bladder). d) Diseases associated with polyuria as diabetes mellitus and diabetes insipidus.

Clinical Picture : In most children with enuresis bladder control at night has never been achieved, and nocturnal incontinence has continued from infancy. Wetting generally occurs every night, often more than once a night. The time of wetting is variable. Some children wet within an hour after going to sleep; others not until the early hours of the morning. Children rarely awake after wetting the bed. The habit may cease alone during childhood often at 6-8 years, but it may continue until the early teens when it ordinarily corrects itself. Urgency and frequency are prominent symptoms of enuretics and frequently persist to a variable degree throughout life after the bed wetting has ceased. Children's psychologic response to enuresis varies considerably. Many children are unconcerned. In most children, however, their anxious feelings about enuresis become apparent readily as the physician gives them the opportunity to express their concern.

Diagnosis :

- 1 — Full medical, psychological and social history.
- 2 — Observation of the child's behaviour and personality.

- 3 — Organic disease, as a cause of bed wetting must be excluded by a thorough clinical examination, and if needed laboratory investigations, before the child is treated for functional enuresis. These investigations include :
 - a) Urine analysis for specific gravity, sugar, pus cells and other cells and casts.
 - b) In some cases pyelography, cystourethrography, cystoscopy and cystometry.
 - c) E.E.G. and myelography may be required.

Management :

- 1 — Proper management of organic causes if present.
- 2 — Psychotherapy if the emotional problem is prominent.
- 3 — *Interview with the parents* : The parents should have an idea about the nature of enuresis and that it is due to no fault or weakness on their part. Shaming, threats and punishment should be avoided. The only reasonable attitude is one of encouragement with praise for a dry night and understanding sympathy after a wet one.
- 4 — *Interview with the child* : Conversations with the child are designed to rid him of feelings of inadequacy, shame and guilt. Special stress is placed on the great frequency of enuresis and on its favourable outcome.
- 5 — Fluid intake may be limited in the late afternoon. Let the child pass urine before going to bed, and pick him up by night once or twice to void.
- 6 — Success can sometimes be attained by training the child during the day-time to drink much fluids and to hold the urine as much as possible. The purpose is to increase the intravesical pressure necessary to initiate the micturition.
- 7 — *Drugs* : The place of drugs is difficult to assess, but the wide variety which has been tried at one time or another reflects their relative inadequacy :
 - a) Imipramine (Tofranil and Tryptizol) : It is one of the best drugs available. It has got anticholinergic, antidepressant and central stimulant effects that inhibit bladder contractions, elevate the mood and increase the level of awareness during sleep. The dose ranges from 25-75 mg. at bed time. Gradual withdrawal is usually started after two months of complete dryness. Resumption of symptoms may occur in some cases upon discontinuance of therapy.

- b) **Belladonna** : It relaxes the bladder wall and so can increase the capacity of the bladder, but its action is short. An initial dose for a 5 year old child is 5 drops of the tincture three times daily. The amount is increased daily by one drop per dose until the earliest manifestation of intolerance occurs (flushing 20-30 minutes after administration). Up to 30 drops or more t.d.s are tolerated by most children. Belladonna has to be continued for two months after improvement has been established.
 - c) **Amphetamine and ritalin** : Are central stimulants that may be used to lighten the sleep and enable the enuretic to wake in response to the stimulus of a full bladder.
 - d) **Tranquilizers** : Are used for emotionally disturbed children.
- 8 — Electric buzzer** : It is a form of treatment which involves the induction of conditioned reflex. The apparatus consists of a wired pad which is placed under the child's buttocks. The first drop of urine completes an electrical circuit which rings a loud bell in the room, the child is awakened and gets up to empty his bladder. In successful cases, the child will begin to awaken spontaneously without the bell and will empty his bladder without having wet the bed.

ABDEL-HADI I. HASSAN

Chapter XVI

THE ENDOCRINE SYSTEM

THE THYROID GLAND

Physiological Considerations :

The functions of the thyroid gland are to concentrate iodide and combine it with tyrosine for the synthesis of thyroid hormones, and to store or release these hormones in accordance with the requirements of the body.

The conversion of inorganic iodine to biologically active hormones takes place through a number of steps. A specific enzyme is needed for every step.

The major part of the circulating thyroid hormones consists of thyroxin (T 4). Triiodothyronine (T 3) is present only in small amounts. Degradation of the thyroid hormone occurs mainly in the liver and kidney.

The activity of the thyroid gland is regulated by the thyroid stimulating hormone (T.S.H.) of the pituitary in accordance with the needs of the body. T.S.H. secretion is controlled by the level of circulating thyroid hormones through a «feed-back» mechanism.

Iodides and antithyroid drugs as thiouracil are readily transmitted from mother to fetus. Congenital goiters are reported in some infants born of mothers receiving propylthiouracil or excessive iodides during pregnancy. The placental transmission of thyroxin which circulates loosely-bound to protein is open to controversy. There are evidences to suggest that the fetus lacking a thyroid gland does not receive sufficient hormones from the mother to afford complete protection.

Hypothyroidism

The term «cretinism» or «congenital hypothyroidism» is applied when the disorder is believed to have been present at or before birth. When a previously normal child develops the deficiency, he is said to have «acquired» or «juvenile hypothyroidism».

Etiology of hypothyroidism :

(A) Congenital (cretinism) :

- 1 — Agenesis or dysgenesis of thyroid gland «athyrotic cretinism» or sporadic cretinism. Cause unknown. Some cases are possibly due to maternal autoimmunization.
- 2 — Inborn error of metabolism (goiterous cretinism). There is inability to produce normally acting thyroid hormone because of hereditary defect at some point in the pathway of thyroid hormone formation (enzymatic defect).
- 3 — Prenatal iodine deficiency (endemic cretinism).
- 4 — Goiterogenic (antithyroid) drugs taken by mother during gestation period, as thiourea, thiouracil, P.A.S., thioyanates and perchlorates.

(B) Acquired :

- 1 — Cause usually unknown (idiopathic).
Possibly due to autoimmunization
- 2 — Thyroidectomy for thyrotoxicosis, lingual thyroid or carcinoma.
- 3 — Irradiation.
- 4 — Thyroiditis or other infiltrative process.
- 5 — Ingestion of anti-thyroid agents.
- 6 — Iodine deficiency.
- 7 — Panhypopituitarism or specific T.S.H. deficiency.

Pathogenesis : The degree of deficiency of hormone production in relation to changing body needs determines the state of development and severity of the clinical picture. As the thyroid hormone level falls, there is an increase in T.S.H. output; if a *respective* gland is present, there is hyperplasia of acini with enlargement of the gland and sometimes an increase in hormone output with amelioration of symptoms.

Clinical manifestations :

- (A) Functional changes :** (1) Physical and mental changes : the patient is sluggish both physically and mentally. (2) Diminished circulation : peripheral circulation is poor, skin pale, greyish and cool. Pulse rate and pulse pressure are decreased. (3) Diminished intestinal activity : constipation.

(4) Poor muscle tone. (5) Diminished sweating. (6) Metabolic and chemical changes (see under investigations).

- (B) **Retardation of growth and Development** : (1) *Height* : stunted. (2) *Skeletal proportions* : upper/lower segment is infantile. (3) *Naso-orbital configuration* : infantile. (4) *Osseous development* : retarded. When the retarded centers of ossification appear, they look in the X-ray as small irregular foci scattered over a considerable area of the cartilage (epiphyseal dysgenesis). (5) *Dental development* : retarded and defective. (6) *Retardation and defect in development of the brain* : There is evidence that in early life thyroid deficiency may cause slowing of mental reactivity and responsiveness, retardation of the development of the brain and in some cases permanent damage.

Thyroid deficiency is most likely to cause damage in earliest life when myelinization is occurring. If thyroid deficiency does not develop until later childhood when the maturation of the nervous system is complete, no retardation or defect in brain development may occur and the patient may have a normal mentality.

- (C) **Other changes** : Subcutaneous and other tissues will show myxedema, skin is thickened and hair is coarse, dry and brittle.

The clinical manifestations of hypothyroidism vary greatly according to the age of the patient when thyroid deficiency begins and to the degree and duration of the deficiency. It is often difficult to diagnose during the first few months and the characteristic delay in growth and development may not attract attention until the second or third year of life. However, in some cases the myxedematous changes in the skin and subcutaneous tissues become so marked as to cause a grotesque facies, so typical that it can be recognized at a glance. In a well developed case, the body is short and stocky with infantile proportions. The head seems large for the body and the fontanel remains open. The hair grows further down on the forehead than normal. The base of the nose is broad and flat, so that the eyes appear wide apart. The eye-lids are puffy, the lips are thick, the mouth half-open and a thick tongue protrudes slightly. The voice is often deep and hoarse. Teeth erupt very late, are poorly formed and decay early. The neck appears short and thick, the hands broad and short. The abdomen is large and distended due to very poor muscle tone, and an umbilical hernia is usually present. The skin has a characteristic dusty greyish appearance, is cool and dry and shows circulatory mottling, and is thick and roughened. Sweating may be absent. The hair is sparse, coarse and dry. The child is overweight but not actually obese. The subcutaneous tissues seem

to be thickened but are loose, soft and flabby, unlike the firm, tense tissues of the obese child

The mental and physical state is as characteristic as the appearance. The cretin is content to sit or lie quietly for a long period of time and is little interested in his surroundings. He is usually dull, placid and of good nature, rarely troublesome or excitable.

Very early manifestations of cretinism include poor sucking ability, diminished appetite, mottling of skin, mental and physical inactivity, constipation and prolonged neonatal jaundice.

Diagnosis :

It is most important to establish the diagnosis and to start therapy in cretins as soon after birth as possible since the risks of permanent brain damage increase the longer the treatment is delayed. The diagnosis depends upon :

- 1 Overall clinical picture : All findings may not be present.
- 2 — X-ray examination of bones which show retarded appearance of ossification centers and epiphyseal dysgenesis.
- 3 Subnormal P.B.I. and B.E.I. (Protein bound iodine and Butanol extractable iodine). Normal for P.B.I. is 4 - 8 ug.% and for B.E.I. 3 - 6 ug.%
- 4 Radioactive iodine uptake by the thyroid gland : Low in athyroid cretins.
- 5 — Blood cholesterol : In the majority of hypothyroid children over the age of 2 years, the serum cholesterol is between 275 and 600 mg.% compared to a normal range of 125 - 300 mg.%. In cretins under two years of age, cholesterol is often not elevated.
- 6 — The therapeutic response is one of the most conclusive proofs of hypothyroidism.

Differential diagnosis : From other causes of mental retardation, gargoylism, chondrodystrophies, pituitary dwarfs and from dry skin of ichthyosis.

Treatment Desiccated thyroid in adequate dosage is entirely satisfactory as substitution therapy. In young untreated cretins, it is safe to begin with an initial dose of 1/4 grain daily as a single dose and increase by 1/4 grain at intervals of 1-2 weeks. One to one and half grains daily is adequate for cretins up to the age of two years. In older children, higher doses are needed and a maintenance of 2-3 grains is usually required. It should be

known that this substitution therapy should be maintained for life. Some workers prefer to use thyroxin on the basis that it is a pure compound not subject to variation; 0.1 mg. of sodium L. thyroxin given orally once/day is equivalent to the activity of about 100 mg. (1.6 grain) of desiccated thyroid.

When treatment is adequate, the physiologic evidences of deficiency disappear rapidly. The patient becomes more active and energetic both physically and mentally. The earliest clinical signs of improvement are warmth of the skin, marked increase in patient's activities and improvement in the bowel movements. There is also a marked diminution of the concentration of serum cholesterol.

Manifestations of excess therapy are marked excitability, nervousness, tremors, tachycardia and hypertension.

Prognosis : With proper treatment the outlook for normal physical growth and for the disappearance of all stigmata of cretinism is excellent. The prognosis for mental development is uncertain and much less favourable.

If in a completely athyrotic cretin treatment is instituted very early, the outlook for mental development is not bad. About half of such cretins when treated adequately before 6 months of age have attained normal mental development. The longer the treatment is delayed beyond 6 months, the greater the likelihood that irreparable cerebral damage will occur.

In acquired hypothyroidism, if the onset occurs after 2-3 years of age, the intelligence quotient (I.Q.) may be restored to pre-disease level.

GOITER

Goiter is abnormal enlargement of the thyroid gland regardless of the cause. Enlarged thyroid glands differ in their functional activity. Those which do not cause the patient to deviate from an euthyroid state are referred to as simple euthyroid goiter. With hyperthyroidism one may speak of toxic goiter. There are also hypothyroid goiters which are either caused by or result in an inability of the thyroid gland to secrete adequate amount of the hormone.

Etiology and types of goiters :—

- (4) Goiters compensatory to impaired production of, or increased needs for, thyroid hormone : Inborn enzymatic defects, Endemic goiters (Iodine deficiency), Goiters due to antithyroid drugs or naturally occurring goiterogens and Simple goiter of adolescence or pregnancy.

(B) Thyrotoxic goiters.

(C) Inflammatory reactions (functional status may be euthyroid, hypo- or hyperthyroid). Acute : Non-suppurative and suppurative. Chronic : Tuberculosis, syphilis, Riedel's thyroiditis and Hashimoto's thyroiditis.

(D) Neoplasms : (functional status may be euthyroid, hypo-or hyperthyroid). Benign tumours or cysts Cancer of the thyroid.

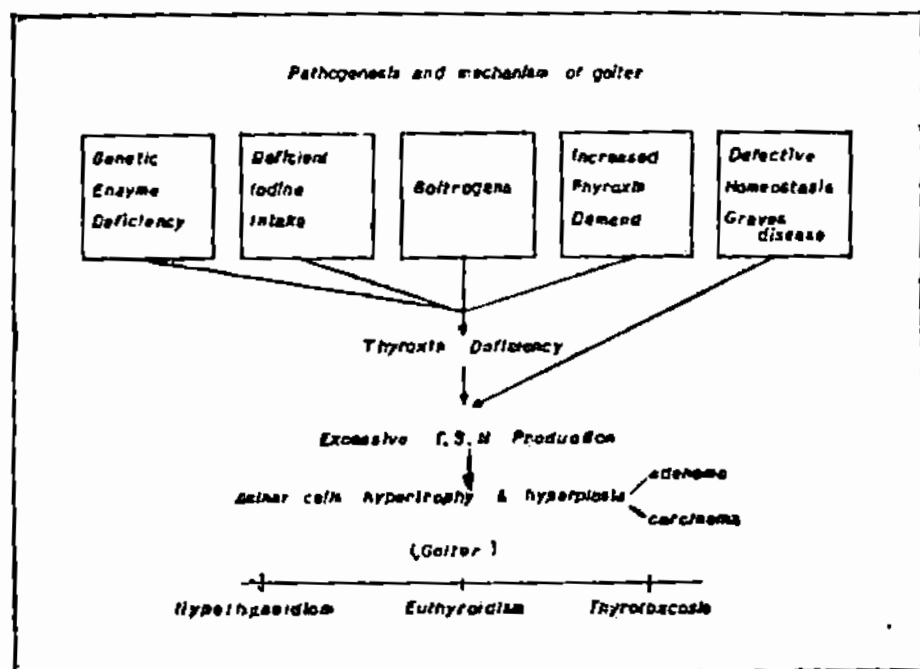


Fig. : 41 Pathogenesis and Mechanism of goiter formation

Simple goiters of adolescence or pregnancy : —

This form of goiter has generally been considered to be due principally to increased needs of the body for thyroid hormone. Adolescent goiters most often occur in girls just prior to puberty, but sometimes are seen in boys. The possibility that these patients might have a mild enzymatic deficiency similar to those which produce goiterous cretinism must be considered.

Simple goiters are usually diffuse and soft and of only moderate size. They often subside spontaneously during or after adolescence. If they cause embarrassment, they may be helped to disappear by giving substitution therapy with 2 — 3 grains of desiccated thyroid daily for one or more years.

Chronic lymphocytic thyroiditis — Auto-Immune thyroiditis — Hashimoto's disease.

This is by far the most common type of thyroiditis and occurs frequently in childhood. It is possible that many of the so-called cases of «adolescent goiter» may actually be of this type. The enlargement of the thyroid gland may be so slight or so localized as to pass unnoticed. Some cases of acquired juvenile hypothyroidism may have been preceded by the disorder. Hashimoto's disease is now considered as an auto-immune disease. Initially it is possible that some injury to the thyroid gland occurs, possibly due to a viral infection, trauma, surgery or irradiation. Destruction of a few acinar cells, or escape of thyroglobulin into the interstitium, liberates antigen into the circulation. The subject develops antibodies to his own thyroid antigen. Antigen-antibody reaction in the thyroid gland leads to further destruction of the gland with lymphocytic infiltration, progressive destruction may eventually lead to hypothyroidism.

The thyroid gland may be very small, firm or hard. Most commonly it is 2 — 3 times its normal size. The enlargement is diffuse, the surface is smooth or irregular and nodular. The patient is asymptomatic except for the goiter. The condition is chronic and the goiter may remain for years.

Treatment consists in administration of desiccated thyroid 2 — 3 grains daily for 2 years. Serial clinical observations are made for development of changes in thyroid function. In some unresponsive patients corticosteroids are added.

Neonatal goiter : The goiter may be attributed to intrauterine exposure to:
(1) Goiterogenic substances (2) A state of maternal thyroid pathology such as iodine deficiency, hypothyroidism or hyperthyroidism.

Clinical manifestations : The size of the gland varies. When pressure on the trachea, esophagus and/or veins is great, alarming symptoms especially respiratory difficulty may occur. Often infants are euthyroid. Some may be hypothyroid but go through a hyperthyroid phase if goiterogen inhibition disappears before hyperplasia subsides. Hyperthyroidism may occur in newborn infants of thyrotoxic mothers.

Treatment : Iodine should not be given since it may cause further thyroid enlargement. If the gland is large or there is hypothyroidism, desiccated thyroid is given in a dose of 1/4—1 grain daily for the first week, and 1 - 2 grains daily thereafter if there has been no decrease in size. If the gland is very large and is causing serious respiratory obstruction, partial thyroidectomy is required. In newborn infants of thyrotoxic mothers thyrotoxic symptoms may require treatment.

THE ADRENAL GLANDS

Each adrenal gland is developmentally and functionally two separate organs; the medulla, and the cortex. Hormones secreted by the adrenal medulla are epinephrine and norepinephrine. The biologically active hormones secreted by the adrenal cortex can be divided into four groups :

(1) The glucocorticoids.	(2) The mineralocorticoids.
(3) The androgens.	(4) The estrogens.

SUPRARENAL CORTICAL HYPERFUNCTION

Oversecretion of adrenocortical hormones may be due to hyperplasia of adrenal cortex or to a benign or malignant tumor. This may result in one of the following :

- (1) — Congenital adrenal hyperplasia.
- (2) — Premature adrenarche.
- (3) — Cushing's syndrome.
- (4) — Virilizing and feminizing tumors.
- (5) — Primary and secondary hyperaldosteronism.

CONGENITAL ADRENAL HYPERPLASIA (CAH)

CAH is the most important cause of adrenogenital syndrome in infancy and childhood. It is a classic example of an inborn error of metabolism and represents the clinical expression of a hereditary defect in the biosynthesis of cortisol due to partial or complete lack of certain enzymes. The clinical symptoms in affected males and females are caused by excessive secretion of adrenal androgens due to excessive stimulation by ACTH secondary to diminished cortisol level in the blood. Adrenocortical activity in the fetus begins as early as the 3rd month of gestation before the completion of the development of the genital ducts and external genitalia. In females, the increased elaboration of androgenic substances during embryonic life in patients with CAH results in hypertrophy of the clitoris and variable degrees of fusion of the labioscrotal folds (female pseudohermaphroditism). The internal duct system has developed normally and normal infantile ovaries are present. These females resemble males with hypospadias and bilateral cryptorchism. In a few cases, a complete penile urethra has been described. In all cases of ambiguous external genitalia,

and in all male babies with bilateral cryptorchism at birth, it is wise to carry out the simple test for sex chromatin.

In the untreated female patient with CAH, clinical signs of virilization will appear. Usually pubic hair grows by the age of 2 to 4 years followed shortly by axillary hair. Other symptoms of progressing virilization are acne, deepening of the voice and further enlargement of the clitoris with frequent erections. At the age of puberty, development of the breasts fails to occur.

In males, CAH cannot usually be recognized in early infancy except when symptoms of the salt losing syndrome occur. After birth, there is rapid sexual development. The penis becomes large and pubic hair appears. The testes remain infantile in size. Acne deepening of the voice and masculine development appear.

In the untreated males and females, somatic growth and osseous development become far advanced for the age of the patient. Epiphyseal fusion occurs early and will lead to a dwarfed adult, despite having been excessively tall in childhood.

Some cases of CAH are accompanied by the salt-losing syndrome due to complete deficiency in the enzyme necessary for aldosterone formation. There is hyponatremia, hyperkalemia and metabolic acidosis; changes typical of Addison's disease. The symptoms usually develop during the first 7 — 14 days of life and are those of acute adrenal insufficiency. If this crisis is not recognized rapidly, severe dehydration, shock and hyperkalemia ensue, with early death. In another group of patients hypertension may occur.

Genetic studies in patients with CAH indicate that the defects in the biosynthesis of adrenocortical steroids are due to a recessive autosomal heredity with clinical expression in the homozygous state.

Treatment : Administration of cortisone in physiological doses for life. The dose should be increased in situations of stress. In the salt losing variety, desoxycorticosterone is also added.

PREMATURE ADRENARCHE

Here, pubic or axillary hair may develop at an early age without the appearance of the other symptoms of sexual maturation. The syndrome has been called premature pubarche and premature adrenarche. Urinary excretion of 17-ketosteroids has been found slightly or moderately raised.

Two explanations are put :

- 1 — Increased sensitivity of sexual hair follicles to normal levels of androgens present during the pre-adolescent period.
- 2 — Premature increase in the secretion of adrenal androgens before the pituitary gonadotrophic mechanism becomes activated.

The condition should be considered as a benign constitutional variation of sexual development.

CUSHING'S SYNDROME

Cushing's syndrome is rare in children, but it has been reported at all ages, even in infancy. In children, the syndrome is usually due to an adrenal carcinoma. The condition may also be due to bilateral hyperplasia (hyperresponsiveness to ACTH, or secondary to increased ACTH production). Pituitary tumors may be responsible for the syndrome.

Clinical manifestations : The most important clinical and laboratory findings are those caused by excessive production of cortisol. Other steroids may also be produced in excess as androgens, estrogens and mineralocorticoids. Outstanding symptoms of the syndrome are obesity (characteristic moonfaced truncal type of obesity), hypertension, glucosuria and purple striae. Virilizing symptoms are common. An important sign in children is stunting of growth.

Treatment : Treatment is surgical in cases due to an adrenal tumor. With adrenal hyperplasia, treatment is more difficult. Several alternatives may be used as total adrenalectomy, subtotal adrenalectomy or irradiation of the pituitary gland.

ADRENAL CORTICAL INSUFFICIENCY

The various causes of adrenal failure are as follows :

- A) Acute adrenal insufficiency : (1) Congenital hypoplasia of the adrenals. (2) Hemorrhage into the adrenal glands in the newborn either from trauma or blood disease. (3) Salt-losing crisis with congenital virilizing adrenal hyperplasia. (4) Meningitis, diphtheria and other fulminating infections causing hemorrhage or necrosis of the adrenals (Waterhouse-Friderichsen Syndrome). (5) Operative removal of an adrenal tumor due to compensatory atrophy of the remaining adrenal. (6) Bilateral adrenalectomy

- (7) In the course of acute stress (surgery and infections) in patients treated for chronic adrenocortical insufficiency or congenital adrenal hyperplasia.
 (8) In the course of acute stress in patients on long-term steroid treatment or in patients after stopping longterm steroid treatment. (9) Crisis in cases of chronic adrenal insufficiency.

B) Chronic adrenal insufficiency : (1) Addison's disease. (2) Iatrogenic chronic adrenocortical insufficiency after stopping corticosteroid therapy.

ADDISON'S DISEASE

Etiology : Addison's disease may be due to primary atrophy of the adrenal glands or destruction of the glands by tuberculosis. It may also occur in association with generalized moniliasis and hypoparathyroidism. There is a good possibility that atrophy of the adrenals, and other endocrine glands may be due to an autoimmune process.

Symptomatology : The presenting symptoms of Addison's disease in children are general weakness, anorexia, weight loss with dehydration and gastro-intestinal symptoms such as nausea, vomiting and diarrhea. Recurrent convulsions, probably of hypoglycemic origin may occur. Pigmentation of mucus membrane and skin is usually present, particularly of areolae and genitalia. In some cases, the first manifestation is that of acute adrenal crisis.

Laboratory findings : Low plasma and urinary 17-hydroxycorticosteroids and their failure to increase after ACTH. Serum sodium decreases and potassium increases. Hypoglycemia.

Treatment : Replacement therapy with cortisone and desoxycorticosterone.

IATROGENIC CHRONIC ADRENOCORTICAL INSUFFICIENCY

Perhaps the most frequent and important cause of chronic adrenocortical insufficiency in childhood is the iatrogenic chronic adrenocortical insufficiency in the patient who has been treated with glucocorticosteroids and who has recently stopped taking them. Administration of glucocorticosteroids results in suppression of pituitary ACTH release, suppression of cortisol production and ultimately adrenocortical atrophy. There is considerable clinical and

experimental evidence that even short periods of glucocorticoid therapy may lead to a severe degree of adrenocortical atrophy.

Prevention : This is through intermittent administration of ACTH during prolonged steroid therapy. This will at least prevent severe adrenal atrophy and will promote rapid recovery of adrenocortical function after stopping therapy. For at least 24 months after discontinuing prolonged therapy, stress doses of cortisol should be given for infection, trauma or surgery (2.5 mg. cortisol/kg./24 hours).

CLINICAL PICTURE OF ACUTE ADRENAL CORTICAL INSUFFICIENCY

Adrenal Crisis

Acute adrenal insufficiency may manifest abruptly and if untreated runs a rapidly fatal course. The patient suddenly becomes cyanotic; skin is cold and clammy and his pulse rapid and weak. Frequently, there is severe abdominal pain suggesting acute abdominal disease; vomiting and diarrhea are often present. The blood pressure falls, respirations are rapid and labored and he becomes comatose. Serum sodium and chlorides are decreased and serum potassium is increased. There is hemoconcentration and metabolic acidosis. This symptom complex is known as adrenal crisis.

Waterhouse-Friderichsen Syndrome

It is a syndrome that occurs mainly in children and young adults; characterized by overwhelming sepsis with extensive purpura and circulatory collapse. Most cases are due to massive invasion with meningococci, though other microorganisms may produce the sepsis. Acute meningococcemia with purpura and vascular collapse may occur without the adrenals showing any obvious disease. The term Waterhouse-Friderichsen syndrome should be restricted to cases in which bilateral adrenal hemorrhage is found at necropsy. In the absence of adrenal pathology, the term «fulminant meningococcemia» should be used. It is advisable in the treatment of this syndrome to give cortisol. Maintenance of normal blood pressure partly depends upon the presence of cortisol, since cortisol potentiates the effects of noradrenaline. In the absence of cortisol, response to the adrenaline is progressively lost.

How to Prevent the Occurrence of Acute Adrenal Crisis :

1 — Children treated for chronic adrenocortical insufficiency should receive maintenance doses of cortisol which are not in excess of the physiological production of cortisol. Major stress situations such as surgery, injuries and infection should be managed by a two to four fold increase in the maintenance dose for the duration of the critical situation. If the patient is not vomiting and is fully conscious, the treatment can be given orally.

2 — Patients with congenital adrenal hyperplasia should be managed exactly as those in group 1.

3 — Patients on long term steroid treatment should never discontinue the steroids during stressful situations. If the dose has been decreased before, it should be increased again as high as stress doses and given parenterally if there is vomiting. Ambulant patients on long-term steroid therapy should carry a card with them containing informations of the treatment. In the child who acquires varicella, the dose should be decreased to the maintenance dose.

4 — When preparing a child for adrenalectomy or surgical removal of an adrenal tumor, he should be given for two days prior to, and on the morning of the operation 100-200 mg. of cortisone I.M. At operation, he should be given glucose-saline by intravenous drip. Intramuscular cortisone 100 mg. daily should be given for 3 days after the operation, then 50 mg. for 3 days and 25 mg. for another 3 days. Substitution therapy is then continued.

Scheme for the Treatment of Acute Adrenal Insufficiency

1. Intravenous fluids (isotonic saline in 10% glucose) approximately 100 ml./kg. during the first 24 hours.

2. Cortisol hemisuccinate intravenously, 1 — 2 mg./kg. at once, then 50 — 250 mg. intravenously in the drip during the first 24 hours.

3. Adrenaline and noradrenaline for the treatment of shock; the vasopressor substance is diluted in 250 ml. of 5% glucose and a slow rate of I.V. drip maintained, under careful control of blood pressure.

4. Aldosterone I.V.; 1.0 mg. at once and if necessary repeated during the first 24 hours.

5. DOCA I.M; 3.0 mg. at once and 2 — 4 mg. per day thereafter.

6. Antibiotics and other supportive treatment.

The intravenous therapy should be continued for at least 24 hours and until the patient is definitely out of shock with well maintained blood pressure and is capable of taking adequate fluids and salt by mouth. After this period of emergency, treatment with cortisone should be given intramuscularly and dose reduced gradually to the amounts required for maintenance.

JUVENILE DIABETES MELLITUS

Although juvenile-onset diabetes (before 15 years of age) constitutes a small percentage of all diabetics, yet it presents disproportionate bigger problems.

Characteristics of juvenile-onset diabetes and differences from maturity-onset (adult) diabetes are the following :

- (1) — Onset is rapid, with progression to severe, ketoacidosis and coma in a matter of hours or days.
- (2) — Early hypertrophy and hyperplasia of islet cells occur, with supranormal levels of plasma insulin, followed by atrophy of cells and complete diabetes in five years.
- (3) — Usually within three months following initiation of insulin therapy there tends to be a temporary remission of the diabetic state. The diabetes then progresses with less frequent and relatively minor remissions to complete insulin insufficiency over a period of four to five years.
- (4) — Insulin replacement is required, and oral hypoglycemic agents are usually not effective.
- (5) — Omission of insulin promptly results in extreme hyperglycemia, and in 24—48 hours ketoacidosis and coma may set in.
- (6) — Variations in insulin response are great, with marked swings from hypoglycemia to hyperglycemia.
- (7) — Exercise exerts a definite lowering effect on blood sugar levels.
- (8) — Complications occur in 90% of juvenile diabetics within twenty years following onset, and the rate of progression is rapid.

Etiology : The precise cause of the common type of diabetes mellitus with ketosis is unknown. In childhood, the disease is invariably insulin sensitive, but whether it is due primarily to diminished insulin production by the *B*-cells of the islets of Langerhans or to a raised level of insulin antagonists

is uncertain. Heredity is an important factor. It has been suggested that transmission is by an autosomal recessive trait in which case, when both parents are diabetics, all their children should ultimately develop the disease. The close relationship with obesity, which is well recognized in adults, does not apply during childhood.

Pathophysiology : Diabetes mellitus is the manifestation of a deficiency of insulin. This will result in hyperglycemia due to deficient utilization of glucose by the peripheral tissues, impaired glycogen formation in the liver and in the muscles and increased glycogenolysis. The hyperglycemia, when it exceeds the renal threshold, is responsible for glycosuria. The diuresis initiated by the hyperglycemia accounts not only for the excretion of excess glucose, but also for excessive losses of electrolytes and water. As a result of the inability to use glucose for fuel, both protein and fat are oxidized at abnormally rapid rates, with excessive catabolism of tissue proteins and body fat. The increased rate of breakdown of fat in the liver results in overproduction of ketones and in their discharge into the blood at a rate exceeding the capacity of the peripheral tissues to oxidize them and of the kidneys to excrete them. Ketonemia with metabolic acidosis will result. Other factors in the development of acidosis are dehydration and renal dysfunction secondary to dehydration and loss of fixed base. The specific causes of coma are not apparent but cerebral vascular activity is adversely affected by the various metabolic derangements.

Clinical manifestations : These are of sudden onset, occurring in a matter of hours or days. They include polyphagia, polyuria, polydipsia and rapid weight loss. The polyuria may lead to nocturnal enuresis. Pallor, malaise and irritability are often present and skin irritation and infection are occasionally associated with diabetes.

The presenting symptoms may be those of diabetic acidosis particularly if there is an existing acute infection. In the precomatose state, there are drowsiness, dryness of the skin, flushed cheeks, cherry-red lips, acetone breath, hyperpnea, nausea and vomiting and abdominal pain. In complete coma, the hyperpnea becomes greater (Kussmaul breathing), the eyeballs are soft and sunken, the abdomen is rigid, the pulse is rapid and weak, and the temperature and blood pressure may be subnormal.

Diagnosis : The recognition of diabetes mellitus would rarely present difficulty if every patient's urine was examined for sugar and, whenever a reducing substance was present, tests for acetonuria were carried

out. In children with diabetes mellitus there are usually large quantities of glucose in every specimen of urine and commonly there is an added ketonuria. These urinary findings in association with the symptoms already described make the diagnosis almost certain. Confirmation is obtained by estimating the blood-sugar level. Provided no carbohydrate has been taken in the previous two hours, a blood-sugar level of 200 mg. per cent or higher establishes the diagnosis of diabetes mellitus. If doubt still persists, a glucose-tolerance test should be performed. It shows an abnormally high fasting blood-sugar level, and after the ingestion of glucose the blood-sugar level rises further and shows little or no fall after two hours.

Transitory glycosuria may be the result of emotional disturbances, overeating, acute infections, cerebral injuries and lead poisoning. Salicylates may be responsible for a reduction of Benedict's solution which may simulate that by sugar. Renal glycosuria is the result of a lowered renal threshold for glucose, but there is no hyperglycemia and the glucose tolerance curve is within normal. It is also important to bear in mind that not all urinary sugar is glucose, and steps should be taken to ensure that the unusual instances of pentosuria and galactosemia are not diagnosed as diabetes mellitus.

Complications : Except in cases of long duration or in inadequately treated ones, complications are uncommon.

- (1) — Stunting of growth, hepatomegaly, failure to develop secondary sexual characters and amenorrhea are seen in adolescents whose diabetes has been uncontrolled over long periods of time.
- (2) — Serious degenerative lesions occur in juvenile diabetics who have had diabetes for ten to twenty years. These complications include principally arteriosclerosis with hypertension, retinal and lenticular changes and nephropathy. The high incidence of vascular degenerative disease constitutes the most important problem in juvenile diabetes.
- (3) — Infections : In poorly controlled diabetic children infections not only are common but also show less tendency to heal. Among these infections are pyoderma, vulvitis and proctitis, dermatophytosis, cystitis and pyelonephritis.
- (4) — Complications associated with insulin therapy : Lipodystrophy (atrophy of subcutaneous fat), lipomatosis, allergy to insulin and hypoglycemia due to overdosage, inadequate caloric intake, or associated with unusual exercise.

Treatment : The aims of treatment are restoration of the diabetic child to average physical status and health, and subsequent maintenance of them.

General treatment : Diabetes mellitus is a permanent disability and great care is required to prevent the child being cast as an invalid. Both the parents and the patient should be instructed in the nature of the disease, for their intelligent cooperation leads automatically to an improvement in the degree of control of the diabetes. The child's daily activity should approximate as closely as possible those of his nondiabetic friends. Extra carbohydrate will be required following unusual exertion. The manifestations and early recognition of hypoglycemia should be described as well as the method of treatment. They should also be instructed about the recognition of early signs of acidosis and of the need for immediate medical assistance. Practical instructions should be given in the measurement and administration of insulin and also in the testing of urine for sugar and ketones. The urine should be examined for sugar at least twice a day and for ketones weekly.

Diet : The essentials of an adequate diet are; sufficient caloric value for activity and growth, a protein intake not less than 2 — 3 grams per kilogram per day, optimal intake of vitamins and minerals, and participation of the diet by the entire family.

The requirements for a child of one year are calculated as 1000 calories daily with an additional 100 calories daily for each subsequent years of life. Calories are given as 50% carbohydrate, 25% protein and 25% fat. A quarter of the total diet should be given at each of the three meals i.e. breakfast, lunch and dinner, and the final quarter divided to provide a snack for mid-afternoon and before retiring to bed.

Most physicians today prefer the free diet, in which the child is allowed the ordinary diet customary for his age and social environment. The advantages of this diet are ease of management, and the lessened risks of hypoglycemic attacks. It does result in somewhat higher blood sugar levels but it is doubtful if this carries any real disadvantage.

It is essential to prevent obesity, and it is preferable that the weight be kept at the lower limits of normal.

Insulin therapy : The severity of juvenile diabetes mellitus makes it imperative for insulin to be used, for in no other way can adequate control be ensured. There are several types of insulin which vary in their speed of action and the period in which they are effective (table 21).

Table 21 — Speed and duration of action of different types of insulin in hours.

Type of insulin	Onset of action in hours	Peak effect in hours	Duration of action
Regular or crystalline	1/2	2 — 4	6 — 8
N.P.H.	2	8 — 12	18 — 24
Lente	2	8 — 12	18 — 24
Protamine zinc (P.Z.I.)	4 — 8	14 — 24	24 — 30

The original soluble quick-acting insulin is the most suitable for initial stabilization. Once diabetes mellitus is recognized, regular insulin should be started. It is given half an hour before each of the three main meals. A convenient starting individual dose is 5 — 10 units, according to the degree of glycosuria. Adjustments are made daily on the basis of the qualitative urine test for sugar in specimens voided about three hours after each meal. Increase of insulin should be by 2 — 4 units each dose. It is safe to keep the evening dose less by 2 — 4 units than the morning and noon doses. When the urine becomes free from ketones and the glycosuria has disappeared or is intermittent, an attempt should be made to maintain stabilization with a single daily injection of insulin. This usually takes from 5 — 7 days. A good plan of therapy is to give 75% of the previous day total dose of regular insulin as lente or N.P.H., and the remainder as unmodified insulin before breakfast. Subsequent adjustments of the dose of each insulin are made on the basis of the presence or absence of sugar in the urine, or by the presence of insulin shock.

The dose of long acting insulin is adjusted so that the urine of the following morning contains little or no sugar, and so that the child does not have insulin shock during the night or prebreakfast hours. The dose of the unmodified insulin is estimated on the basis of the urinalysis preceding the noon and evening meals or the occurrence of insulin shock during this portion of the day. Occasionally satisfactory glycaemic equilibrium is obtained with only long acting insulin but most often regular insulin will have to be continued in the pre-breakfast injection.

Temporary mild hyperglycemia with glycosuria is tolerated. Strict control is not practical and sometimes unwise because recurrent hypoglycemia is more frequent. Repeated moderate or severe hyperglycemia however, is to be avoided.

It is often observed that a few weeks after the beginning of treatment some

recovery of pancreatic function may take place, enabling a reduction in insulin dosage.

Exercise enhances the oxidation of sugar and thus diminishes the need for insulin. Therefore exercise in moderation is beneficial. However, patients taking insulin should be cautioned against strenuous exercise unless they fortify themselves beforehand with extra carbohydrate.

Infection increases the requirement for insulin and is the most potent factor in initiating acidosis. During mild infections sufficient extra insulin is required to prevent excessive glycosuria. In more severe infections the fat should be decreased, extra carbohydrate administered, and additional insulin of the regular type should be injected as required before the three principal meals. It is important to bear in mind that the dose of insulin must be reduced again during convalescence.

Prior to and during surgery, crystalline insulin is usually preferable. Intravenous fluids are given. Urine and blood sugar levels are followed carefully as to the adequacy of the insulin and to prevent hypoglycemia.

Insulin shocks (hypoglycemic reactions) :

These occur sometimes in almost every diabetic child. The most common early manifestations are hunger, pallor, weakness or dizziness, sweating and rapid pulse.

Older children may have epigastric discomfort, tremors or diplopia. With severe reactions, there may be semiconsciousness and paralysis. Unless treatment is promptly given, convulsions, coma and even death may supervene.

Insulin shock may result from an overdose of insulin, from reduction in diet, or from increase in exercise without a corresponding reduction in insulin.

Treatment : Mild symptoms of hypoglycemia respond promptly to the oral administration of 4 - 5 ounces of fruit juice or a few teaspoonfuls of sugar or syrup. A school child should always take a lump of sugar, candy, or fruit in his pocket to be used in such emergencies. If the hypoglycemia has led to unconsciousness, epinephrine may arouse the patient so that he can take carbohydrates by mouth. If not, or if there is vomiting, it is necessary to give glucose intravenously.

Diabetic acidosis and Coma : Diabetic acidosis is the most serious hazard in the life of the diabetic. Diabetic acidosis and coma may be the initial episode which leads to the recognition of the disease, or it may develop in cases under treatment as a result of omission of in-

sulin, injudiciously decreased dosage of insulin and/or failure to increase the dose as needed in the presence of infection or other illness.

In the precomatose state there is drowsiness, dryness of the skin, flushed cheeks, cherry-red lips, acetone breath, hyperpnea, nausea vomiting, abdominal pain and often general body pains. In complete coma the hyperpnea becomes greater (Kussmaul breathing), the eyeballs are soft and sunken, the abdomen is rigid, the pulse is rapid and weak, and the temperature and blood pressure may be subnormal.

Diabetic acidosis with or without coma must be differentiated from acidosis or coma resulting from other causes such as hypoglycemia, uremia, gastroenteritis, encephalitis, cerebral hemorrhage, lead poisoning, and salicylate poisoning. Abdominal pain, tenderness, muscular rigidity, vomiting and leukocytosis may simulate an acute abdomen.

Treatment : The essential needs of the child in diabetic coma are insulin, fluids (table 22) and the skilled nursing required for the unconscious patient.

Table 22 : Fluid therapy : The amount of fluid and electrolytes required during the first 24 hours (per kg.)

Requirements	ml. H ₂ O	mEq./L.			
		Na	Cl	K	P
Deficit Therapy	80-125	5-10	3-7	1-3	1-1.5
Maintenance Therapy*	70-120	1-2.5	1-2	1-2.5	2-3

* The larger amounts are indicated for the infant; the smaller amounts for the child.

First we correct extracellular *dehydration*, shock, anoxia, and impaired renal function with Ringer's lactate solution 15 - 25 ml./kg. intravenously during the first hour of therapy, followed by 10-20 ml./kg. hourly thereafter.

Glucose is best omitted from the solution initially but as soon as the blood sugar level begins to fall (levels below 300 mg.%) the parenteral fluids should contain 5% glucose.

When urine flow and circulatory efficiency are satisfactory, replace intracellular electrolytes (potassium and phosphorus).

As the ketosis declines, the child will gradually regain consciousness and oral feeding will become possible. Only fluids and in small quantity should be administered initially, and as the amount is increased the intravenous drip can be discontinued.

Insulin : Enough crystalline insulin to effect clearing of the ketosis by accelerating the utilization of carbohydrate should be given with carbohydrate to prevent development of hypoglycemia.

An initial dose of 2 units per kilogram body weight is satisfactory; half subcutaneously and half intravenously. An immediate blood sugar level should be estimated before giving the first dose of insulin. Further blood-sugar levels should be ascertained every two hours and half the initial dose repeated subcutaneously until the glucose level begins to fall. Insulin dosage can then be reduced and the interval between injections prolonged. With a blood sugar level of 300 mg. per cent or less, the sugar content of the urine can be used as a guide to further insulin requirements with blood sugar estimations at six to twelve hourly intervals. It should be remembered that 1-2 gm. of carbohydrate per unit of insulin are necessary to prevent hypoglycemia (included as 5% glucose in the parenteral fluids and oral fluids). The parenteral administration of vitamins of the B-complex is advised. Gastric aspiration early in therapy is helpful in relieving the massive distention which may occur, and to avoid pulmonary aspiration of vomitus. Administration of large doses of appropriate antibiotics, if bacterial infection is present, may rapidly improve the response of the patient to insulin.

Oral feeding can usually be started cautiously within twenty four hours and parenteral therapy may be discontinued in favour of oral carbohydrate and electrolyte mixtures and other liquid diets. Insulin is given 6 hourly as required for two to three days before we shift to long acting types of insulin.

DWARFISM (SHORT STATURE)

A dwarf may be broadly defined as an individual who is conspicuously smaller than others of his kind.

Growth in height requires :

- 1 — The inherent capacity of skeletal and other tissues to respond to appropriate hormonal stimuli.

- 2 — The presence of anabolic hormone.
- 3 — Adequate nutrition for maintenance of a positive nitrogen balance.
- 4 — A properly functioning assimilative and metabolic processes for the utilization of nutritional substances.

Defective growth may result from

- 1 — Hereditary factors.
- 2 — Nutritional deficiencies or disease interfering with the supply or transport of amounts of amino-acids, vitamins, minerals and oxygen necessary for the building of body tissues.
- 3 — Endocrinal factors: Growth and development are influenced by at least 3 types of hormones: (a) Thyroid hormone, (b) Pituitary growth hormone and/or (c) Androgens derived either from the adrenals or testes. All 3 of these hormones have been shown to stimulate protein anabolism and increase nitrogen retention. Each of these hormones manifests its effects at a somewhat different period of life and in a different way.

Etiological Classification of Dwarfism · In studying a dwarfed child, the following possibilities must be kept in mind :

1 — Bone diseases :

- Chondrodystrophy, Hurler's syndrome, .. etc.
- Rickets, all types.
- Osteogenesis imperfecta with multiple fractures.
- Diseases and anomalies of the spine (as Pott's disease).

2 — Nutritional or metabolic disorders :

- Nutritional defects.
- Chronic infections.
Hepatic diseases (including glycogen storage disease).
- Celiac disease and cystic fibrosis of the pancreas.
- Chronic renal disease with acidosis and/or rickets.
Poorly controlled diabetes.
- Electrolyte disturbances (hypokalemia & hypercalcemia).

3 — Circulatory or respiratory disorders :

- Some congenital abnormalities of the heart as patent ductus arteriosus and cyanotic heart disease.
- Extensive chronic pulmonary disease with anoxemia.

4 — Constitutional delayed growth and adolescence.

5 — Endocrine disorders

- Hypothyroidism
- Hypopituitarism.
- Sexual precocity with early epiphyseal fusion

6 Primordial or genetic dwarfism :

- Familial.
- Sporadic.
- Syndrome of gonadal aplasia and dwarfism.

7 - Other types :

- Progeria.
- Dwarfism with severe brain defects

Etiological Diagnosis : There is usually no much difficulty in diagnosing dwarfism due to bone disease, nutritional or metabolic disorders and to circulatory or respiratory disorders. If these possibilities are always put in mind, a good history, careful clinical examination and few investigations will lead to the proper diagnosis. It should be emphasized that the kidneys are always worthy of careful investigation since unsuspected renal disease is frequently responsible for retardation of growth. Dwarfism may develop before the appearance of bone lesions that are typical of secondary renal hyperparathyroidism

It is only when bone diseases and somatic disease have been excluded, should the endocrine, genetic and constitutional types of dwarfism be considered.

Hypothyroid dwarfism

Can be diagnosed most readily from the clinical picture and investigations.

Sexual precocity :

Cases are very rare. There is at first an abnormally rapid rate of growth and osseous development, but premature fusion of the epiphyses usually causes cessation of growth before adult height has been attained.

Syndrome of Gonadal Aplasia and Stunted Growth :

It is a form of primordial dwarfism. There is no response to growth hormone.

Epiphyseal ossification is only slightly delayed. Epiphyseal fusion is delayed but eventually occurs. The face is characteristic with rather immature features and poorly developed jaw and chin. Patients with this syndrome frequently have various somatic anomalies such as webbed neck, coarctation of the aorta and lymphedema of the extremities. In this syndrome there is a congenital defect in the development of the gonads.

There is a normal vulva, vagina, uterus and fallopian tubes. Because the fetal glands have failed to develop, there will be no estrogens and therefore breasts and female secondary characteristics fail to develop, but pubic and axillary hair appears (due to adrenal androgens).

Recent studies have shown that they have an XO sex chromosomal constitution (45 chromosomal number).

When the causes of stunted growth already mentioned have been excluded, there remains a group of dwarfs who are hard to classify during early childhood. These are : Primordial dwarfs, Delayed adolescence with retarded growth and Pituitary dwarfs.

During the pre-adolescent years, one cannot predict with certainty which children will mature sexually at approximately the average time, which will have a late but normal adolescence and which will remain sexually infantile. After the patients have reached adult years, they may be divided into these three groups according to the pattern of sexual development.

Primordial dwarfs :

Here sexual maturation takes place normally and at the usual time. These dwarfs are usually small at birth, growth is slow from early infancy, the centers of ossification usually appear at the normal times and epiphyseal union occurs normally. The mental development is average.

Delayed Adolescence with Retarded Growth:

This forms a large group of patients who fail to show the normal spurt of growth and sexual development at the usual time. Puberty starts late (at the age of 16 — 17 years. Many of them finally attain heights within the normal adult range. These children are often smaller than the average throughout childhood and have consistently shown a delay of 2 — 4 years in their epiphyseal development. Family history may reveal similar cases.

Pituitary Dwarfs :

Usually pituitary dwarfs have panhypopituitarism. At the age of puberty

no sexual maturation occurs. They remain sexually infantile for the rest of their lives. Pituitary dwarfs are frequently of normal size at birth and may grow fairly normally during the first few years of life. After stunting becomes apparent, growth does not cease but usually continues at a very slow rate. There is a delay in osseous development. Features are usually immature.

Treatment: The correction of nutritional and metabolic disturbances usually leads to a resumption of growth only when these factors are the primary cause of stunting.

In hypothyroidism, the response to thyroid therapy is most gratifying.

Cases of delayed adolescence if not treated, they eventually mature into entirely normal adults and may attain average height. Therefore, treatment of these is not required. However, if the delay in onset of adolescence leads to psychologic maladjustment of a severe degree, then it is justifiable to attempt to accelerate testicular development by the intramuscular administration of chorionic gonadotrophins (anterior pituitary-like hormone) in dose of 500-2000 units 3 times a week. If there is no development after 3-4 months, one may give in addition 10-20 mg. of methyl testosterone orally daily. In females, chorionic gonadotropins are unsatisfactory and may cause cystic ovaries. If there are marked psychological disturbances estrogens are administered.

Patients with the syndrome of gonadal aplasia and dwarfism are greatly improved from the psychologic standpoint by estrogen therapy, but little growth can be expected because of the advanced state of epiphyseal development.

Pituitary dwarfs : Human growth hormone is effective. However, it is not available commercially. Hormone of animal origin is ineffective. For secondary sexual development chorionic gonadotropins, testosterone or estrogens are indicated. No treatment is indicated or effective for primordial dwarfs.

ABDEL-HADI I. HASSAN

Chapter XVII

THE NERVOUS SYSTEM

HYDROCEPHALUS

Hydrocephalus refers to distension of the ventricular system of the brain, caused by accumulation of cerebrospinal fluid, which is under increased pressure.

The cerebrospinal fluid : Is contained and flows within a closed system, originating primarily in the lateral ventricles, continuing into the foramina of **Monro** to the third ventricle, through the aqueduct to the fourth ventricle. There are exits from the roof of the fourth ventricle by way of the lateral foramina of **Luschka** and the central foramen of **Magendie**. This allows free communication dorsally with the cisterna magna cerebellomedullaris. From the latter, the fluid flows caudally into the subarachnoid space surrounding the spinal cord and anteriorly or ventrally around the bulb into the cisterna basalis and a series of cisterns under the pons and mid-brain. The CSF resurfaces the subarachnoid spaces over the convexity by way of the lateral surfaces of the cortical hemispheres. It is finally absorbed into the dural venous sinuses, especially the superior longitudinal, by way of the arachnoid villi.

The formation of the CSF occurs primarily in the ventricles, especially the lateral, but also the third and fourth. The fluid is essentially a secretion of the choroid plexuses located in these ventricles. There is some quantity of fluid which enters by way of the ependyma and walls of the subarachnoid space.

The absorption takes place in various ways. Primarily the CSF is absorbed by way of arachnoid villi which protrude into the large dural sinuses. The venous blood has a lower pressure and is hypertonic relative to the fluid in the villi. There is also some absorption into the blood by way of the subarachnoid space, both cortical around the cranial nerves and spinal around the peripheral nerves, and in the ventricles by way of the choroid plexus.

Etiology : There are three possible mechanisms for the development of hydrocephalus; viz., overproduction of CSF, defective absorption of CSF and obstruction of CSF circulation.

1) *Overproduction* of CSF occurs in the rare instance of tumor of the choroid plexus.

2) *Impaired absorption* of CSF may result from a rise in the intracranial venous pressure, due to compression of the venous sinuses by an intracranial tumor. Thrombosis of the superior longitudinal sinus by extension of infection from the lateral sinus seems the probable cause of the condition described as otitic hydrocephalus in which symptoms of hydrocephalus complicate otitis media or mastoiditis. Obliteration of the arachnoid villi by inflammatory material may occur in meningitis.

3) *Obstruction* in the pathway of CSF which results in dilatation of the channels proximal to the site of obstruction is the most common cause in the majority of cases.

When obstruction to the circulation of the CSF is either within the ventricles or at the outlet from the fourth ventricle, there is no free communication between the ventricles and the subarachnoid space and the resulting hydrocephalus is referred to as obstructive or non-communicating hydrocephalus. When free communication between the ventricles and the subarachnoid space exists, the obstruction to CSF circulation is in the subarachnoid space itself. Increased production or impaired absorption of CSF may also result in communicating hydrocephalus.

The three major causes of obstructed CSF circulation producing hydrocephalus are :

- 1 — **Neoplastic obstructions** : In a patient with a neoplasm, hydrocephalus is due to obstruction. The most common neoplasms in children producing hydrocephalus are gliomas of the third ventricle, periaqueductal region or cerebellum and fourth ventricle.
- 2 — **Congenital malformations** : These are present in a number of cases of hydrocephalus, many of them are secondary to :
 - (i) *Arnold-Chiari* hind brain anomaly often seen in association with spina bifida and with meningocele. In these patients the basilar subarachnoid pathways are underdeveloped resulting in blocking and subsequent dilatation of the ventricles.
 - (ii) *Stenosis of the aqueduct of Sylvius or forking of the aqueduct* produces early severe hydrocephalus. It can also appear later secondary to a progressive periaqueductal glioma or gliosis.
 - (iii) *Congenital septa or membranes* are occasionally described occluding the outlets of the fourth ventricle (Dandy-Walker syndrome). That

they may not be truly congenital, but possibly the result of inflammatory process, is suggested by the fact that these patients have obliterated basal cisterns as well, hence simple opening of these membranes may not relieve hydrocephalus.

3 - Post Inflammatory or traumatic obstruction There is ample evidence that the most frequent cause of hydrocephalus is related to post inflammatory or post traumatic obstruction of the basilar cisterns and the region of the tentorium cerebri. Two pathological mechanisms come into play:

- (i) *Intracranial bleedings* at the time of normal birth.
- (ii) *Episodes of meningitis*, at times unrecognized, during pre or postnatal periods. These processes lead to a progressive impairment to the absorption of CSF. Cysticercosis, toxoplasmosis and other parasitic infections may produce ventricular or subarachnoid obstruction.

The occurrence of spontaneous arrest of hydrocephalus is most likely related to reopening of these channels when they have not been irreversibly obliterated.

Diagnosis : In a classical case of advanced hydrocephalus characterized by a large head, distended scalp veins, deviation of the eyes and retarded development, the diagnosis is obvious.

Although the actual head size is of importance, repeated observations of the rate of head growth are more significant. Additional information can be obtained from measurements of the anterior fontanel as active hydrocephalus does not occur in conjunction with a closing fontanel. If the anterior fontanel is enlarging from month to month, the infant will have increased intracranial tension and further investigations are necessary.

X-rays of the skull confirm the disproportion between the facial bones and the enlarged vault and may show thinning of the bone and separation of the cranial sutures.

The final diagnosis of hydrocephalus rests on ventriculography and/or pneumoencephalography. Since chronic large subdural hematomas can produce the same characteristics including enlargement of the head as in hydrocephalus; ventriculography may be the only way to differentiate between these cases. It can also give some indication as to the thickness of the cortical mantle of the hydrocephalic individual. If the ventricle is not tapped at the depth of 4 cms., hydrocephalus-if present-is not sufficiently advanced to require treatment.

When the ventricular fluid is obtained, a sample is immediately set aside

for laboratory study. It is often helpful at this point to inject 0.5 to 1 ml. neutral phenolsulphonphthalein into lateral ventricle and time its appearance from lumbar needle as indicated by pink coloration of gauze soaked with alkali to receiving drops of CSF from lumbar puncture needle. Collect all urine usually by catheterization, for two hours from time dye is injected. Normal appearance time in the lumbar CSF is 2 to 12 minutes. If dye did not appear in lumbar CSF after 20 minutes complete block is present. Normal appearance time in the lumbar CSF but less than 15% excretion in two hours indicates obstruction of surface subarachnoid pathways distal to the cisterna magna. If the dye did not appear in the lumbar CSF and less than 15% excretion in urine in 2 hours, the block is in the ventricular system, aqueduct or cisterna magna.

Forty to sixty ml. of air are injected into one ventricle and subsequent bubble ventriculographic studies will demonstrate :

- a -- Whether the ventricles communicate via the foramen of Monro.
- b -- How thick the cortical mantle is.
- c -- Whether there is unsuspected midline neoplasm.
- d -- Whether communication exists between the ventricular system and the subarachnoid space.

Prognosis : Poor at present. Spontaneous correction of the obstruction occurs rarely. Surgery offers a small hope for success. Correction either spontaneous or surgical will not cure damaged and destroyed brain tissue and subsequent mental retardation of varying degree is the rule.

Treatment : *Medical therapy :* is not encouraging and is based on influencing the rate of CSF production. Hydrocephalus complicating syphilitic meningitis is responsive to antisyphilitic treatment.

Choroid plexectomy : removal of the choroid plexus of the lateral ventricles results in decreased production of CSF and drainage of CSF directly through cisternae venae magnae and cisterna ambiens through individual openings made in the floor of the lateral ventricles thus permitting fluid absorption and circulation.

Shunting or bypassing procedures : Several operative procedures were devised to establish artificial channels for reducing CSF pressure. If the block to flow exists in the third ventricle aqueduct or fourth ventricle, the procedure described by Torkildsen is often employed, viz. Ventriculo-cisternostomy.

A catheter is passed from one or both lateral ventricles depending on the patency of the interventricular foramen of Monro over the occiput into the cisterna

magna. If the cisterna magna is scarred or inadequate for the distal end of the tube, Matson advocates the ventral subarachnoid space in the upper cervical area. Both operations merely change a non-communicating to a communicating hydrocephalus.

If a kidney is sacrificed, the ureter can be used to accept a plastic tube draining CSF from the ventricle or the lumbar subarachnoid space. Two conditions threaten life in such shunting operation, viz. meningitis and salt loss without replacement.

The use of the peritoneal cavity as a drainage site from either the ventricle or the lumbar subarachnoid space has been proposed. Difficulty arises from blockage of the peritoneal end of the tube by omentum or other extraneous tissue.

The pleural cavity may be used as a drainage site for the CSF from the ventricular system. The tube is inserted into the ventricle and its distal end is carried subcutaneously into the right posterior thorax.

The development of competent valves allowing for one way flow has led to successful shunts from the ventricle to the right atrium via the jugular vein.

The choice of operation to be used on a given infant should be governed by the personal experience of the neurosurgeon as well as the details of the disease.

SPINA BIFIDA

In spina bifida there is failure of fusion of the vertebral column, leaving a cleft or defect due to the lack of closure of the posterior arches. A number of types have been described.

Spina bifida occulta : This is the most common type. It is stated to be present in about 25 per cent of the normal population. There is no protrusion of intraspinal tissues, and the defective closure of the spinal column can only be demonstrated by X-ray. There may be a tuft of hair or a subcutaneous pad of fat overlying the area which is almost always in the lumbosacral region. In other children, dimpling or wine stain of the skin may be noted.

The majority of children with this condition have no symptoms since the spinal cord is unaffected. The peculiar appearance of the skin in the lumbosacral region may be noted during routine examination, but there are no other abnormal physical signs, and hence no therapy is needed.

Myelodysplasia with spina bifida occulta : In some instances there may be failure of bladder or rectal control, dribbling of urine or enuresis. In others there may be difficulty in beginning to walk, bilateral talipes equinovarus or valgus, or deformities of the toes. Examination may reveal a relaxed rectal sphincter, dribbling of urine with pressure on the abdomen, loss of deep tendon reflexes, sensory defects in the extremities or trophic changes.

Pathologically the lumbosacral area of the spinal canal is filled with fatty mass to which is attached the lower end of the spinal cord, or there may be numerous strands of connective tissue attached to the cord, which bind it to the spinal canal. As a result, the cord is prevented from ascending cephalad as the spinal column grows.

Surgery may be attempted to relieve some of the pathological conditions with which spina bifida occulta may be associated, especially if there is progression of symptoms. These include lipomas of the spinal cord, fibrous bands, *tigh-filum terminale*, or a bony spicule which fixes the cord.

Myelo-Meningocele : There is opaque protrusion of the spinal cord and or nerve roots along with membrane into a sac covered with skin or epithelial membrane, or the spinal cord may be completely exposed. This latter type often ulcerates, is easily infected and associated with complete paralysis of the lower limbs. Paralysis is flaccid. There is loss of sphincteric control and death usually occurs in a few months.

Meningocele : There is protrusion of the spinal cord membranes only, into a sac with overlying normal skin. Neurologic abnormalities are uncommon because the spinal cord and its roots are usually not disturbed. The swelling is most commonly located in the lumbosacral region, rarely in the cervical or thoracic regions and is transilluminant.

The accurate diagnosis of pure meningocele cannot be made until exploration is done. After exclusion of the presence of nerve elements, the meningocele must be removed. It is erroneous to believe that surgical repair of a meningocele or a meningomyelocele leads to the development of hydrocephalus. Hydrocephalus is commonly associated with such anomalies, but does not result from the surgical repair. It is either the result of anomalies in the brain or is due to the pull of the brain stem and the lower part of the cerebellum downward by the spinal cord that is anchored low in the spinal canal, occluding the foramen magnum, the so called Arnold-Chiari malformation.

Two views are present as regards the treatment of meningomyelocele. Some authors question the value of surgery in meningomyelocele, when there is

paralysis and the addition of hydrocephalus and mental retardation lessens the indication for repair of the sac. Others, however, advise surgery in the first day of life to deflate the sac by aspiration. This improves the morale of the family.

ENCEPHALITIS

The term encephalitis literally means inflammation of the brain tissue that is caused most frequently by viruses, hence, it has almost become synonymous with viral encephalitis. Other agents including bacteria, fungi, protozoa, spirochetes and rickettsia can cause encephalitis.

VIRAL ENCEPHALITIS

Some viruses attack the brain directly and are referred to as neurotropic viruses. In other types, the brain is indirectly attacked; no viruses being demonstrated; in other words the brain is secondarily involved, perhaps through an allergic reaction. Those in which a viral etiology is known or strongly suspected include :

- 1) *Type A encephalitis* (*Encephalitis lethargica, Von Economo's disease*).
- 2) *Type B encephalitis*, caused by arthropod-borne viruses (ARFOR).

These are primary neurotropic virus infections occurring essentially in epidemic form and usually seasonally, especially in the summer. They are transmitted by either mosquitoes or ticks or by both and they include :

a) *Eastern, Western and Venezuelan Equine viruses.* (b) *St. Louis encephalitis.* (c) *Japanese B encephalitis.* (d) *Murray valley encephalitis.* (e) *West Nile valley encephalitis* (f) *Russian summer and louping ill.* (g) *others.*

3) *Non-Arthropod-Borne Encephalitis* : This is a heterogeneous group and includes:

- i) *Enteroviruses* : a) ECHO, types 4, 5, 6, 7, 9, 14 and 16.
b) Coxsackie group A, types 1, 4, 7, 8, & 10 and group B types 1 - 6.
c) Polio, types I, II, & III.

ii) *Myxo viruses* that include mumps and influenza viruses.

iii) *Herpes virus group* that includes herpes simplex, herpes zoster, herpes, virus simii and subacute inclusion encephalitis.

iv) *Miscellaneous viruses* as rabies, benign myalgic encephalomyelitis, infectious mononucleosis, cat scratch fever, lymphogranuloma venereum adenoviruses and infectious hepatitis virus.

DEMYELINATING ENCEPHALITIDES

Also known as acute disseminated encephalomyelitis. These may occur following infections or vaccinations.

- 1) **POSTINFECTIOUS ENCEPHALITIS** : Encephalitic manifestations occur as a complication of certain systemic infections such as measles (one per 600 to 1000 cases), chicken pox (one per 1000 cases), small pox (one per 2000 cases) and German measles (one per 6000 cases). Some patients with mumps may have a postinfectious form of encephalitis in addition to or without a preceding recognized viral encephalitis. A similar type of encephalitis has been described as occurring after upper respiratory tract infections of unidentified viral origin.
- 2) **POSTVACCINAL ENCEPHALITIS** : Encephalitis is a complication of a number of vaccination procedures, including those for small pox, rabies, pertussis, influenza, poliomyelitis and yellow fever (only in infants less than one year of age).

Pathology : In viral encephalitis, the cells of the brain including their fibers may be destroyed. There is also evidence of inflammatory reaction in the sheaths of the small blood vessels. The gray matter of the brain stem, including the basal ganglia and cerebellum, is often primarily attacked in some forms as in the original acute epidemic type, but the cortex and the subcortical white matter as well as the gray and the white matter of the spinal cord, are also involved in other types.

In the postinfectious or the postvaccinal types, there is a marked diffuse demyelinating process-regardless of the primary disease. These findings are attributable to antigen-antibody reaction, resulting from the development of antibodies against nervous tissue. Some alteration of brain substance to make it antigenic, possibly as a result of initial virus damage is thought to occur.

Clinical manifestations : The child presents with a sudden or insidious onset of headache, followed by drowsiness which may proceed to deep coma. Fever is usual. A convulsion may be the initial symptom particularly in infancy. Sometimes the onset is marked by hyperactivity, bizarre behaviour or mental disturbances. Palsy or paresis of one or more cranial nerves, disorders of speech, ataxia, weakness of muscle groups, diplopia, alteration of reflexes and disturbances of the autonomic nervous system

are usually found as single or combined signs. In general, the clinical picture depends on the areas of the brain involved irrespective of the type of virus.

Lumbar puncture usually reveals a clear fluid under normal or increased pressure. The sugar content is usually normal. The protein content is either normal or moderately elevated. There is moderate increase in cells (10-200 cells/c.mm.) in which the lymphocytes predominate after the first 48 hours.

Differential diagnosis : Encephalitis should be differentiated from : Tuberculous meningitis, purulent meningitis, poliomyelitis, brain abscess and brain tumor.

Diagnosis : Ideally the diagnosis of encephalitis should be made on isolating the virus, but this is impractical because it is time consuming and expensive. Therefore, serological methods as neutralization or complement fixation tests are utilized. Similar methods are used for the post-infectious and other demyelinating types where no virus has been demonstrated.

Prognosis : Recovery may be dramatically sudden within a few hours after the onset, or may be delayed for days, weeks or months. Permanent residual damage may result at all ages, although the incidence appears to be much greater in very young infants and decreases with increasing age. The presence of persistent neurologic involvement is evidenced by such symptoms as seizures, hemiplegia, monoplegia, bizarre behaviour patterns and mental retardation. Residual damage may not be immediately obvious but may manifest itself later as deficiency in motor skills or learning ability. Apart from permanent residuals transient neurologic changes and behaviour disorders may be noted shortly after apparent recovery from the acute phase.

Treatment : *In the acute phase :*

- 1) Clear the airway. 2) Control convulsions. 3) Give fluids and nutrients. 4) General measures including oxygen, reduction of temperature, frequent turning, emptying the bladder and maintenance of adequate sedation. 5) Special measures include broad spectrum antibiotics to prevent secondary infections, corticosteroids for post-infectious types and control increased intracranial tension.

Convalescent Care : Anticonvulsants, physiotherapy, occupational therapy and corrective surgery.

This term is used to include a number of meningeal disorders which have in common an acute onset, usually a self-limited course with a critical period of varying degree, an increase in the cells of the cerebrospinal fluid and absence of organisms on direct smear. The majority of these disorders are caused by viruses especially enteroviruses, but there are other causes listed below :

Infections : (1) *Viral :* a) Transmissible from man to man as caused by enteroviruses, viz. Coxsackie A and C, ECHO viruses and polioviruses. Less frequently mumps, measles, rubella, varicella, herpes simplex herpes zoster and very rarely infectious hepatitis, influenza and others. b) Transmission from rodent to man as in lymphocytic choriomeningitis. c) Transmission from arthropod to man as the arthropod-borne encephalitides, including Eastern, Western Equine and St. Louis.

(2) *Presumably viral infections :* include infectious mononucleosis, infectious lymphocytosis and cat scratch fever.

(3) *Rickettsial :* Rocky mountain spotted fever.

(4) *Bacterial :* Mycobacterial tuberculosis, atypical mycobacteria or bacteria causing purulent meningitis, especially *H. influenza*, either insipient or partially suppressed by suboptimal therapy.

(5) *Spirochetal :* as in leptospirosis and syphilis.

(6) *Mycotic :* in systemic histoplasmosis, coccidiomycosis and candidiasis.

(7) *Protozoal :* as in toxoplasmosis.

(8) *Helminthic :* as in trichinosis.

Post Infections and/or Allergic : Acute aseptic meningitis syndrome may occur following natural infections e.g. rubella, rubella, varicella and mumps, or may follow vaccinations against small pox, rabies, or influenza.

Non-Infections : and may result from: a) Irritation of the meninges, from lesions within or adjacent to the central nervous system including abscesses, granulomas, hematomas, tumors and thromboses.

b) Allergy e.g. serum sickness or reaction to antibiotics.

ACUTE ASEPTIC MENINGITIS SYNDROME

- c) Miscellaneous reactions to : (i) Systemic poisons e.g. lead, (ii) Intrathecal injections e.g. serum, antibiotics, contrast media, (iii) Leukemic infiltrates.]

Clinical Manifestations : Although the onset may be insidious over a week or so, or even be preceded by a non-specific febrile illness for a few days, it is generally fairly acute. The presenting manifestation of older children are headache and hypersthesia; of infants, are irritability and resentment at being handled. Fever, nausea and vomiting are frequent but convulsions are rare. Coryza, cough, pharyngeal exudate and diarrhea are uncommon. Preceding or accompanying exanthems may occur especially with the ECHO viruses. Examination reveals nuchal-spinal rigidity without significant localizing neurologic changes.

The *cerebrospinal fluid* shows pleocytosis which ranges from 20 to several thousand cells; early in the disease these are often polymorphonuclear; later they are chiefly mononuclear. No organisms are seen on direct smears and there are normal or slightly elevated levels of proteins and glucose. In all instances, the spinal fluid should be cultured for bacteria and mycobacteria, and in some instances special examinations are indicated for fungi protozoa and other pathogens.

Careful analysis of the history and epidemiologic circumstances may point to one of the specific causes. Especially during the summer and autumn, the presence of pleurodynia, of unexplained febrile eruptions in the community suggests the possibility of Coxsackie or ECHO viral infections; the coexistence of acute paralytic disorders in other patients suggests poliomyelitis; the encephalitic infections in horses point to the possibilities of Eastern and Western Equine encephalitis. Knowledge of exposure to or concurrent evidence of mumps or one of the common exanthems can help in the differential diagnosis.

Most difficult from the diagnostic point of view are instances of bacterial meningitis especially *H. influenza* or mycobacterial meningitis. The clinical findings, the dosage of antibiotics previously used, and the spinal fluid smear culture and glucose level may be helpful in the former. When tuberculous meningitis is suspected, a careful evaluation of contacts, and a positive tuberculin reaction may suggest the correct diagnosis. The possibility that the observed meningeal reaction is neither viral nor bacterial in origin must be recognized.

Symptomatic treatment to relieve the headache consists of aspirin, sponging and a cool room. The withdrawal of cerebrospinal fluid for diagnosis often relieves the headache. Codeine, morphine and phenothiazine derivatives are

best avoided, since they may induce misleading signs and symptoms. When the etiological factor is doubtful, the patient should be carefully isolated. Several weeks after apparent recovery, careful neuromuscular assessment should be conducted to assure that muscular weakness has not been missed.

POLYNEURITIS

Polyneuritis refers to multiple involvement of the peripheral nerves resulting in pain, motor weakness and sensory disturbance. Only the most common types will be described here.

LANDRY - GUILLAIN BARRE SYNDROME (INFECTIOUS NEURONITIS)

This is the most frequent form of polyneuritis seen in the pediatric age group and its etiology is not known. It is thought by some to be due to viral infection, basing their concept on the occurrence of polyneuritis following measles, chicken pox and mumps. Others hold that it is due to a toxic effect of the original infection. Some cases have been considered as an allergic phenomenon, following small pox or rabies vaccine injection or serum sickness.

Pathologically there is degeneration of the peripheral nerves which is maximal where the anterior and posterior roots fuse, with chromatolysis of the intraspinal part of the motor neurons.

The onset may occur at any age in either sex. The symptoms may occur suddenly one week or more after acute infection of the respiratory or gastro-intestinal tracts and consists of symmetrical weakness of the lower extremities with paresthesia and sensory loss. The muscles are tender. Other segments are involved in an ascending fashion, including the trunk muscles, upper extremities, diaphragm and cranial nerves, especially the facial. Tendon reflexes are diminished or lost. Plantar response is not elicitable, and sphincters are intact.

Alternatively the symptoms may occur insidiously without preceding illness or infection, progressing for days or weeks. Both motor and sensory neurons may be involved or one type may predominate. The paralysis may ascend the cord; in others it may begin in the cranial nerves and descend. Fever is not a constant feature.

The duration of the illness is variable. The majority show signs of

increasing paralysis for the first two weeks; then slow recovery sets in, requiring weeks or several months for completion. Relapses may occur. Very acute cases may die within two weeks with involvement of the respiratory muscles and / or the medulla.

The major CSF finding is an increase in proteins without corresponding increase in cells, and is referred to as albuminocytologic dissociation.

Diagnosis : depends on the presence of polyneuritis. Paralysis is usually symmetrical and may be ascending involving spinal and/or facial muscles. The history of antecedent infection, vaccination or injection of sera may be of diagnostic help. The albuminocytologic dissociation in the spinal fluid, present in some cases, is not pathognomonic since it may occur in other diseases, namely, poliomyelitis, diphtheria, infratentorial tumors, spinal compression, venous sinus thrombosis and lead poisoning.

Diphtheritic polyneuritis may present a diagnostic problem, however, the onset of polyneuritis occurs four to six weeks after the initial attack of diphtheria. If previous diagnosis of diphtheria was not made, involvement of the muscles of accommodation or a preceding history of regurgitation of fluid through the nose or a nasal twang to the voice will help in the diagnosis.

In *poliomyelitis*, the onset is usually sudden with fever, stiffness of the neck and back indicating meningeal irritation, increased spinal fluid cytology early in the disease with asymmetric paralysis. In the second week albuminocytologic dissociation may be present and diagnosis depends on the presence of asymmetrical paralysis and the history.

Polyneuritis due to lead can be ruled out by the absence of history of ingestion of lead and the absence of excess of lead in blood and urine.

Encephalomyelitis due to other causes, e.g. viral or post vaccinal can be differentiated by serological tests or a history of vaccination.

It is difficult to give prognosis in an individual case. Unless mortality occurs in the first weeks, recovery may occur over many weeks or months. There may remain residual weakness or paralysis of the face or of the muscles of the extremities. Antibiotics are used for intercurrent infection. Corticosteroids have proved to be promising.

DIPHTHERITIC POLYNEURITIS

Polyneuritis occurs in diphtheria from the effect of the toxin elaborated by the *Corynebacterium diphtheria*, which has a strong affinity for the peripheral nerves.

Clinical picture : The incidence of neuritis as a complication in diphtheria is about fifty per cent. The frequency of involvement and its degree depend upon the severity of the diphtheritic attack and the length of time which has elapsed prior to the administration of antitoxin. Occasionally the illness is so mild that the family considered the child to have had a simple cold. A few weeks later the paralysis is observed. It is this latter type in which differential diagnosis may be difficult.

Usually the first manifestation is involvement of the soft palate. This occurs towards the end of the first week. There is regurgitation of fluids through the nose and a nasal tone to the voice. Either accompanying the palatal palsy or shortly thereafter, paralysis of accommodation occurs due to involvement of the ciliary muscles. There is difficulty in reading when the book is held close because vision is blurred. Spread to other cranial nerves occurs resulting in pharyngeal palsy, dilatation of the pupils, strabismus and facial palsy. After the third or fourth week following the cranial nerve palsies, signs of polyneuritis appear. These are evident in the extremities. The changes include loss of vibratory joint and stereognostic senses. To a lesser degree there are also loss of temperature, touch and pain senses. The motor phenomena include muscle weakness, diminished or absent deep tendon reflexes and abdominal reflexes, and some muscular incoordination. Foot and wrist drop may occur. In other instances there is weakness of the muscles of the neck with head drop. The most severe type includes paralysis of the phrenic nerve, with dyspnea and thoracic breathing. The peak of paralysis occurs in one to two weeks and then slow improvement sets in which may take months. In most of the children there is full recovery, but in some there may remain atrophy of some of the muscles. The spinal fluid is negative except for the albuminocytologic dissociation.

Recovery from peripheral neuritis will be aided by rest. Later physical and occupational therapy should be offered.

SEIZURES.

Seizures are one of the more common symptoms encountered in children with disease or functional disturbances of the CNS. The cause of seizures may or may not be known in a particular case. They are characterized physiologically by paroxysmal cerebral dysrhythmia and clinically by muscular movements or loss of consciousness or more commonly by both.

Incidence : 6 to 7% of all children under the age of five years are said to have convulsions. Over 50% of all seizures in children occur in age groups of six months to three years.

Pathological Physiology Seizures are probably due to sudden electrical discharge of cortical neurons, originating from disturbances of physicochemical function within the brain. The nature of the abnormality is not clearly understood. In high percentage of cases a predisposition is inherited and the importance of constitutional factor in the etiology of seizures is well established.

Etiological Classification :

A — ACUTE CONVULSIONS :

(1) *Febrile convulsions* : Seizures associated with fever are divided into two categories : (a) Those in which fever is essential contributory factor and are known as true (*primary*) febrile convulsions. (b) Epileptic seizures in which the fever acts as a precipitating factor (*secondary*).

In the primary the age ranges from three months to 6 years. Seizures are always generalized and occur only with elevation of body temperature, but the threshold varies. Seizures are of short duration (less than 15 min.) may be single or repeated. If repeated, this usually occurs within 18 hours from the first seizure. E.E.G. in the afebrile state is always normal. Seizures usually subside with age, but 3% will develop epilepsy.

Secondary febrile seizures occur in potentially epileptic children; 90-95% will develop subsequent seizure disorders. There is abnormal E.E.G. in the afebrile state, with a history of significant head trauma or family history of epilepsy.

- (2) *Intracranial Infection* : Meningitis, encephalitis, sinus thrombophlebitis and brain abscess.
- (3) *Intracranial hemorrhage* : Complicating birth trauma, blood disease or rupture of a defective vessel.
- (4) *Intracranial Developmental Defect* : Porencephaly, hydrocephalus, microgyria, aplasia, tuberous sclerosis or cerebral angiomatosis (Sturge-Weber).
- (5) *Toxic* : Lead, arsenic, thallium, insecticides, narcotics & tranquillizers, nitrites, anesthetic agents, salicylates, snake bites.
- (6) *Anoxic* : due to Asphyxia.
- (7) *Degenerative and metabolic disorders* : Kernicterus, Wilson's disease, Lipidoses, Gargoylism, Metachromatic leukoencephalopathy, hypertensive encephalopathy, hypoparathyroidism, hypoglycemia, hypocalcemia, hypernatremia, hypomagnesemia, infantile beri-beri, vitamin B₆ deficiency and dependency.
- (8) *Space occupying lesions* : Abscess, hematoma, neoplasm or cysts.

B -- CHRONIC OR RECURRENT CONVULSIVE DISORDERS (EPILEPSY).

Idiopathic : a — genetic or hereditary.

b Non-genetic or acquired idiopathic.

Organic : Resulting from residual brain damage from previous focal or diffuse injury. This type may be : — (i) Post-traumatic. (ii) Post-hemorrhagic. (iii) Post-anoxic. (iv) Post-ischemic. (v) Post-infectious e.g syphilis or toxoplasmosis. (vi) Post-toxic. (vii) Degenerative (viii) Congenital developmental defect.

Types of Seizures.

- (1) Major Motor : (Generalised or focal).
- (2) Myoclonic seizures :
 - a — myoclonic epilepsy of infancy, designated as minor motor epilepsy, hypsarrhythmia and massive myoclonic epilepsy.
 - b — myoclonic epilepsy of older children, also designated as petit mal variant, head dropping spells and akinetic seizures.

- (3) Petit Mal.
- (4) Psychomotor.
- (5) Mixed Seizures.
- (6) Seizure Equivalents.

GRAND MAL

Is the most frequent type of seizures, both alone and in combination with other forms. The attack may begin with an aura and is characterized by a sudden loss of consciousness, followed by tonic and clonic spasms of the muscles. The aura may be of a motor or a sensory type. It consists of numbness, tingling, dizziness and or pain in the abdomen. During the seizure there may be fecal and urinary incontinence, the eyes may deviate to any direction, the tongue may be bitten and there may be intense salivation. In the tonic spasm the respiration is interfered with, so that pallor then cyanosis develop. Subsequent to the fit the patient falls asleep. On rising there is headache, a feeling of dullness, depression and confusion. The usual seizures may last several minutes but occasionally much longer. The number of attacks vary, usually one, occasionally two in a day. There may then follow an interval of weeks, months or a year or two between seizures. *Status epilepticus* is the term used when one attack is followed by another in rapid succession without an intervening period of returning consciousness. This results in extreme dehydration and unless extreme measures are used may end in a fatality.

FOCAL SEIZURES

Originate from a specific pathologic area in the gray matter of the cerebral hemisphere. It refers to location rather than anatomic type of pathology. A specific form of focal seizure is the Jacksonian. The seizure begins locally in any part of the body and then spreads in a definite manner corresponding to areas in the precentral gyrus. The seizure is usually contralateral and clonic in type.

Focal seizures may originate from areas other than the precentral gyrus. They may be sensory with tingling or numbness arising from the postcentral gyrus, visual from the occipital lobe (flashes of light before the eyes), auditory from the temporal lobe, or olfactory from the uncinate gyrus.

INFANTILE SPASMS (MASSIVE MYOCLONIC SEIZURES)

These seizures occur mainly in the first three years of life and begin during the first year. The spasms are of short duration, abrupt and generalized, involving groups of muscles, especially of the arms, legs and head and are rhythmically repeated as in petit mal. There may be sudden bending or jerking of the head with simultaneous flinging of the arms and flexion of the thighs upon the abdomen, accompanied by a cry. There may be many spasms per day, each lasting about a second or a continuous series. In one third of the children there may be major seizures as well. The vast majority of these infants are mentally retarded.

Encephalitis, prenatal developmental factors and birth injury are the main etiologic agents. Some cases have occurred secondary to pertussis immunization. The E.E.G. is characterized by what was called by Gibbs as «hypsarrhythmia» and consists of high voltage, slow waves and random spikes. The E.E.G. pattern and seizures usually disappear about the fourth year. If infantile spasm is associated with normal E.E.G., as it was shown recently, there is 55% chance that the infant will develop normally.

AKINETIC SEIZURES

These attacks are characterized by transient loss of postural tone with sudden fall to the floor or nodding of the head. Clinical manifestations are due to sudden inhibition of the postural control. There is usually transient loss of consciousness. The term salaam seizures is applied to a type of akinetic seizure in infants and young children, during which the head drops forward, as the upper extremities are raised above the head.

[MYOCLONIC] SEIZURES,

Consist simply of spasmodic contractions of the muscles of the trunk or extremities most commonly the flexors of the upper extremities. Other types of convulsive seizures commonly occur in these patients.

PETIT MAL

This term was originally used to describe all minor seizures, but now is reserved for brief lapses of consciousness or absence associated with the three

per second spike and wave pattern in the E.E.G. The lapse of consciousness occurs without warning and may be accompanied with slight rhythmic movements of eyelids, eyebrows, lower jaw and upper limbs. Voluntary purposive movements are interrupted but posture is not disturbed. Occasionally a history of head trauma, birth injury or encephalitis may be obtained, but in general a genetically determined predisposition to seizures is the only finding.

Petit mal status consists of an almost continuous series of petit mal discharges which may persist for as long as three or four days.

PSYCHOMOTOR EPILEPSY

The anatomic site responsible for this type of epilepsy is the anterior portion of the temporal lobe. It is uncommon in childhood. Symptoms are extremely varied. Manifestations may be chiefly motor in the form of automatism such as rubbing masticatory movements, laughing, running, shouting and so forth, or psychic in the form of confused dream-like state, hallucinations or delinquent behaviour, temper outbursts and so on. The patient may or may not have amnesia of these events.

MIXED SEIZURES

Almost any combination of the previously mentioned attacks may occur in the same patient. Any minor seizure may spread in the brain, if conditions are optimum to produce a major convulsion.

SEIZURE EQUIVALENTS

May be manifest in the form of abdominal pain, headache, nausea, cyclic vomiting, nightmares, night terrors, behaviour disorders, enuresis, hypo and hyperthermia. The E.E.G. is abnormal in 85% of children with seizure equivalents. The seizures may be generalized or focal. The 14 and 6 per second positive spike pattern is a frequent finding in patients with seizure equivalents.

Diagnosis : The diagnostic procedures are somewhat dependent upon the age of onset, the type and frequency of seizures. The following examinations are included in a complete study : (i) History, physical, neurological and fundus examinations. (ii) Determination of the blood glucose, calcium and serological tests. (iii) CSF examination. (iv) Urinalysis

(v) X-ray of skull and long bones. (vi) EEG with activating procedures as hyperventilation, sleep and photic stimulation. (vii) Pneumoencephalography, ventriculography or cerebral angiography.

Treatment : Is divided in two categories according to the availability of a specific therapeutic agent.

I - Seizures amenable to specific therapy and include :

(1) Fever and extracranial infections. (2) Intracranial infections
(3) Electrolyte disturbances. (4) Metabolic disorders. (5) Toxic encephalopathy. (6) Hypertensive encephalopathy. (7) Acute Anoxia.
(8) Light stimulus (Photic seizures). (9) Intracranial structural lesions (hematoma, cyst, tumor or vascular). (10) Miscellaneous. Emotional disturbances or allergy. Empirical anticonvulsant therapy is often required in addition.

II - Seizures amenable to empiric therapy : Include idiopathic and secondary epilepsy.

DRUG THERAPY :

— *Phenobarbital sodium* : 4 to 10 mg./kg./day in divided doses. Side reactions are rare and include drowsiness, increased excitability and dermatitis. Effective in the treatment of grand mal epilepsy.

Mebaral (Mephobarbital) : in a dose of 8 to 20 mg./kg./day. It is not superior to phenobarbital in controlling grand mal epilepsy.

— *Gemonil* (Diphenyl barbituric acid) : Useful in grand mal and petit mal and myoclonic epilepsy in particular. The dose for infants is 50 mg once to three times per day. For older children 100 mg. are given 1 to 3 times per day. Side reactions are drowsiness, irritability and skin rash.

— *Epanutin* (Diphenyl hydantion sodium) : Useful in grand mal, dose is 2-8 mg. / kg. / day. Side reactions are gum hypertrophy, nausea, vomiting, nervousness, ataxia, nystagmus, rash lymphadenopathy, rickets and lowering of IgA.

— *Mesantion* (Methylphenylethyl hydantion) : Useful in grand mal. Dose 3 to 10 mg./kg./day. Side reactions are nervousness, ataxia, nystagmus, pancytopenia and exfoliative dermatitis.

Mysoline (phenyl ethyl hexahydropyrimidine dione) : Useful in grand mal and psychomotor epilepsy either alone or in combination with dilantin (T = 250 mg.). We start with one tablet daily and the dose is increased by one tablet weekly till 4 Gm. per day are given. Side reactions are nausea, vomiting, drowsiness and ataxia

Tridione and paradione : (Trimethadione and paramethadione) Useful in petit mal, dose 20 to 70mg./kg./day. Side reactions are pancytopenia, hiccup, nephrosis, exfoliative dermatitis and photophobia

Phenurone (phenacemide) : for refractory cases of psychomotor epilepsy. May be used with tridione or paradione especially in infants. Under 6 years the dosage is one 0.3 Gm. tablet t.d.s. Over 6 years the initial dose is 0.5 Gm. tablet twice daily. It may be increased slowly. Side reactions are behaviour changes, hepatitis, pancytopenia, abdominal pain, proteinuria, headache and dermatitis

- *Milontin* (phenyl succinimide) : used when tridione and paradione are ineffective in the control of petit mal or toxic. The dose is 0.5 Gm 2 to 3 times per day to a maximum of 2 Gm. Side reactions are drowsiness, nausea, vertigo and pancytopenia.

Gelontin (methyl succinimide) : useful in petit mal and psychomotor seizures. The dose is 30 to 40 mg./kg./day. Maximum dose 4 capsules (1200 mg.).

Zarontin (Ethosuccinimide) : used in petit mal. The initial dose below 6 years of age is 250 mg/day; above 6 years the initial dose is 500 mg/day, the dose is then increased by one capsule every 4 to 7 days until control is achieved with minimal side effects. Four to 6 capsules are used. Side reactions are nausea, gastric irritation, drowsiness, dizziness and headache.

Dilantin (Acetazolamide) : a carbonic anhydrase inhibitor.

- *ACTH* Used in infantile spasms

Benzedrine : may be used in epilepsy to counteract the lethargy produced by drugs like phenobarbital. The dosage is 5 mg. twice daily in the morning and mid afternoon.

- *Valium* (Diazepam) : is effective in the treatment of status epilepticus available as 10 mg. ampoules in 2 ml solution for intravenous administration. The solution should not be diluted and must be administered very slowly. The usual dose is 0.2 to 0.3 mg./kg. and no more than 30 mg. is recommended.

Mesdona (Nitrazepam) is the most effective drug against infantile spasms.

- *Rivotril* (Clonazepam) : is the most effective drug for the akinetic-myoclonic group of seizures.
- *Tegretol* (Carbamazepine) : is helpful in controlling psychomotor seizures. Initial dose 100 mg ($\frac{1}{2}$ tablet) t.d.s. with or without other medications

and can be increased to 400 mg. 2 to 3 times daily in adolescents.

The principal advantage is lack of sedation. Side effects are dizziness, nausea and vomiting.

KETOGENIC DIET: This diet, high in fat, low in CHO is beneficial in reducing seizures. It has been used along with fasting and restricted fluid intake. Ketogenic effect leads to acidosis with loss of tissue fluids.

SURGERY : When there is evidence of brain tumor, brain abscess, progressive hydrocephalus, cyst or hematoma, surgery is indicated. In many of these, drug therapy may be continued. In psychomotor seizures where there may be incisural sclerosis of the temporal lobe, as a result of head compression or birth injury, causing arrest of the flow of the blood, this is corrected by partial temporal lobectomy.

Hemispherectomy is valuable in children with infantile hemiplegia accompanied with personality changes, mental impairment and severe epilepsy

GENERAL MEASURES : (1) Keep the patient from being injured.

(2) Acquaint the family with the disease and strict adherence to drug regimen.

(3) Attention to the physical status of the patient.

(4) Avoid excess fatigue

(5) Treatment of emotional factors as indicated.

CEREBRAL PALSY

The term cerebral palsy is applied to describe the motor disability in children resulting from a non-progressive lesion in the immature brain* affecting motor control†. It may be associated with other evidences of brain damage involving other areas. These comprise sensory changes (speech, visual and auditory disturbances), impairment of growth, intellectual retardation, convulsions and behaviour changes.

Etiology : The etiology may be divided into those factors operating prenatally, paranatally and postnatally. In some cases more than one condition is at fault, e.g. there may be prematurity with toxemia in the mother

* from embryonic life till about 2 years of postnatal life.

† motor cortex, cerebellum and basal ganglia.

and difficult labour. Knowledge of the cause of cerebral palsy in an individual case aids the pediatrician in estimating the prognosis and in the advice he offers to the parents concerning future pregnancies.

I *Prenatal Factors* : 1. *Hereditary (genetic)* as in congenital cerebellar ataxia and familial tremor.

2. *Environmental (Acquired)* :

(a) Infections - viral (Rubella, mumps and infectious hepatitis), protozoal (Toxoplasmosis) or spirochetal (Syphilis). (b) Toxemia of pregnancy (causes fetal cerebral hemorrhage). (c) Maternal trauma. (d) Nutritional and vitamin deficiencies in the mother. (e) Pelvic radiation in the first trimester. (f) Maternal diabetes. (g) Causes of fetal anoxia, viz. improper fetal implantation, placental infarct, premature separation of the placenta, maternal anemia, carditis or hypotension.

II — *Natal and Perinatal Factors* : (1) *Anoxia* resulting from : excessive anesthesia, oversedation, cord abnormalities, fetal air way obstruction and placenta previa. (2) *Trauma and Hemorrhage* occurring in malposition, cephalopelvic disproportion, high forceps, breech presentation, delivery by suction and prematurity.

III — *Postnatal Factors* : a) Intracranial infections (meningitis and encephalitis) b) Skull fracture with hemorrhage. c) Postkernicterus resulting from hyper-bilirubinemia of the indirect type mainly due to blood group incompatibility. d) Lead encephalopathy e) Vascular embolism, thrombosis or hemorrhage

By far the most frequent etiological factors fall into the antenatal and natal periods. It has previously been estimated that about 85% of cerebral palsy occurs from brain damage produced at these periods. Prematurity is a tremendous hazard as it means that the infant is much more vulnerable to the effects of anoxia and hemorrhage. Over a third of all cerebral palsied children are prematures.

Pathology and Pathogenesis : As might be expected from the rather extensive list of etiologic factors in cerebral palsy, there is no specific lesion definitely related to it; but rather a wide variety of lesions. Alternatively, lesions may not be found. Negative pathological studies of the brain do not necessarily mean that alterations of the structure of the brain are not present. Irrespective of the etiological factor involved, damage to the brain is the result of anoxia and hemorrhage. Anoxia results in diffuse atrophy of the motor cortex, with loss of nerve cells, scars, focal cortical necrosis and gliosis.

CLINICAL SYNDROMES OF CEREBRAL PALSY

SPASTIC GROUP

This group comprises about 50 to 60% of cerebral palsied children. The pathology is present in areas 4, 4S and 6. The latter two have extrapyramidal association with basal ganglia and lower centers. When damage occurs in the pyramidal tract alone, flaccidity with mild spasticity result. However, the adjacent areas are almost always involved in cerebral palsy. Spasticity is due to an upper motor neuron lesion and is considered by the majority as the expression of the removal of inhibition on the lower spinal reflex area by virtue of damage of the pre-Rolandic area and basal ganglia. The various types of spasticity include quadriplegia, hemiplegia, paraplegia, monoplegia and triplegia.

Spastic Quadriplegia :

Spastic paralysis of the four extremities in which spasticity is more marked in the lower extremities. When the child is held standing, he stands on his toes with ankle equinus, the limbs are markedly spastic in extension with adduction of the thighs and internal rotation of the hips. Tendon reflexes are increased. Babinski's sign is present and there is hyper-active stretch reflex. Mental retardation indicates that the brain is so badly damaged and the infant will not walk.

The presence of spastic quadriplegia in a child who has a normal mentality and no seizures or athetosis suggests the diagnosis of high spinal spastic quadriplegia. The pathology is located in the cervical cord at the level of the junction between the skull and atlas, and results from birth injury of the cervical spine producing displaced fracture and dislocation with resulting pressure on the pyramidal tract.

Infantile Spastic Hemiplegia

Is the most frequent type of cerebral palsy. Clinical manifestations appear early in infancy as inability to use the arm and leg on one side. This is because in the majority of cases the pathology is the result of birth trauma. A similar type of hemiplegia is observed in those children with postnatal onset.

In the fully developed picture, there is flexion of the arm, marked flexion deformity of the hand and extension with equinus of the foot. The limbs are underdeveloped and there is shortening. Atrophy and growth disturbances

of the muscles may be due to involvement of the post-central gyrus as well as the precentral areas. Function of the affected side is poor. In addition to the motor effects there are sensory changes including loss of proprioception and discrimination of form (Astereognosis). The tendon reflexes are hyperactive and the Babinski's sign is present. The EEG shows abnormal patterns. Convulsions and mental retardation may occur. In children with right hemiplegia, there may be aphasia. Emotional and behavior disturbances may be marked.

Etiology and pathology : The brain shows marked cortical atrophy on the side opposite the hemiplegia. Abnormalities associated with prenatal pathology such as a true aplasia or porencephaly rarely occur. In the majority damage occurs at birth due to trauma associated with intracranial vascular occlusion of an artery. Prematures and infants of excessive birth weights are particularly vulnerable. Postnatal factors are next in frequency. In the latter the pathology is most often of a vascular nature. The hemiplegia may occur in a variety of infectious diseases e.g. encephalitis, meningitis, acute hemorrhagic encephalitis of Marie-Strumpell type or pertussis. There may be hemorrhage from head trauma or vascular thrombosis associated with blood diseases such as sickle-cell anemia. Infantile hemiplegia is also associated with Sturge-Weber syndrome.

Double Hemiplegia

In this type while all the extremities are affected, one side has a greater degree of hemiplegia than the other and the arms are more involved than the legs. It is usually associated with mental retardation and pseudobulbar palsy (disturbance in speech, swallowing and facial expression). Jaw reflexes are increased. There may be emotional outbursts of laughing and crying. The pathology involves cortical or subcortical areas or the internal capsule. As a result corticobulbar pathways which serve the medullary nuclei are affected.

Monoplegia : Very rare to occur as an isolated manifestation. There are usually other parts of the body that are very slightly involved too. Where the upper limb is palsied there is also associated weakness on the same side of the face (monoplegia faciobrachialis).

Paraplegia : Very rare to occur as the only manifestation.

Triplegia : This usually involves both legs and one arm.

ATHETOTIC GROUP

The clinical picture results from involvement of the basal ganglia and the extrapyramidal system. The motor cortex and its relay system (pyramidal tract) are intact in the isolated forms of athetosis. The following syndromes have been included in this group : congenital double athetosis, congenital double choreo-athetosis, torsion spasm and hemi-ballismus. Initial complaints at the fifth or sixth month of life are in the form of delay in motor development with inability to respond to normal stimuli, difficulty in suckling, swallowing and inability to follow objects. Examination at this stage shows hypotonia that is replaced at the age of one to two years by athetoid movements. Dysarthria then becomes manifest, and in athetosis following kernicterus partial deafness is an added feature. The persistence of the tonic neck and Moro reflexes in some cases interferes with feeding, dressing and creates the anxiety of fear of falling due to loss of balance. The involuntary movements disappear during sleep. Convulsions are less frequent in the athetotic than in the spastic group. It is common to see athetotic cerebral palsy mixed with other forms, than to find it isolated.

RIGIDITY

This type results from severe brain damage that is likely to be widespread involving the cerebral cortex and basal ganglia. The muscles are extremely tight and hypertonic "lead pipe". There is no hyperactive stretch reflex or hyperactive tendon reflexes. Mental retardation is marked in the majority.

ATAXIC

This type is a manifestation of a lesion in the cerebellum or its pathways. Generally defective development is at fault. Initial complaints are delay in motor development and lack of equilibrium. Later the child walks on a broad base with evident muscular incoordination. Tremors may be present and increase with excitement. Nystagmus may be seen.

ATONIC DIPLEGIA

This is a rare form of cerebral palsy characterized by loss of muscle tone, and active deep tendon reflexes. Spontaneous movements are possible, though purposeful movements are lost. Mental retardation is marked. Little is known about the pathology of atonic diplegia. A reaction that is peculiar

to atonic diplegia is elicited by lifting the infant by placing the hands around the trunk, his legs will become rigid; being flexed at the hip, flexed or extended at the knees. This reaction is the expression of a postural reflex. Incoordination is almost always present. Electrical reactions are normal. Ultimately the hypotonia may change to spasticity during the second year with arms more markedly involved (double hemiplegia). The etiology is thought to be either prenatal or neonatal asphyxia with cerebral anoxia. This condition has to be differentiated from other causes of hypotonia.

MIXED TYPES. These are types in which there may be spasticity and athetosis combined in the same patient or various forms of athetosis may occur in the same patient at different times.

Diagnosis of Cerebral Palsy :

To reach a proper diagnosis one must go in detail in the history of the patient including the antenatal, natal and postnatal periods, his developmental history; maternal history including the history of the present and previous pregnancies and the family history. This is followed by physical examination including examination of the nervous system, optic fundi and other accessory examinations as X-rays, blood studies, EEG, pneumoencephalography when needed, speech, visual and hearing tests.

The presence of hyperactive stretch and deep tendon reflexes, Babinski's sign and clonus constitute important data in recognizing the spastic type of cerebral palsy. When this type is associated with normal mentality, the possibility of spinal type must be searched for and a normal X-ray of the cervical spine eliminates this possibility. Athetoids are readily recognizable. The ataxic type must be differentiated from heredo-familial degenerative diseases that are progressive. Atonic diplegia has to be differentiated from poliomyelitis, muscular dystrophy, amyotonia congenita, cretinism and congenital laxity of the ligaments. Developmental retardation due to mental retardation may be easily mixed with that resulting from cerebral palsy. The presence of evidences of cerebral palsy as spasticity, atonia, increased stretch reflex, persistence of tonic neck reflex or Moro reflex, abnormal movements, hyperactive deep tendon reflexes or clenched fists beyond the first three months, will clinch the diagnosis. Otherwise, diagnosis of mental retardation is made. Mental retardation, however, may occur in association with cerebral palsy.

Management of Cerebral Palsy :

This is best accomplished by the cooperation of the pediatrician, physiotherapist, orthopedist, social worker, surgeon, psychiatrist and the family.

It is the job of the pediatrician to take care of the patient throughout infancy and childhood, supervising his nutrition, prescribe muscle relaxants for spasms, medication to induce sleep or to minimize irritability. The pediatrician with the assistance of the social worker and the psychologist will explain to the parents the nature of the disease so that better understanding will be associated with better cooperation. The physiotherapist through passive stretching and exercises will assist in producing muscular relaxation, prevention of contractures and deformities of the joints in spasms. In athetoids training is directed toward voluntary control of muscles. The ataxic child must be taught to use tactile and visual sensation in a functional position by doing balance and coordination exercises in front of large mirrors, and stress is laid on improvement of gait. Efforts must be spent in training the patient in the daily living activities. Bracing is useful in spasms to avoid or correct deformity, and in athetoids to control overactive movements. Crutches may be needed for ambulation. Wheelchairs are used for the child to get about until walking begins.

Seizures are treated by the use of anticonvulsants. Ataraxic drugs may be utilized in behaviour disorders or hyperkinetic children.

Speech therapy is intended to obtain intelligible speech to facilitate communication with others. This is achieved through teaching proper breathing and speech relationship and to correct articulatory errors, emissions and substitutions. In educating cerebral palsied children special technique must be used.

Orthopedic surgery may be employed to improve function by increasing the range or strength of motion, correct deformities, provide stability or for cosmetic reasons.

Neurosurgical procedures are used when the brain pathology can be removed or its effects can be overcome. This is obvious in subdural hematoma or hydrocephalus. Hemispherectomy may be resorted to in cases of infantile hemiplegia if convulsions failed to respond to medical therapy, and pneumoencephalographic studies showed cortical atrophy.

Prognosis of Cerebral Palsy :

Two factors control the prognosis in cerebral palsy, viz. the intelligence quotient of the child and the degree of motor involvement. In 40% of cerebral palsied children where there is mild motor disability and the intelligence quotient is average or high there is good chance for good outcome. In about 15%, physical disability is too severe to accomplish progress even though the I.Q. is close to normal. The remainder have very low I.Q. and have a poor prognosis.

MENTAL RETARDATION

Mental retardation refers to inadequate mental development which results or may be expected to result in incapacity for independent social adaptation. It results from cerebral malfunction during prenatal life or infancy. The incidence varies from one country to the other and its value in childhood and adolescence is several fold's its value in the general population.

For academic purposes the intelligence quotient (I.Q.) is useful for categorizing mentally defective children in regard to the degree of defect. The I.Q. is the percentage of the mental age in relation to the chronologic age. When the value of the I.Q. ranges between 0 and 20, this category is referred to as idiot or low grade retardates. When the value of the I.Q. ranges between 21 and 50 the category is referred to as imbeciles (middle grade retardates or trainable). When the I.Q. ranges between 51 and 75, the category is referred to as morons or high grade retardates or educable. The proportionate distribution of these categories in the general population is usually estimated as 5 : 20 : 75 respectively.

Clinical Classification :

The clinical classification which follows is based, when possible, on etiology and only those conditions that occur often enough to have practical importance are included. The following clinical conditions are grouped according to the period of life during the which the causative factor is operative, namely, prenatal, natal and postnatal.

- 1 — **PRENATAL** . A — **GENETICALLY DETERMINED** : 1. Familial or subcultural, 2. Phenylketonuria, 3. Galactosemia, 4. Cerebral lipidosis, 5. Gargoylism, 6. Cerebral demyelinating disease, 7. Cranial anomalies (microcephaly, craniosynostosis, hypertelorism, congenital hydrocephalus), 8. Congenital ectodermoses (tuberous sclerosis, neurofibromatosis, cerebral angiomas), 9. Hereditary cerebral maldevelopment not classifiable clinically. 10. Chromosomal aberrations (Mongolism, Klinefelter's syndrome, triple X syndrome, hermaphroditism and other miscellaneous conditions)

B **NON-GENETIC, KNOWN CAUSE** : 1. Infection (syphilis, German measles, toxoplasmosis, cytomegalic inclusion disease). 2. Fetal radiation. 3. Kernicterus. 4. Cretinism.

C — **UNKNOWN OR INDEFINITE CAUSE** Associated with placental abnormalities; toxemias of pregnancy; prematurity, maternal

medication: nutritional deficiencies; anoxia, poisoning, trauma etc. (congenital cerebral maldevelopment)

- II **NATAL** . Birth injuries (direct cerebral trauma, hemorrhage, anoxia).
- III **POSTNATAL** : 1. Cerebral infections (meningitis, encephalitis, abscess). 2. Cerebral trauma. 3. Poisoning (lead, carbon monoxide and others). 4. Cerebrovascular accidents; occlusions and hemorrhages of varying or unknown cause. 5. Post immunization encephalopathies (pertussis, smallpox, rabies and others).

FAMILIAL OR SUBCULTURAL RETARDATION

This category comprises from 60 to 75% of all mentally retarded in the community. These patients are doubly handicapped, as besides the inherited diminished intelligence capacity, the majority have been born into families in which either one or both parents and most of the siblings tend to be intellectually inferior or even retarded and consequently are placed in the lowest economic and cultural strata. The physical examination reveals no evidence of abnormality and neurologic examination indicates an essentially intact central nervous system. The psychological profile reveals the principal defect to be in the verbal and abstract sphere with relatively better accomplishment in the performance of items of concrete nature dependent on manual dexterity and visuo-motor coordination. The handicap becomes increasingly evident during the school years, which are essentially a verbal experience, and less striking in later life when exposed to an occupational experience in which verbalization and abstraction are less important than performance ability. When special school and training facilities and even minor efforts at community supervision are available, very few of these retardates require residential institutional care, and the prognosis for successful social integration is good.

Practically all the offspring resulting from a mating of two mentally defective parents of this category have defective or inferior intelligence. As the intellectual level of either parents approaches the average, the proportion of children with defective and inferior intelligence tends to decrease. It is apparent that this type of hereditary transmission must depend on many independent genetic determinants whose effects are cumulative rather than on a single abnormal gene as in most hereditary conditions.

PHENYLKETONURIA

Phenylketonuria is a metabolic disorder where there is excretion of phenylpyruvic acid. The basic enzymatic defect is absence or inactivation of phenylalanin hydroxylase in the liver, resulting in failure in hydroxylation of phenyl-

alanine to tyrosine and the accumulation of phenylalanine in the blood and body fluids, which after transamination appears in the urine as phenylpyruvic acid. The condition is transmitted by a recessive gene. Heterozygotes are asymptomatic and can be identified by the phenylalanine loading tests.

A high percentage of these children have abnormal electroencephalographic tracings, and about one third of them have epileptic seizures. Most of the children have serious personality disorders. Infants with phenylketonuria appear normal at birth and during the neonatal period, and phenylalanine level in the plasma is normal (0.4 to 2 mg/100 ml.). Plasma phenylalanine level of 15 mg./100 ml. is reached by the age of 6 to 30 days of life at which time progressive cerebral damage begins, reaching its maximum at the age of two to three years of age. As a rule increased levels of phenylalanine in the blood are associated with mental retardation.

Diets low in phenylalanine begun in the first few months of life have appeared to prevent the development of mental retardation in many cases.

GALACTOSEMIA

Galactosemia is a congenital error in the metabolism of galactose, inherited as a recessive condition. In normal metabolism galactose is phosphorylated to galactose-1-phosphate, by the enzyme galactokinase and adenosine triphosphate. Galactose-1-phosphate is subsequently converted to glucose-1-phosphate through the activity of galactose transferase. In galactosemia this enzyme is absent, resulting in the accumulation of galactose which is toxic to the tissues including the nervous system. Hypoglycemia is also a possible cause for the central nervous system manifestations.

The infant appears normal at birth. As milk feeding continues for several days, the infant develops vomiting, diarrhea, loss of weight and lethargy. Jaundice soon appears, the liver and spleen become enlarged. Ascites and edema may be present. Cataracts are also seen in 50% of cases at this time.

If the condition is recognized early, and the infant received lactose-free mixture, the outlook is good for a return to normal. If unrecognized, the infant either dies or remains physically and mentally retarded.

HURLER'S SYNDROME (GARGOYLISM)

Hurler's syndrome is a heritable metabolic disorder of mucopolysaccharide metabolism. Transmission is autosomal recessive in the majority of cases, and sex linked recessive gene in a minority.

In a typical case the patient is dwarf with constant kyphosis in the upper lumbar region. The head is relatively large being either scaphocephalic or acrocephalic. The face is grotesque, the nose is flattened, the root recedes and the nostrils flare widely above thickened lips. The ears are low-set and the neck is very short. The extremities are short and the joints admit only a limited range of movements. The abdomen is protuberant and umbilical and inguinal hernias are common. A smooth enlargement of the liver and spleen is a feature of the classical case. Sexual development usually remains infantile. In a large percentage of cases the corneas are opaque. Deafness may develop and progressive mental deterioration is evident in most of the cases.

The roentgenographic manifestations of gargoylism are characteristic. A lateral view of the spine shows the vertebral bodies shortened in the sagittal plane with concave anterior and posterior outlines and characteristic beaking in some vertebrae.

The excretion of excess acid mucopolysaccharides in the urine of cases even before the appearance of clinical or radiological manifestations is helpful to establish a final diagnosis. Reilly granules in the granulocytes is another diagnostic finding.

As there is no specific therapy, the majority of children die prior to adulthood, either from cardiac disease or intercurrent infection.

CRANIAL ANOMALIES

The four most common cranial conditions showing rather characteristic configuration are microcephaly, craniosynostosis, hypertelorism and hydrocephalus.

MICROCEPHALY

The terms primary or genetic microcephaly are used to express the type of microcephaly which is of genetic origin. Here, the skull is smaller than normal and is of peculiar configuration, with a receding forehead and a flat occiput. Mental retardation is the rule.

Though the peculiar clinical features are related to the skull, the pathology is in the brain, in which there are general hypoplasia of the cerebral hemispheres and a paucity of cells. Cerebral atrophy may result in false porencephaly. The pyramidal tracts and most of the spinal cord are poorly developed. The peculiar clinical features in the skull are the result of the brain pathology.

Clinically, there is also underdevelopment of the body resulting in short stature and underweight. All milestones are delayed. Seizures are present in about 15% of the cases. Occasionally there is spasticity with hyperactive deep tendon reflexes. The E.E.G. shows some abnormalities, especially reduction in voltage, but there is nothing diagnostic. Most microcephalics have an I.Q. less than 50 and some are idiots.

The diagnosis is based on the characteristic appearance of the skull, mental retardation, associated at times with convulsions and hypofunction of the pyramidal system.

In exogenous or secondary microcephaly, the etiology is prenatal or natal, but non-genetic. Pelvic irradiation of the pregnant mother by X-ray or radium, prenatal viral infections, toxoplasmosis, or anoxia in the first trimester of pregnancy may produce secondary microcephaly.

Microcephaly, must be differentiated from other conditions in which a small head may be present, especially craniosynostosis and familial microcrania. In the latter condition the child is perfectly normal, both physically and mentally.

Most microcephalics have poor resistance to infection, but with the advent of antibiotics, their lives are prolonged beyond the childhood period. As there is no specific therapy, microcephalics must be institutionalized.

CRANIOSYNOSTOSIS

Craniosynostosis refers to the premature closure of one or more of the cranial sutures. In contradistinction to microcephaly, where the skull bones unite to form a small head following the failure of normal brain development, there is primary premature union of sutures, which prevents the growing brain from expanding resulting in symptoms and signs of increased intracranial tension.

The mechanism that produces normal suture closing is not understood, and the time when this occurs is not fixed.

Clinically : The various cranial deformities depend on the sutures involved.

The expansion and shape of the skull occurs in a line parallel to the closed suture. When the sagittal suture closes prematurely, there is greater expansion anteroposteriorly because the coronal and lambdoidal sutures allow it resulting in an elongated narrow skull known as *scaphocephaly*. With premature closure of the coronal suture, the sagittal and squamosal sutures allow for lateral expansion of the skull resulting in *brachycephaly*. When premature union of sutures involve the lateral parts of the coronal suture and the posterior part of the sagittal suture, growth of the skull will occur along the

anterior fontanel and the resulting deformity is referred to as *oxycephaly*. In the latter type there is proptosis resulting from pressure on the roofs of the orbits, and increased intracranial tension may result in optic atrophy with or without pyramidal signs and mental retardation. Premature union of the coronal and squamosal sutures (on one side) results in flattening of that side of the forehead and is referred to as *plagiocephaly*. When premature union involves all sutures, the head expands upwards toward the anterior fontanel, forming a tower skull; the base of the skull becomes deeper, the sinuses undeveloped or obliterated and the orbits shallow.

X-ray is helpful in demonstrating evidence of increased intracranial tension and in showing which sutures are closed.

Treatment is surgical. Craniectomy and insertion of polyethylene film over the inner and outer surfaces of the bone.

If the surgical procedure is done in the first few months, the cosmetic effects are good, the mentality is preserved, and the prognosis is excellent. If done later, there is still some good effects, but the chances for changing the skull contour after two years are poor and there may be mental retardation.

HYPERTELORISM

This condition is characterized by an abnormally large distance between the eyes and a broadening of the root of the nose, and may be associated with mental retardation and other congenital defects. The lesser wings of the sphenoid are overdeveloped while the greater wings are relatively small. Hypertelorism can be transmitted through several generations.

CONGENITAL ECTODERMOSIS

This group includes tuberous sclerosis, neurofibromatosis and cerebral angiomas. In a sense these are combined disorders of the skin and brain both of which are derived from ectoderm, and are referred to as neurocutaneous syndromes.

TUBEROUS SCLEROSIS (Epiloia)

This disease in its complete form consists of mental retardation, epileptic seizures, and adenoma sebaceum. The characteristic skin lesion which is rarely apparent before the fifth to the eighth year of life, is the small slightly elevated pale pink to reddish papules almost always seen on the cheeks in a butterfly fashion across the nose. Histologically these are fibroangiomas which enlarge

with age. At or around adolescence one occasionally finds the small grapelike skin tumors at the nasolabial folds. About the same time there may occur intracranial calcification, usually in the periventricular regions. Retinal tumors usually mulberrylike, may be present in very early life and occasionally may be the only manifestation to suggest the diagnosis in a young infant.

NEUROFIBROMATOSIS

Neurofibromas may involve any nerve and vary in size from the smallest beadlike structure to grotesque overgrowth of parts or of entire extremities, resulting in symptomatic elephantiasis. Mental retardation is less common than in tuberous sclerosis. The peculiar pigmentary lesions known as café au lait spots are almost always present and occasionally characteristic osseous defects occur.

Cerebral Angiomatosis (Sturge-Weber Syndrome)

The distinctive feature is a large port-wine stain, trigeminal in distribution, involving skin, scalp, skull and meninges, associated with angiomatosis of the brain on the same side. As a result of the pathology in the cortex there are usually focal convulsions, contralateral to the side of the brain involved. The typical doublecontoured opacities in the skull radiograms represent intracortical calcification. Mental retardation is not always associated with this syndrome and when present is usually mild.

MONGOLIAN IDIOCY (DOWN'S SYNDROME)

Down's syndrome is one of the most common forms of mental retardation. Its incidence is estimated at 1.5 per 1000 births. All patients with Down's syndrome have a total of 47 chromosomes. The extra chromosome is the result of trisomy of chromosome number 21, and almost certainly arises as a result of non-disjunction at gametogenesis. The known association of mongolian idiocy with advancing maternal age makes it likely that non-disjunction generally occurs at oogenesis; the possibility of non-disjunction occurring at spermatogenesis occasionally giving rise to mongolism has not been excluded. In a few instances there has been a translocation of one of the parts of a 21 chromosome without an extra chromosome being present. In these the main portion of a number 21 chromosome has attached itself to another chromosome usually one in the 13-15 group, the resulting joint chromosome thereafter acting as a single unit. Under these conditions the total number of chromosomes would be 46.

The clinical diagnosis depends on the presence of mental retardation associated with certain pathognomonic clinical features resulting from a disordered growth of the skeletal system, especially of the skull and long bones. Findings resulting from defective development of other tissues and organs are frequently present. The disorder in the growth of the skull bones gives rise to most of the characteristic features. The skull is small and tends to be flattened anteriorly and posteriorly. There is a lateral upward slope of the eyes. An epicanthic fold is present in the younger child which differs from that of Asiatic races by being confined to the inner angle, rather than including most of the upper lid. This fold tends to disappear after the tenth year of life. Cataracts appear in about 5 to 8 per cent of cases. Developmental anomalies of the external ears are common. The tongue is usually protruded, owing to the smallness of the oral cavity. Sucking of it usually results in fissuring and furrowing (scrotal tongue) which does not become evident until about 6 months of age. The nose is short, with a flat bridge resulting from the underdevelopment of the nasal bone. The teeth are delayed in eruption, small and abnormally aligned. The neck is short and broad, and there is laxity of the skin at the lateral aspects. In the young child the abdomen is prominent, owing to hypotonia of the abdominal muscles. The extremities are shortened especially the phalanges, so that the hands and feet tend to be broad, flat and square. The fifth finger is proportionately small, and tends to curve inward. Roentgenographic examination demonstrates that the second phalanx of the fifth finger is rudimentary in about 40% of mongols. The spaces between the first and second fingers and toes are increased. The genitals are poorly developed and the secondary sex characteristics are delayed.

The most frequently associated developmental anomalies are those of the eyes and heart. Generalized hypotonia of the skeletal musculature is present but wanes as the child becomes older. The mental status is usually in the imbecile range, infrequently in that of idiocy or the moron level. Mongols are usually pleasant and affectionate, and rarely exhibit behaviour disorders. In the absence of serious extracerebral and cardiac defects, and when given reasonable medical care, their life span need not be shortened. The mongoloid children are also susceptible to infection of the upper respiratory tract including the sinuses and middle ears, possibly because the abnormal skull development adversely affects drainage from these areas. Infections, however, respond to the antibiotics.

The diagnosis of mongolism in the older child is relatively simple. Significant difficulties may be encountered in the early weeks of life when most of the signs are not too obvious, the abnormal configuration of the skull however, is established at birth, and the peculiar formation of the orbits and palpebral fissures are frequently the only specific findings on which a diagnosis can be

be made. Restraint in making the diagnosis in the first few months of life is wise, since occasionally facial appearances suggestive of mongolism occur in infants of normal intelligence. Detailed chromosomal analysis should usually yield results which are pathognomonic in questionable cases.

Translocation Mongolism

Though the clinical features of mongolism described above also occur in mongolism resulting from translocation, there are certain differences between nondisjunction and translocation mongolism. The latter is familial. The mother's age at birth is usually younger than the average. Mongols have forty-six chromosomes including a normal pair of 21 and an abnormal chromosome replacing one of the 13-15 group. Mothers of those children are phenotypically normal and have often had normal as well as mongol children. They have 45 chromosomes including one normal 21 and an abnormal chromosome indistinguishable from that of their mongol offspring. The abnormal one is the result of translocation between chromosome number 21 and a chromosome of the 13-15 group, or rarely chromosome number 22.

Genetic Counseling in Mongolism :

Mothers giving birth to mongols before the age of 25, have 50 fold chance of getting another mongol. Mothers getting mongols between 25 and 34 have five fold risk. Mothers getting mongols at the age of 35 or older have no increased risks than in the general population. Presence of previous abortions, stillbirths or neonatal deaths in her sisters, her mothers sisters, and her maternal grand mother increases risk. If such a history is found in a mother who has had one mongol child, the risk of her having a second mongol should be regarded as that of translocation carrier until the possibility has been excluded by chromosome studies.

There is no evidence that the course of mongolism is benefited in any way by the use of endocrine or other medications.

CONGENITAL SYPHILIS

Congenital syphilis is relatively uncommon cause of mental retardation. In affected patients the mental level is usually in the high grade category, and practically all of them have additional signs of central nervous system abnormality in the form of serious personality disorders, palsies, incoordination, pupillary changes and deafness. The cerebrospinal fluid in untreated or inadequately treated patients is almost always normal.

DIAGNOSIS OF MENTAL RETARDATION :

Diagnosis involves a consideration of the most common conditions that may be mistaken for mental retardation or that may so interfere with the capacity to learn as to result in a clinical picture characterized by depressed intellectual functioning. Since psychologic tests are as a general rule based on the acquisition of learned experience, the following conditions, by impairing the learning process, may also adversely affect the results of these tests and add to the diagnostic difficulties.

Delayed Maturation, especially educational. This is a normal variation in the development of readiness to partake of organized learning experiences, especially those involving academic schooling.

Peripheral sensory defects, such as hearing and vision.

Cerebral Palsy : In infancy, assessment of development is in great part pendent on such motor achievements as holding the head, sitting, hand manipulations, crawling, standing, walking and the like. Low developmental quotients based on these considerations, may erroneously be attributed to mental retardation in the presence of cerebral palsy. In the older child such motor defects may actually interfere with learning opportunities. This is especially true for children with athetosis.

Language and speech disorders : These can seriously affect the learning capacity and may be erroneously mistaken for mental retardation.

Deprivation effects : Deprivation of adequate learning opportunities, or emotional stimulation may result in a picture not unlike that seen in mentally retarded children. These conditions are as a rule reversible if corrected in reasonable time.

Environmentally induced psychogenic disorders : Improper handling and other environmental factors may result in abnormal behaviour and emotional patterns that significantly impair the learning process.

Primary personality disorders : These include basic personality defects which may be the result of faulty cerebral development. The basic clinical manifestation is a failure to properly relate to the environment and a failure in the development of normal interpersonal relationships. The presence of such defects seriously impairs the learning capacity and is frequently mistaken for mental retardation.

TREATMENT AND MANAGEMENT :

There are no known drugs which are appreciably effective in raising the mental level, except for specific defects like cretinism where thyroid extract is of value. If seizures are present these should be treated as previously indicated. Tranquilizing drugs like chlorpromazine, may be of value in hyperactivity, withdrawal and restlessness seen in some of these children.

Defectives may be divided into (1) a trainable group which includes most of the moron group and those of the upper imbecile level, and (2) a permanently custodial group.

Trainable Group Most of the high grade mental defectives are educable and trainable for social adjustment. Specialized educational techniques are necessary for optimal development. Occupational training can result in definite but limited skills. Training and education are best handled in the home and community if possible. Institutionalization of mentally defective children should be resorted to only after home care has proved unsuccessful.

Custodial Group The problem is simply one of supplying custodial care. Institutionalization depends on such factors as economic status of the family, the availability of space in a government sponsored institution, the presence of other children in the family and the emotional stability of the parents. As a rule, practically all mentally defective children of low grade will eventually require institutional care before the fifth or the sixth year of life.

The parents should be told the truth as soon as the diagnosis is established. This information must include whether the condition is inherited or acquired, or whether the cause is unknown. The chances of recurrences in future pregnancies must be discussed in the light of the factor productive of mental retardation in the case under discussion. Also the effect of the presence of mentally retarded child on the other children and whether anything can happen to normal children in the way of subsequent deterioration must be clarified to the parents.

INTRACRANIAL TUMORS

Neoplasms of the CNS make up a large proportion of tumors of childhood. There is no general predilection for the race or sex. There is a definite age incidence; tumors are rare in infancy but increase rapidly to a peak at 5 to 6 years age level, probably owing to high incidence of medulloblastoma at this age. Thereafter a more uniform level is maintained through childhood.

CLASSIFICATION · I — Extracerebral Tumors : Examples of which are meningioma, acoustic nerve tumor and tumors of the pituitary gland.

II — Intracerebral Tumors : Are either primary or secondary. In this chapter we will be concerned with primary intracerebral tumors.

Sixty to seventy per cent of intracranial tumors are infratentorial, in contrast to a reverse pattern in the adult. Of the supratentorial tumors more than half are in the midline. The gravity of the problem in childhood is pointed out by the fact that about 3/4 of all brain tumors are incompletely removed owing to their cellular pattern; that about half of them are difficult or impossible to remove owing to their location and that others are so situated in relation to the brain stem or to the ventricular system that functional embarrassment of these structures is a possibility.

INFRATENTORIAL TUMORS

The common infratentorial tumors are :

1 — Cerebellar Medulloblastoma.	2 — Cerebellar Astrocytoma.
3 — Brain stem Gliomas.	4 — Ependymoma.
5 — Hemangioblastomas.	

CEREBELLAR MEDULLOBLASTOMA

Most common of all brain tumors of childhood, has its peak incidence around 5 years of age, and occurs twice as often in boys as in girls. The tumor usually originates in the posterior vermis and spreads most frequently to the meninges of the brain and cord. The course is rapid. Early morning vomiting and unsteadiness of gait being soon followed by head enlargement. Most children

have sutural separation and papilledema. The gait disturbance is one of disequilibrium. Except for hypotonia, cerebellar signs are slight in the limbs. Fifth or seventh cranial nerve palsies and pyramidal signs are evidence of compression or invasion of the brain stem. Nystagmus is common. Obstructive hydrocephalus is constant. Nuchal rigidity, cerebellar seizures and cord signs are late events. Total removal is impossible. The best treatment is decompression and X-ray therapy. Survival is usually less than one year.

CEREBELLAR ASTROCYTOMA

Astrocytoma is considered perhaps the most benign. It comprises about 20% of brain tumors in childhood. The tumor is usually located in the midline or nearby. It is either solid or cystic and grows slowly. It may extend into the cerebellar hemispheres, rarely into the brain stem.

The onset of symptoms is usually insidious in the form of increased intracranial pressure. In others the first symptom is disturbance of gait or impaired vision before the onset of cerebellar signs. In older children there may be lethargy or lack of cooperation. Unilateral cerebellar involvement may be indicated by a slow, coarse nystagmus to the side of the lesion, hypotonia, dysmetria and ataxia of the extremity on the side of the lesion. Evolution of the clinical picture usually takes three to eight years in the majority of cases.

Best results are achieved by surgery. If the tumor is in the lateral lobes, the results are good with no sequelae with cure rate of 80% to 90%. If the tumor is located in the vermis, removal often cannot be accomplished without some cranial nerve damage. There is no response to radiotherapy.

BRAIN STEM GLIOMAS

These tumors occur mostly in the pons, but may involve the medulla and upper cervical cord or may extend into the cerebellum or cerebral peduncles. As these tumors grow within the pons, they increase its size, but rarely block the aqueduct. Damage is usually produced through infiltration and destruction of the nerve cells.

The peak incidence is about the 7th year of age but no age except perhaps infancy is exempt. The syndrome is one of multiple cranial nerve palsies particularly of the 7th, 9th and 10th nerves and of the sensory portion of the 5th nerve combined with ataxia of the trunk, mild pyramidal signs usually without spasticity, little sensory loss and vomiting without other evidence of increased intracranial tension. CSF pressure is usually elevated only late and

the fluid which is usually normal, infrequently contains 5 to 20 lymphocytes and a slight excess of protein. Pneumoencephalography demonstrates backward and upward shift of the floor of fourth ventricle, encroachment on the pontine centers and some ventricular dilatation. Hypersomnia and hyperthermia are evidences of extension into the upper brain stem and hypothalamic area. The tumor usually begins in the deep strata of the pons and thus are inoperable. When the course is slow, as happens sometimes, X-ray therapy may permit a surprising long survival in few cases.

EPENDYMOMA

Ependymoma in childhood has no sex or age predilection. The initial symptom is almost always vomiting followed by headache, unsteady gait, enlarged head and pyramidal and cerebellar signs. The clinical pattern is variable since the tumor invades and exerts pressure in widely differing directions. Regression of symptoms is also often a feature. Fleck like calcifications evident on the roentgenogram and internal hydrocephalus are common. The tumor is best treated by internal decompression and roentgen therapy.

HEMANGIOBLASTOMAS

These tumors of embryonic origin, often familial are occasionally confined to the cerebellum. The tumors are of vascular origin with a tendency to become cystic, in which cases there is solid nodule attached to the wall. Rarely the tumor originates in the cerebral cortex as a cavernoma. Hemangioblastomas are benign tumors but may turn malignant.

These tumors are rare in childhood. Symptoms and signs are those of all other types of cerebellar tumors, but often come on late. Early, there may be suboccipital headache and discomfort, later vomiting and papilledema.

Differentiation from other cerebellar tumors cannot be made when hemangioblastoma exists alone. However, in some instances when there is a retinal lesion (Von Hippel disease), examination of the discs will show a tortuous dilated vein and beeding of the accompanying artery which together reach the periphery of the retina to enter a nodule.

The prognosis of hemangioblastoma is good if it is solitary. If however there is involvement of the retina or angiomatous nodules in either the spinal cord or brain stem or viscera, the outlook is poor. Treatment is by removal of the hemangioblastoma.

SUPRATENTORIAL TUMORS

The common supratentorial tumors are those of the suprasellar and chiasmatic region, of the thalamus and the posterior third ventricle and of the hemispheres. Tumors of the suprasellar and chiasmatic region include craniopharyngioma and glioma of the optic chiasm.

CRANIOPHARYNGIOMA

This tumor is the most common neoplasm of the supratentorial region in children. It originates from the epithelial cell rests of Rathke's pouch. The tumor is usually cystic containing yellow fluid. It is usually located in the suprasellar region, occasionally in the sella and often calcifies.

The onset in children is usually marked by early evidence of increased intracranial tension due to blocking of the third ventricle by the tumor. Headache may be persistent or recurrent with progressive diminution in vision. papilledema is often present. The visual defects depend upon the location of the tumor. If it is behind the chiasma papilledema results; if in front of the chiasma optic atrophy may result. The visual field defects may be asymmetric but since the tumor is usually suprasellar, there are lower quadrant field defects and bitemporal hemianopia. Pressure on one tract results in homonymous hemianopia; if on the nerve there is blindness and atrophy. The third and fourth and sixth cranial nerves may be involved producing diplopia and ocular palsies. Inclusion of the seventh nerve results in facial palsy.

With involvement of the pituitary gland evident retarded skeletal development and growth occurs. In older children there are sexual infantilism; hairlessness and smooth skin. The syndrome of *Simmonds cachexia* or *Lorain dwarfism* with infantilism may be seen. Hypothalamic pressure is noted by the presence of diabetes insipidus, drowsiness, hypothermia or the adiposogenital *Frohlich's* syndrome.

X-ray skull shows calcification in about 80% of cases, usually suprasellar. Signs of increased intracranial pressure include suture separation, wide flat sella and erosion of the posterior clinoid processes.

Total removal of the tumor is rarely possible because of the close adherence of the cyst wall to the pituitary and hypothalamus. The cyst is evacuated and removal of the capsule is attempted. When the tumor blocks the flow of the spinal fluid Torkildsen operation may be performed. Cortisone and ACTH

may be used to make up for poor adrenal function due to pituitary disturbances, both pre and postoperatively. Deep X-ray therapy may be tried. The outlook however is poor. About twenty per cent survive five to ten years after surgery.

GLIOMA OF THE OPTIC CHIASMA

Initially causes visual disturbances, later there are manifestations of increased intracranial pressure and of hypothalamic involvement. It is often accompanied by extensive cutaneous café-au-lait spots. Optic atrophy is more frequent than papilledema. Excavation beneath the anterior clinoids is a common roentgen finding. The tumor is inoperable. Roentgen therapy is indicated.

TUMORS OF THE POSTERIOR THIRD VENTRICLE

Are pinealomas, gliomas and hamartomas. All produce obstruction early in the course with signs of increased intracranial pressure. The pineal neoplasms compress the mesencephalon from above and cause pupillary dilatation and failure of upward conjugate gaze (the syndrome of Parinaud). They may produce precocious puberty in the male by pressure on the hypothalamic area. Gliomas in the thalamus or hypothalamus may cause similar hypothalamic disturbances together with increased pressure and frequently hemiplegia. They are best treated by draining.

TUMORS OF THE HEMISPHERES

Are gliomas, ependymomas of the ventricles and sometimes sarcomas. Clinical manifestations are hemiplegia, seizures and those of increased intracranial pressure. They are frequently enormous in size. Treatment is surgical or by radiation.

SHAWKI EL - KHATEEB

Chapter XVIII

DISORDERS OF BODY DEFENCE & ALLERGIC DISEASES

Normal Body Defence :

Non-specific : there are natural barriers to infection which include the skin, the mucous membranes, the movements of the cilia, the secretion of mucus, tears, saliva, sweat, gastric acidity, bile and natural reflexes like coughing and sneezing. *Lysozymes* present in tears, saliva, nose secretions and intestinal secretions and in the leukocytes possess bactericidal activity. *Interferon* is a protein produced by cells infected by viruses and has viral inhibiting properties. *Complement* (C') consists of components that react in sequential manner starting by C₁ and ending by C₉. *Properdin* system includes a protein, magnesium ion and complement.

Specific : the specific body defence depends on the phagocytes. These can be wandering phagocytes (leukocytes) and fixed phagocytes (Kupfer cells, sinusoidal cells, reticulum cells). The phagocytic cell captures, kills and digests the microorganism intracellularly. The immunologically competent cell takes this digested product, recognizes it as foreign and develops a memory for future encounter.

The Immune System : (see fig. 42) the stem cell gives a lymphoid cell which either migrates to the Thymus to become a *T-lymphocyte* concerned with Cell-mediated (Delayed) Immunity, or migrates to the gastrointestinal lymphoid tissue (counterpart of Bursa of Fabricius in Birds) to become a *B-lymphocyte* concerned with Humoral (Immediate) Immunity through the production of immunoglobulins (IgG, IgM, IgA, IgE and IgD).

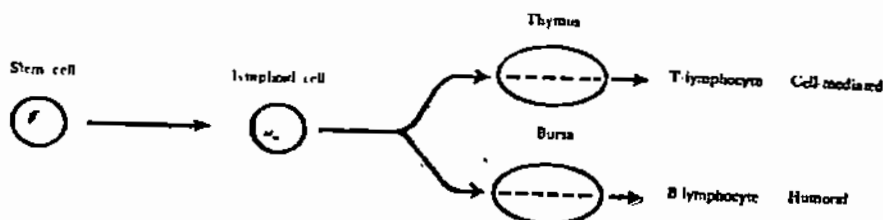


Fig. 42 : The Immune System

ALLERGIC DISORDERS

The allergic disorders of children form a large group of conditions that have in common an immunologic basis. Allergic diseases are due to a sensitivity which certain persons develop to normally harmless substances. A susceptible person who is exposed to these substances has symptoms of disorder in the respiratory organs, the digestive organs or the skin. The most common of these disorders are hay fever, asthma, eczema, urticaria and gastrointestinal disturbances.

Substances capable of producing allergy are called «*allergens*» and are usually proteinic in nature. Simple chemical compounds or drugs need to combine with proteins to become allergenic or antigenic, and are therefore called «*haptens*».

When a particular allergen enters the body, the plasma cells or preplasma cells manufacture special substances ... «*antibodies*» ... which interact with it. This produces an irritation in the susceptible tissues ... «*shock tissues*» ...; e.g., the nose, the bronchial tree or the skin.

The range and variety of things to which susceptible persons may become sensitive are almost endless. Sensitivity usually occurs only after repeated exposure to the substance. Allergic patients may be sensitive to more than one allergen.

«*Atopy*» means clinical allergy which results from hereditary influences and is thought to be peculiar to human beings. Any individual can manifest an allergic disease (e.g. serum sickness), but only certain «*atopic*» individuals with a special constitution can manifest an atopic disease (e.g. hay fever). These atopic individuals are capable of producing a special type of antibodies called «*reagins*» or «*skin sensitizing antibodies*». These harmful antibodies differ from the beneficial ones produced in non-atopic individuals (circulating antibodies which can agglutinate an antigen, precipitate it or adsorb it).

Allergic Disorders are classified as :

I. Immediate Allergic Reactions :

1. Anaphylactic Type — can be induced experimentally, heredity is a negligible factor, are associated with agglutinating, precipitating, complement fixing antibodies.. etc Examples Anaphylactic Shock, and Serum Sickness.
2. Atopic Type — not induced experimentally, heredity is a major factor, are associated with reagins (skin sensitizing antibodies). Examples :

Infantile and Childhood Eczema, Allergic Rhinitis, Bronchial Asthma, and certain Food and Drug Allergies.

II. *Delayed Allergic Reactions* :

1. Non-Infectious Type — represented by Contact Dermatitis, from plants, drugs, chemicals, ... etc. Example : Poison Ivy.
2. Infectious Type — represented by Allergy to Infection, whether viral, bacterial, or mycotic. Example : Tuberculin Reaction.

Methods of Study of an Allergic Child

Infants and young children are quite suitable for a full and comprehensive allergic work-up. This should include the following :

- (1) *History* — In the study of known or suspected allergic disorders, a careful and complete history is the first and most important step in the diagnosis. The history serves two functions; to establish the existence of an allergic disorder, and to disclose the specific causative agent or agents. The history must combine the features of a general pediatric history, and a specific allergy history. Family history of atopic diseases, past history of the same disease, or of other allergic disorders, seasonal variations, and the effect of the environment, are all quite important. Environment questioning should include the house, the residential area, the patient's own room, the effect of dust, temperature, humidity, heating, air-conditioning..., etc, on the disease. Question should also include inquiry about the patient's toys, pets, effect of exertion, hyperventilation (laughing), fumes, paints, smoke, perfumes and the like. Dietary history is also very important, and history of immunizations and handling of infections should not be omitted.
- (2) *Physical Examination* — This is a general pediatric examination, laying stress on certain points :

Nose — the colour of the mucosa, the discharge, and the nose wrinkle (pale boggy mucosa, clear discharge, and wrinkle in allergic rhinitis).

Sinuses — tenderness on the ethmoid, or maxillary sinuses, and frontal (after the 6th year).

Ears — the external canal and ear-drum.

Pharynx — the tonsils, the posterior pharyngeal wall, or any post-nasal drip.

Lymph nodes — tonsillar, cervical, or otherwise.

Chest — shape, presence of emphysema, or any orthopedic deformity.

Lungs — intensity of breath sounds (air entry), prolonged expiration, and wheezing.

Heart - rate, sounds, murmurs.

Abdomen — movements of the diaphragm.

Skin — condition of the scalp, dryness of the skin, rashes.

- (3) *Laboratory Tests* : (a) Blood Count — peripheral eosinophilia exceeding 7% is often present in allergic diseases. However, counts higher than 25% should arouse the suspicion for parasitic infestations, especially visceral larva migrans, collagen diseases, especially periarteritis nodosa, eosinophilic leukemia and familial eosinophilia. Leukocytosis with shift to the left is present when secondary bacterial infection complicates the picture. (b) X-ray Chest — should be done in cases of wheezing, especially when first seen, to assess the state of aeration of the lungs, to detect the presence of any complications (pneumonia, collapse, ... etc), or to discover an etiology other than allergy (foreign body). (c) Tuberculin Testing. (d) Urine and Stool analyses. (e) Cytologic Study of the mucus (Nasal, Conjunctival, Bronchial, or Gastro-intestinal). Nasal smears, stained by Hansel or Wright, showing 10% or more of the cells to be eosinophils is very much suggestive of an allergic reaction. (f) Pulmonary Function Tests—these are not practical in infancy and preschool years. Later, the vital capacity, timed vital capacity, and maximal breathing capacity are very useful. (g) Special Tests resorted to in certain occasions, like the estimation of Sweat Chlorides (Cystic Fibrosis of the Pancreas), Immunoglobulins (Dys- and Agammaglobulinemia), cultures from the nasopharynx, bronchoscopy, ... etc.
- (4) *Elimination Procedures* elimination of foods or environmental allergens is often of great help in establishing the etiology of an allergic state. Below the age of 2 years, the most common offenders are foods and house-hold inhalants. After that age, many can be added to the list, especially seasonal allergens. Young infants can have a strict environmental control first, and watched. After a reasonable period (10 days), elimination diet can be tried. This usually comprises a milk substitute, rice cereal, beef, two fruits, and two vegetables. If in 10 days the allergic manifestations disappear or improve markedly, this is suggestive of food allergy. Add various foods slowly, at 10 day intervals, and the most important ones first (e.g. milk).
- (5) *Allergy Skin Testing* — do not skin test for all the possible allergens, but select the ones that fit most the history. Start always with the scratch test, and read the results in 15-20 minutes. Positive tests show a wheal and flare reaction. If scratch tests are negative, intracutaneous tests can be done,

first 1/100 concentration, then 1/10, and lastly concentrated solutions. Mucous membrane tests can be done in the conjunctival sac, or intranasally, or by a respirometer. Patch tests are done only in contact dermatitis. These are read after 48 hours (delayed, Tuberculin-like), and positive ones show erythema, induration and vesiculation.

Prophylaxis of the Allergic State.

(1) *Diet* - nature protects the newborn infant against the potentially noxious effects of food by providing human breast milk, the only natural food for the infant. Probably a good prophylaxis of allergic diseases is breast feeding. It seems reasonable to suppose that the mother should be on a controlled diet to avoid foods of high sensitization potential during lactation, and perhaps during pregnancy. If breast feeding is not practical, the use of milk substitutes proved adequate in suspected milk allergy (soy bean milk). It should be also remembered not to give cow's milk in the period before breast feeding is established. In infancy and early childhood, additions to the diet should be in the form of simple foods, rather than mixed foods. If possible, avoid common allergens such as wheat, chocolate, oranges, bananas and eggs.

(2) *Environment* - the room of the infant and child should be kept dust-free as much as possible. Avoid rugs, carpets, heavy curtains, storing of clothes or furs in the room. It is safer to use synthetic pillows (polyester, dacron), instead of cotton or feathers, or new foam rubber ones, and to cover the mattress with tightfitting plastic. Blankets should be washable, synthetic (Acrylic, Orlon), and not wool. No fuzzy toys should be allowed in the room and particularly in the bed with the child.

(3) *Pets* - animal dander (hair) is potent allergen and so its avoidance is advisable. Attention must also be paid to birds, parrots, . . . etc. If a pet is essential for the allergic child, choice of gold-fish, turtle, . . . etc. can be allowed.

(4) *Exercise* - should be permitted within tolerance. Swimming is a good exercise for breathing and for muscle development of the chest wall. Blowing of balloons, and using a wind instrument as a musical passtime recreation is also recommended.

(5) *Respiratory Infections* - these usually aggravate the allergic symptoms. We cannot prevent most of them, but prompt treatment proves helpful.

(6) *Temperature and Humidity* - sudden changes in these should be avoided as much as possible by the allergic child.

(7) *Emotional Problems* - the knowledge of the true state of the atopic disorder can minimize the anxiety of the parents which is undoubtedly reflected on the child. Also, the care of the allergic child should be directed towards making his life as much like that of his non-allergic companions as symptoms permit.

(8) *Immunizations* - the usual immunizations should be given to the allergic child. The only major exception is small pox vaccination of the eczematous infant. Siblings or contacts of an eczematous infant are also not vaccinated. On the other hand, it is important to maintain active immunity by repeated booster doses to avoid the use of animal sera as in Diphtheria or Tetanus. The allergic child is more prone to anaphylactic reactions to heterologous sera.

ANAPHYLACTIC SHOCK

Etiology : (1) Heterologous serum injections. (2) Antibiotics, especially penicillin. (3) Insect stings (bites). (4) Biologic medications (e.g. insulin).

The child who had had a previous contact with any of the mentioned antigens, will react on re-exposure, due to antigen/antibody union. There is release of chemical mediators (histamine, serotonin, acetyl choline, heparine and others), and most of the symptoms are due to the liberation of histamine.

Clinical Picture : (1) The skin — itching, flushing, burning sensation, urticaria and angioedema. (2) The respiratory system — tightness and chest pain, cough, wheezing, dyspnea and cyanosis. (3) The circulation — circulatory failure manifested by marked drop in blood pressure, pallor, vertigo and coma. Death may issue.

Diagnosis : The dramatic sequence of events leaves no doubt in the diagnosis. Simple fainting from the needle prick should be differentiated.

Treatment : Prevention by history taking and skin testing is very important.

Treatment must be prompt and vigorous. A tourniquet should be applied immediately above the level of the injection, if this is in a limb. Adrenaline 1/1000 0.2 - 0.5 ml. is injected i.m., and another dose at the site of the antigen. The adrenaline can be repeated every 5 - 10 minutes until an effect is obtained. Antihistaminics can be given i.m. or i.v. (e.g. 10 mg. chlor-trimeton). Coramine, levophed, oxygen inhalation, and other measures of treating shock may be necessary. Steroids are not of value in the emergency state, but are useful later on to minimize the urticaria and angioedema.

SERUM SICKNESS

Etiology : It is due to injection of heterologous serum in a child who was not sensitive when the serum was administered. Examples are diphtheria antitoxic and antitetanic serum.

Accelerated serum sickness occurs in previously sensitized children, and these might even develop anaphylactic shock.

Clinical Picture : The incubation period is 6 — 12 days. There is low grade fever, skin rashes, lymphadenopathy and polyarthropathy.

- (1) *Fever* — varies in severity, but usually low grade, and stays from a day to a week.
 - (2) *Skin rashes* — urticaria, erythema and purpura may occur, usually first at the site of serum injection, then generalized.
 - (3) *Lymphadenopathy* — most marked in the nodes draining the site of injected serum, but also generalized. The nodes are slightly tender, 2 cm. or more in size, and the spleen may be palpable.
 - (4) *Polyarthropathy* — occurs in half the cases, and affects knees, ankles, elbows, wrists and small joints of hands and feet. The affection varies from pain and stiffness, to definite swelling and effusion.
- Laboratory findings — moderately elevated E.S.R., leucopenia, and urinary albumin and casts in severe cases.

Treatment : *Mild* — antihistaminics, ephedrine, aspirin, and local applications (calamine lotion).

Severe — steroids (prednisone 20 -- 40 mg./day) are given for about 7 days.

Prognosis is good, and the symptoms rarely exceed one week.

INFANTILE ECZEMA

Eczema or Atopic Dermatitis is most common in infants over 2 or 3 months of age (usually between 2 and 6 months). Most cases clear spontaneously by the 2nd or 3rd birthday. There is a high family incidence of allergic diseases. Eczema is frequently associated with or progresses to respiratory allergies. Blood eosinophilia is common, skin tests are positive, and the Prausnitz Kustner test can be demonstrated. All these implicate allergy as the basis of infantile eczema.

Etiology : Predisposition - Heredity (atopic disease). Skin character (sweating and overhydration).

- (1) *Food Allergy* - The incidence of eczema is more in artificially fed babies, and less in breast fed ones. Cow's milk is the most frequently suspected allergen, and eggs play an important role, though other foods may be also responsible.
- (2) *Inhalants* - Dust, animal dander, wool, moulds and pollens are common offenders. Direct contact with wool is usually irritating to the eczematous skin, but this is due more often to mechanical irritation than to specific sensitization.
- (3) *Skin infection* - There are observations which indicate that bacterial infection may be an important etiologic factor in certain cases of atopic eczema.

Clinical Picture : Itching is the most distressing and most persisting symptom, often accompanied by discomfort, irritability and insomnia.

The eruption begins in the majority of cases on the cheeks, then spreads to the rest of the face, and later on may become generalized. It tends to localize in chronic cases in the so called atopic areas (behind the ears, in the neck, in the antecubital and popliteal spaces, wrists, hands and ankles.)

The lesion in the early stage is a vesicle on an erythematous base. Quickly, this is scratched off, the skin becoming excoriated. There is exudation of serum (weeping), and crusting. Thickening of the skin (lichenification), and secondary infection (impetiginization), with adenopathy are common.

Diagnosis : The most important conditions that should be differentiated from infantile eczema are :

- (1) *Seborrheic dermatitis* - mainly affects the scalp and the intertriginous areas. The scales are thick, grayish and waxy, and a scalp dermatitis with greasy crusts is common (cradle - cap). There is no vesiculation or weeping, itching is absent or slight, and there is no family history of allergic disorders.
- (2) *Exfoliative Dermatitis* - occurs much earlier (one to 3 months), no itching, no eosinophilia, but usually severe and protracted diarrhea. It is now considered to be a form of staphylococcal infection.
- (3) *Moniliasis* - lesions are bright red in colour, with sharp margin, and festooned edge. Satellites are common in the adjacent free skin, itching slight, and the candida (monilia) can be demonstrated.

Treatment : (1) *Avoidance of allergens* - includes elimination diets, environmental control, . . . etc.

- (2) *Symptomatic treatment* - this includes : a) support for the entire family. b) prevention of mechanical trauma (cutting of nails, restraints, . . . etc). c) sedatives and antihistaminics. d) systemic steroid therapy (in very selected cases). e) topical therapy — in the weeping acute stage, the best will be compresses with Burrow's solution (aluminum acetate), 1 : 20, and hydrocortisone lotion or cream (1%). If there is secondary infection, neomycin or a similar antibiotic, is added to the topical cream. In chronic eczema, coal tar derivatives are the best (3 to 5% coal tar in Lassar's paste or Zinc Oxide). Generalized corn starch baths may be helpful. Avoidance of soaps and the use of skin emollients is also useful.
- (3) *Desensitization (immunization) therapy* is resorted to occasionally, especially when infantile eczema is associated with respiratory allergy.

Complications : (1) Thickened, rough, or scarred skin. (2) Secondary infections (with sequelae as nephritis). (3) Generalized edema due to hypoproteinemia (extensive weeping of serum). (4) Eczema vaccinatum and eczema herpeticum (Kaposi's eruption) may be fatal. (5) Persistence into late childhood and adult life. (6) Frequent association with respiratory allergy. (7) Cataracts in severe protracted cases.

ALLERGIC RHINITIS

- (1) Seasonal Allergic Rhinitis (Hay Fever).
 (2) Non-seasonal Allergic Rhinitis (Perennial Allergic Rhinitis).

Etiology : *Hay Fever* — its most important cause is the inhalation of pollens (called sometimes «Pollinosis». These have definite seasons :

Trees & Shrubs.....March & April.....e.g. date palm, pecan,.....etc.
 Grasses.....May & June.....e.g. bluegrass, bermuda,..... etc.
 Weeds.....August & September....e.g. hemp, plantain,.....,etc.

Other causes of hay fever are air-borne moulds, or the seasonal contact with animal dander, ... etc.

Perennial Allergic Rhinitis — is most commonly due to house-hold inhalants (house-dust, kapok, other fabrics, feathers and some indoor moulds), and or animal dander.

Clinical Picture Sneezing, rhinorrhea, tearing, itching of the nose, palate, and pharynx are the main symptoms. Nasal congestion and stuffiness are common, especially as the case gets chronic. Bacterial complications are favoured by the presence of congestion, obstructions and mucoid discharge.

The mucous membrane of the nose looks grossly edematous, pale, and purple-gray in colour. The discharge is thin and watery if there is no secondary infection.

Treatment . (1) Avoidance of the allergens if possible (2) Antihistaminics, generally. (3) Ephedrine (4) Nose drops, sparingly, preferably at bed time, and not more than 7 days in a row (5) Steroids in severe cases, especially if seasonal. (6) Desensitization therapy

Complications : (1) Bacterial infection, changing the discharge to purulent, sinusitis, otitis media, or serous otitis. (2) Nasal polyps. (3) Epistaxis. (4) Frequent association or progress to Bronchial Asthma

BRONCHIAL ASTHMA

This is a wheezing type of dyspnea due to generalized obstructive emphysema, caused by spasm of the bronchi and bronchioles, with outpouring of thick tenacious secretions in the bronchial lumen, and edema of the lining mucous membranes. It can be seasonal (comparable to hay fever), or recurrent. It is commonly preceded by infantile eczema and allergic rhinitis

Etiology . Predisposition Heredity (Atopy)

- (1) Allergens act through immunologic encounter with reagins (IgE) and release of chemical mediators (histamine, serotonin, etc). Foods are important especially in infancy and their importance decreases after the 3rd or 4th year of life. The most important ingestants are eggs, wheat and milk. Inhalants play a much more important role particularly house-dust. Pollens are important after the age of 5 years. Other house-hold inhalants like animal dander, feathers, moulds and mites play a significant role
- (2) Defect in autonomic nervous system may be significant. The parasympathetic system stimulates bronchoconstriction, while the sympathetic system stimulates bronchodilatation. This last effect is achieved through β -adrenergic receptors, which if blocked or defective, increased bronchospasm through α -adrenergic receptors will result. Respiratory infection plays an important role here as well as physical factors (hot and cold environment, humidity, hyperventilation, emotional instability and air pollution. Strong

smells (paint, varnish, smoke, and perfumes) may also aggravate the condition.

Pathology . (1) Spasm of the smooth muscles of the bronchi and bronchioles.

(2) Hypersecretion of tenacious mucus. (3) Edema of the mucosa.

Generalized emphysema will be the result of the previous 3 factors. Emphysema is observed during acute attacks only in the beginning, but if neglected, bronchial asthma will lead to chronic changes. The thoracic cage may become fixed in a form of expiration, the diaphragm will be depressed, and the accessory muscles of respiration called upon.

Clinical Picture : The onset of the attack can be gradual or abrupt. Nasal symptoms (sneezing, and stuffy nose) and slight cough may precede the attack, or it may start suddenly with tightness of chest, audible wheezing, and dyspnea. In very severe attacks, the child will be anxious, perspiring, cyanotic or even shocked.

On examination, the nose looks allergic, there is hyperinflated chest, working accessory muscles of respiration, hyperresonant percussion note, prolonged expiratory phase, and rhonchi together with audible wheezing. The intensity of air sounds (air entry) may be diminished. Signs of atelectasis may be added to the clinical picture.

Diagnosis : Bronchial asthma should be differentiated from other causes of bronchial obstruction, and from cardiac asthma.

- I. *Bronchial Obstruction*. (1) Congenital—usually these give rise to stridor more than wheezing (vascular anomalies, especially double aortic arch) except congenital lobar emphysema. (2) Foreign body inhalation. (3) Respiratory infections (URI, Acute Bronchiolitis, viral pneumonias, pertussis and miliary tuberculosis). (4) Fibrocystic disease of the lungs. (5) Compression by hilar and mediastinal lymph nodes (T.B., Hodgkin, Leukemia, etc). (6) Rarely tumours (Adenoma, Fibroma, Chondroma . . . etc).
- II. *Cardiac Asthma*. This dyspnea of cardiac origin, occurs in left ventricular failure, especially in acute diffuse glomerulonephritis.

Laboratory studies - blood count (eosinophilia), nasal smear (eosinophils), tuberculin test, x-ray chest, nasopharyngeal culture and deep or sputum culture, and bronchoscopic examination.

Allergy skin tests. (See page 488).

Treatment : - *Management of the Acute Attack*.

- (1) Bed rest, away from allergens and exciting factors.

- (2) Drugs to relieve the spasm. *Adrenaline* 0.1 to 0.3 ml. 1/1000 subcutaneously every 20 minutes for 2 or 3 doses. *Isoproterenol* (Isuprel, Norisodrine) is effective by inhalation (nebulizer), or sublingually in the older child. *Aminophylline*— of particular value to those resistant to adrenaline. It is best given i.v. in 100-150 ml. of 5% glucose solution, but can be administered rectally (instillation preferable to suppositories) or orally. The dose is 2-5 mg per Kg. body weight per dose. Avoid overdosage and do not repeat before 6 hours. *Ephedrine* is useful in mild attacks, and for the relief of cough. It can be combined orally with phenobarbital and aminophylline. Its dose is 0.5-1 mg./Kg./dose, and can be repeated after 6 hours.

Methyl-isoproterenol a β -adrenergic stimulant, can be given orally. *Salbutamol*, which stimulates the β -adrenergic receptors in the bronchial muscles only, can be given orally or by inhalation (nebulizer).

- (3) *Expectorants*, are very useful to liquefy the sticky bronchial secretions, and to help coughing up the plugging mucus pellets. The best are Potassium Iodide, (0.1 - 0.3 ml. saturated solution orally), Sodium Iodide (i.v.) in the infusion or Calcium Iodide orally (bitter taste). Syrup of Ipecac is also useful (4 to 8 ml.) as emetic, and if the first dose is not effective, it may be repeated.

If by all these measures the attack is not under control, the case is considered «Status Asthmaticus» and should be hospitalized.

- (4) Steroids are administered i.v., and later orally. (5) Humidified Oxygen. (6) Hydration. (7) Mild sedation (avoid opiates). (8) Bronchoscopy if necessary. (9) Proper antimicrobial therapy.

Long Term Therapy.

(1) Environmental Control. (2) Emotional Support. (3) Prompt treatment of infections especially respiratory ones. (4) Bronchodilators; combination of Ephedrine, Phenobarbital, Aminophylline, and β -adrenergic stimulants. (5) Antihistaminics may help to prevent attacks, but are of no definite value during an attack, as they may even dry and thicken the already viscid mucus. (6) Breathing Exercises. (7) Hyposensitization or Immunization therapy. (8) The use of Disodium chromoglycate (Intal) by way of inhalation may prevent or lengthen the interval between the attacks.

Complications Specific therapy increases the chance of recovery, and helps to prevent the complications of bronchial asthma. (1) Atelectasis and massive collapse of the lung. (2) Emphysema, and later on chest de-

formity. (3) Cor pulmonale. (4) Pulmonary infections, and later on bronchiectasis. (5) Air in the extrapulmonary spaces (Subcutaneous emphysema and Pneumothorax). (6) Mortality rate in the acute attack of about 1%.

URTICARIA AND ANGIOEDEMA

This is an allergic, acute or chronic skin reaction, that may be atopic.

Etiology : (1) Foods — most common cause. (2) Drugs. (3) Sera and Vaccines. (4) Physical and Psychogenic factors.

Clinical Picture : (1) Urticaria — is a very itchy skin condition, characterized by erythematous macules, or wheal and flare reaction that may coalesce to cover large areas of the skin.

(2) Angioedema — occurs mostly on the lips, eye-lids, genitalia, tongue, or larynx (serious, and may cause respiratory obstruction). The lesions do not itch, but they are tense and pale.

Treatment : (1) Adrenaline 1/1000, 0.1 — 0.3 ml, to be repeated every 20 minutes if necessary. (2) Antihistaminics and Ephedrine. (3) Avoidance of allergens. (4) Steroids in selective cases (severe or resistant).

PAPULAR URTICARIA

Etiology : (1) Insect Allergy — especially to flea, mosquito and bed-bug bites. (2) Foods play a minor role.

Clinical Picture : Papular urticaria appears usually in infancy, and presents as small papules which itch markedly, and soon become excoriated. Vesiculation is common, especially in palms and soles. It is commoner in the warm months of the year, and the lesions tend to occur on the periphery and the exposed parts of the body; arms, legs, face, and neck.

Treatment : (1) Control of insects. (2) Antihistaminics. (3) Local calamine lotion or cream, and in severe cases local steroids.

GALAL H. AREF

Chapter XIX

COLLAGEN DISEASES

JUVENILE RHEUMATOID ARTHRITIS

(Still's disease)

Etiology : Is yet unknown, but the following hypotheses are introduced :

Infection : The search for an infectious organism as the etiologic agent has so far been unsuccessful. It seems that infection with some unknown agent provides the most likely explanation for the pathogenesis of this disease. The following are some of the features which suggest that infection could represent the basis for rheumatoid arthritis :

- a) Septic temperature. b) Peculiar and characteristic erythema. c) Leukocytosis.
- d) Splenomegaly. These may precede the development of frank arthritis by months or years. e) Frequent occurrence in cases of agammaglobulinemia. f) Simulate rubella arthritis. g) High incidence of group A beta-hemolytic streptococci isolated from nasopharynx in some series.

Autoimmunity : It is likely that rheumatoid arthritis is related either to : 1) An abnormal response of antibody forming cells to normal self antigen or 2) A normal response of antibody forming cells to modified self antigens. The connective tissue cells of predisposed individuals take up the components of the bacterial cell walls or capsules and incorporate them into their protein polysaccharides, which now altered, result in local cellular damage through immunological mechanism.

Heredity : There is a relative high familial incidence of rheumatic diseases.

Age : Onset between 1½ and 5 years, with slight rise towards puberty.

Sex : More in females, 2 : 1

Clinical features : *Mode of onset* : Varies considerably from :

- a) Involvement of a single joint; usually a knee with no constitutional reaction.
- b) More wide spread polyarthritis of varying severity with or without systemic manifestations.

- c) General systemic onset with high fever, rash and arthralgia (no visible swelling) or even no arthralgia, and this may remain for many months, (here the rash is the most useful diagnostic pointer).
- d) Occasionally one of the extra articular manifestations such as iridocyclitis or pericarditis may be the presenting feature, preceding by weeks or months the onset of joint symptoms.

Joint manifestations : Frequently, the large joints are affected; knees, hips, ankles, elbows and wrists. The cervical spine is commonly affected and presents with pain, limitation of movement and torticollis. The affected joints may swell with fluid or show more of a periarticular thickening. The surrounding muscles atrophy, and sometimes rapidly. Increasing limitation of movement and muscle weakness can lead to severe crippling. Carpi and tarsi are also frequently affected.

Other joints less frequently affected :

- Temporomandibular joints : difficulty in eating. Once involved it rarely recovers completely.
- Rarely the sternoclavicular joints and chondrocostal junctions can become swollen and very painful.
- In few children, stridor and hoarseness can reach alarming proportions due to involvement of the crico-arytenoid joints.

Fever: Shows a daily swing with temperature as high as 40° C in the evening and normal in the morning.

Rash : Erythematous maculopapular and blotchy and it usually changes its shape and distribution continuously, and is distributed widely on the extremities and trunk but can involve the face. It tends to occur in patients who are running a high fever and is frequently manifest only at the height of temperature i.e. towards the evening.

Lymphadenopathy : Generalized glandular enlargement occurs particularly during the early stages of the illness. It tends to decrease as the acute stage subsides.

Splenomegaly : Less frequent than lymphadenopathy. As amyloidosis has been seen to develop within a year of onset, it should always be considered when splenomegaly is present with a disease duration more than a year.

Heart involvement : Pericarditis is almost the only type of cardiac involvement found, and occurs in about 7% of the cases.

Rheumatic fever can occur in a patient who coincidentally has Still's disease.

The possibility of aortitis causing aortic insufficiency must be considered. It occurs in 1% of ankylosing spondylitis in adults, but never recorded in children.

Iridocyclitis : Chronic iridocyclitis is usually severe, and before introduction of steroids often caused blindness.

It may precede the onset of arthritis by 2 years or more. It is necessary to do regular slit lamp examinations even in absence of symptoms or obvious eye changes.

The diagnosis must rest upon the typical features and course of the disease. Inequality of pupils or pigmentary deposits call for immediate consultation. Prompt treatment with steroids is indicated.

Tendon sheath involvement : Effusion may occur in tendon sheathes, most evident in the proximal phalynx. Tendonitis with adhesions between the tendon and its sheath producing a claw-hand may be the main presenting feature of the disease.

Nodules : Rare in childhood. The majority resemble more closely those of rheumatic fever. If present they are usually few and are found on the elbows.

X-rays : a) In the early stages of arthritis no abnormality except soft tissue swelling around the affected joint may be seen. Muscle atrophy may be also visualized. b) As the articular cartilage is eroded, there is progressive narrowing of joint space. c) Ultimately true bony union will result. d) Osteoporosis is frequently marked in the bones near the affected joints. Small foci of bone destruction may be seen in the juxta-articular ends of the bone.

Growth : Apart from ankylosis, interference with growth occurs as a part of the general metabolic disorder.

Premature epiphyseal fusion tends to involve particularly the metacarpal, metatarsal, pharyngeal and ulnar bones, and gives rise to local growth defects particularly in the 10 — 15 years old group.

Course and prognosis : The disease frequently runs a course of remissions and relapses. In most instances it burns itself out after some years. In general there are three possible end results :

- The disease may resolve leaving the child physically fit or only mildly handicapped.
- It may lead to severe crippling.
- Death due to intercurrent infection or amyloid disease.

Diagnostic Aids :

- Hb level tends to fall but seldom below 60%. No response to hematinics. Sedimentation rate is always raised when the disease is active.
- Serum protein : increase in the alpha - 2, gamma globulin and haptoglobin.
 - Test for rheumatoid factor in the serum (Latex fixation test, Rose-Waaler test) which are usually positive in adult sufferers, and are rarely positive in even severely affected young children.

Treatment : The aim of the therapy is to maintain motion in affected joints, to prevent deformity and to ensure as far as possible the normal growth and development of the child physically, mentally and emotionally.

General measures :

- 1) — Rest in bed only during acute febrile episodes.
 - May be harmful and predisposing to contractures.
 - Weight bearing does not seem to increase the amount of joint damage.
- 2) Diet : There is no special diet.
- 3) Infections : The disease is occasionally reactivated by infection with group A beta-hemolytic streptococci.
- 4) Prophylactic therapy with penicillin may be indicated. Physical therapy by exercise and walking in the hydrotherapy pool.
- 5) Prevention of deformity : Prevention of permanent flexion deformities is best achieved by the use of plaster of Paris splints, especially for knees and wrists (worn by night). If flexion contractures of knee joints occur, correct by serial splinting. Knee contractures are almost always concomitant with hip flexion, and both should be corrected at the same time. To prevent flexion deformity of the neck, a collar should be worn especially when sitting.
- 6) Ophthalmic care : Periodic slit lamp examination for early diagnosis of iridocyclitis is recommended.
- 7) Psychological care: The family should be made to understand the necessity of fulfilling the patient's social, educational and psychologic needs.

Drugs . No specific therapy, however the following could be tried :

- a) Aspirin : 100 mg./kg./ day, to be divided into 4 or 6 daily doses. This is the most satisfactory suppressive agent. The response occurs within 3 —4 days.
- b) Corticosteroids : They do not alter the natural remission rate, the length of the illness or the ultimate prognosis.

Therapy is indicated in cases of pericarditis with or without myocarditis, in iritis and any case where the disease appears to be life threatening.

Some authors have the impression that better results are obtained by using aspirin and cortisone together. In mild cases, aspirin may suffice, but in most cases corticosteroids are also used. The dose of prednisone used is the same as in rheumatic fever. The effects are usually dramatic, with rapid subsidence of arthritis, fever, rash, malaise, lymphadenopathy and splenomegaly. When the corticosteroid is withdrawn, there is often a rebound phenomenon with a flare up in the symptoms. This may be controlled with aspirin, but in some cases a maintenance dosage of corticosteroids must be continued for years.

SYSTEMIC LUPUS ERYTHEMATOSUS

S.L.E. is a generalized disease involving many systems, due to formation by the affected person of autoimmune antibodies (against his own tissues).

Etiology : unknown, but a) Many family members are affected with greater frequency than in the general population. b) Rheumatoid factors, antinuclear factors and high or low levels of gamma globulin have all been frequent in such families. c) Increased incidence of rheumatoid arthritis in such families.

So, an inherited abnormality of the immunologic mechanism might account not only for the disease itself, but also for the gammaglobulinopathies observed in family members. Such a genetic factor might predispose a person to S.L.E. given other appropriate precipitating stimuli.

Age at onset : Rare in children, not uncommon during the years of puberty and maximal incidence 20-40 years.

Sex : female : male. 9 : 1.

Clinical Manifestations :

1 — *Rash :* a) Butterfly rash :

— characters : — erythematous, over malar areas and bridge of nose, upper lids not involved, may be photosensitive and may spread to neck and chest.

- onset : — may be the initial finding in half of cases but may occur sometime during the disease.
 - frequency : — over 3/4 of cases.
 - b) Occasionally small papules and urticarial lesions on arms and legs.
 - c) Minute erythematous puncta on the palms, soles and finger tips which may be petechial.
 - d) Purpura on dependent or traumatized areas.
- 2 — *Arthritis* : Character : tenderness and swelling of joints. The joints involved are those commonly involved in rheumatoid arthritis and the arthritis is chronic and not migratory as in rheumatic fever.
Onset : presenting complaint in most cases. In children, the early multisystem manifestations of S.L.E. differentiates it from rheumatoid arthritis.
 - 3 — *Fever* : Irregular, moderate to high spikes of fever associated with malaise, anorexia and debility.
 - 4 — *Renal Disease* : The kidney is almost always involved at the onset of S.L.E. Usually there are persistent albuminuria, microscopic hematuria, pyuria and cylinderuria. Proteinuria may be massive (Nephrotic syndrome).
 - 5 — *Liver, Spleen and Lymph nodes* : Enlargement of liver or spleen in 1/5 of cases. Not a prominent initial finding but becomes apparent as the disease persists. Splenomegaly may be accompanied with hepatomegaly, but may occur independently.
Generalized lymphadenopathy may occur at the onset and may simulate Hodgkin's disease.
Jaundice is not observed (to differentiate from plasma-cell hepatitis).
 - 6 — *Cardiac* : About 40% have some manifestations of heart disease during the course : cardiomegaly unassociated with other symptoms (commonest), pericardial rub, apical systolic murmur, mitral systolic and diastolic murmurs which mimic rheumatic heart may be present.
 - 7 — *Pulmonary* : About 25% have pneumonia or pleurisy early in the course. Several patients develop fulminant and fatal pneumonia apparently as complication of steroid therapy.
 - 8 — *C.N.S.* : Hemiplegia, convulsions, psychosis and chorea but are rare.
 - 9 — *Hematologic abnormalities* : Hb usually less than 12 Gm%, W.B.Cs. 5000

or less, sometimes Coombs test is positive, S.R. increased, platelets less than 100,000 and Thrombotic thrombocytopenic purpura may occur.

Laboratory Data : 1 — L.E. cell Phenomenon : found in all cases.

2 — Hematologic abnormalities described before.

3 — Serum proteins : a decrease in serum albumin and increase in globulin in all cases (increase in gamma & alpha 2).

Course and Prognosis : Mortality rate extremely high. Permanent remissions are uncommon.

Management Rest during acute phase. A high S.R. does not contraindicate physical activity. Blood transfusion should be avoided. There is great difficulty in cross matching blood donors with these patients. Steroids are the only form therapy today. There is suppression of most of the symptoms but there is no control over the progressive renal disease.

POLYARTERITIS NODOSA

Etiology is unknown, but this rare disease is included in the family of collagen or hypersensitivity disorders. The diffuse involvement of arteries, arterioles and capillaries supplying many different organs accounts for its protean clinical manifestations. All three layers of the arteriolar wall are involved. There is fibrinoid necrosis of media and destruction of the intimal elastic tissue. All coats of the vessel wall become edematous and infiltrated with leukocytes; eosinophils being the most conspicuous cell form. Infiltration is followed by granuloma formation, fibroblastic proliferation and healing with fibrous tissue (scarring). Thrombosis of the vessel leading to infarction, recanalization and aneurysmal dilation at points of bifurcation (Nodosa) are common accompaniment.

Two groups of cases are recognized according to presence or absence of lung involvement :

A) **Polyarteritis nodosa without lung involvement** : accounts for 2/3 of all cases. Males : Females, 3 : 1. Onset : any age from infancy throughout life, increasing incidence with advancing age. Season : winter.

Usually preceded by a respiratory illness which is either :

- acute : Hemolytic streptococci in 75%.
- chronic with bronchitis, bronchiectasis and chronic otitis media.

Clinical Manifestations :

- 1 — *Constitutional illness* with weight loss and fever at some stage of the disease (in all patients).

Anemia and leukocytosis are common.

Eosinophilia : in one third of the cases.

Serum proteins : increased globulin and diminished albumin.

- 2 — *Gastrointestinal tract* frequently involved. Polyarteritic lesions confined to terminal branches of mesenteric arteries leading to submucous hemorrhages and ulcers. The symptoms are poorly localized abdominal pain or severe pain or severe hemorrhage which necessitates surgery. The signs are absent, no liver dysfunction. Spleen infrequently palpable.

- 3 — *Skin* : a) Focal indurated skin lesions (local polyarteritis), range from superficial papules to crops of tender, erythematous, subcutaneous nodules which may ulcerate. Their site is arms or legs and they occur in 1/4 of patients.

b) Later in course : subcutaneous hemorrhages, skin ulceration and even gangrene of fingers or toes may occur.

c) Less frequently : recurrent urticaria, angioneurotic edema, maculopapular eruptions, purpuric rashes and painful subcutaneous areas.

- 4 — *Muscle pain and tenderness* : frequent and are often initial manifestation.

- 5 — *Arthritis* : not uncommon at sometime of the course, may be the initial manifestation, may be acute and transitory, may be migratory as rheumatic fever, or chronic as rheumatoid arthritis.

- 6 — *Cardiac (Coronary)* : tachycardia, cardiac enlargement or congestive heart failure.

- 7 — *Retinal hemorrhage* : late and associated with hypertension.

- 8 — *Asymmetric peripheral neuritis*.

— *Renal* : at some stage in 80%, proteinuria and/or hematuria. The B.P. rises during the healing or healed stages. Rapidly progressive.

Two thirds of cases die from renal and one third from coronary disease and gastroenteritis.

- B) **Polyarteritis with lung involvement** : One third of cases with no sex predilection.

Clinical Manifestations Main symptoms are similar to those of :

(1) Asthma. (2) Pneumonia : ranges from transient, symptomless infiltrations to large chronic abscesses unresponsive to antimicrobials. (3) Chronic bronchitis.

Incidence of polyarteritis in other organs and their signs and symptoms are similar to those without lung involvement.

Polyarteritis Nodosa in the first year of life : Most have rash, pyuria, upper respiratory tract manifestations and progressive cardiac failure or sudden death. The prognosis is poor. Cortisone may have some benefit.

ANAPHYLACTOID PURPURA

(SCHOENLEIN — HENOCHE SYNDROME)

The term «Schoenlein — Henoch» syndrome includes :

- 1 — Schoenlein's purpura : purpura with arthralgia.
- 2 — Henoch's purpura : purpura with visceral manifestations.
- 3 — Anaphylactoid or allergic non-thrombocytopenic purpura.

Etiology : There is angitis involving the capillaries. The cause is unknown, but is regarded to be an autoimmune response to a variety of antigenic stimuli.

Age : Mostly between 3-7 years. **Sex** : Male : Female, 2 : 1.

Clinical manifestations : In about half of the cases there is a preceding upper respiratory infection. In about one third, beta hemolytic streptococci can be cultured from the nasopharynx. A week or two after infection, though in others without a preceding infection, arthralgia and/or abdominal pain appear, followed within hours to a day or two by a skin rash. Sometimes, the rash precedes the visceral manifestations while sometimes all occur simultaneously.

Skin changes : The rash is of characteristic appearance and distribution. Diagnosis of the disease is based on the rash.

The rash appears first as small separate urticarial lesions. These soon become dusky red or frankly purpuric and they no longer fade on pressure. The usual site is over the extensor surfaces of the knees, ankles and dorsum of the feet, arms,

elbows and forearms. It is also marked over the buttocks. The face is completely spared, but when the disease appears in an infant (quite rare), the face is often markedly involved.

Gastrointestinal manifestations Occur in two thirds of children : a) Colicky abdominal pain. b) Vomiting and may be hematemesis. c) Melena : either gross or microscopic.

Joint manifestations : Occur in two thirds. Knees or ankles : mild pain and swelling, (Periarticular edema). No tenderness.

Renal manifestations : a) In about 20% of cases frank acute nephritis develops b) Addis count is raised, indicating glomerular involvement in over half of the cases. Prognosis is less favourable than post-streptococcal form. While most cases make a complete recovery, persistent or recurrent proteinuria and hematuria occur in some. (Renal biopsy shows a progressive and irreversible lesion in the glomeruli).

Course and Prognosis : The course is variable, average duration 4-6 weeks, may be only few days or may smoulder for 1-2 years. Mortality rate in acute phase is less than 2% and the cause is gastrointestinal hemorrhage. Five to 25% of children with renal involvement have chronic nephritis.

Treatment : No specific treatment. Bed rest should be enforced until fresh lesions cease to appear.

- Penicillin only if hemolytic streptococci are isolated.
- Glomerulonephritis is managed in the usual lines.
- Cortisone is of no value.

PURPURA FULMINANS

This is probably an atypical form of anaphylactoid purpura, usually seen in young infants. It is rare. Large ecchymotic areas appear all over the trunk and extremities. Superficial gangrene is common. Anemia may be present due to hemorrhage into the skin. Recovery is rare.

DERMATOMYOSITIS

This is a chronic inflammatory condition involving the skin, subcutaneous tissues and the striated muscles. The pathological process can, and sometimes does involve the gastrointestinal tract and the C.N.S.

Dermatomyositis appears to be a vascular process leading to arteritis and phlebitis.

Etiology : unknown. An immunologic mechanism may play a role :

- a) presence of abnormal gamma globulin in serum of patients which has a binding affinity for one or more intranuclear nucleoprotein
- b) sometimes associated with agammaglobulinemia.

Clinical features : Age : 2-13 years, females are affected twice as males. Onset is insidious without apparent precipitating cause. There is general malaise, anorexia and low grade fever.

Weakness (first noted in legs when climbing upstairs) and stiffness of extremities are first indication of myositis. Painful tender muscles.

Erythematous facial rash with a malar distribution. Violaceous, erythematous periorbital edema (sometimes involving only the upper lid). Erythematous rash over the knuckles, elbows and knees. This is associated with scaling and later atrophy.

In most cases there is induration of the skin and subcutaneous tissues, this may progress so that there is generalized edema with pitting. Spleen is palpable in 15% of cases.

Course : The active phase may continue for several months and then complete reversal of symptoms and signs occur. The disease may be progressive for several years before the active process ceases, or it progresses rapidly to death from respiratory failure.

Sequelae : Atrophy of muscles. Decreased mobility of all joints. This limitation is secondary to atrophy and scarring of muscles. Destruction of subcutaneous tissues and muscles is associated with calcium deposits which may be circumscribed or extensive.

Treatment : Symptomatic and physiotherapy.

M. K. BADR EL-DIN

Chapter XX

MUSCLES, BONES & JOINTS

THE HYPOTONIC INFANT

Hypotonia is characterized by diminished resistance to passive motion of the limbs than normally expected for the age of the child. Normal muscle tone is dependent upon viscoelastic properties of muscle, joint and tendon resistance and the tonic stretch reflex.

The causes of hypotonia in children under 24 months of age could be classified according to the presumed site of pathology into :

- A. Hypotonia due to diseases of the central nervous system.**
- B. Hypotonia due to diseases of the spinal cord.**
- C. Hypotonia due to diseases of the spinal roots or peripheral nerves.**
- D. Hypotonia due to abnormalities of the myoneural junction.**
- E. Hypotonia due to diseases of the muscle.**
- F. Hypotonia due to diseases other than those of the neuromuscular apparatus.**

Hypotonia as a manifestation of central nervous system disease :

Congenital atonic diplegia : This is manifested in early infancy by marked hypotonia, retained deep tendon reflexes and mental retardation (chapter XVII).

Congenital cerebellar ataxia : Infants and children with this disease may have mild hypotonia and mild retardation of motor development during the first year of life. With standing, ataxia of the extremities and trunk appears. Late, staccato speech is noted, but horizontal jerky nystagmus may or may not be acquired. The symptoms improve with time.

Kernicterus : (chapter XIV).

Mongolism or Down's syndrome : It is diagnosed by the characteristic features. Hypotonia is marked in this syndrome (chapter XVII).

Tay-sach's disease (Ganglioside storage disease) : This disease is characterized by progressive nervous system degeneration with loss of function and the appearance of hypotonia usually between the ages of 4 and 8 months followed by progressively developing spasticity. Macular degeneration of the retina producing

the so-called «cherry-red spot» surrounded by a white halo of ganglioside-containing terminal neurons can be seen.

Hypotonia as a manifestation of spinal cord disease :

Infantile spinal muscular atrophy (Werdnig-Hoffman's disease) :

This is a familial disease, frequently fatal before puberty. Clinical manifestations may be present at birth or may appear in infancy from 2 to 18 months of age. Weakness is usually first evident in the lower extremities and gradually progresses upwards to involve the intercostal muscles, the tongue, muscles of deglutition and facial muscles. Deep tendon reflexes are gradually lost. Electromyography may reveal fibrillations, fasciculations and decreased number of action potentials.

Biopsy of muscles reveals atrophy of fibers in a «motor unit» or grouped distribution. There is atrophy of the neurons of the ventral horns in the spinal cord with replacement by astrocytes. The muscle atrophy which is noted is secondary to the neuronal disease.

Poliomyelitis : When it occurs in infants under 6 months of age, about half of them usually develop total or diffuse flaccidity (chapter IX).

Hypotonia secondary to disease of spinal roots or nerves :

Acute infectious polyneuritis (Guillain-Barre disease) :

It occurs 10 to 21 days after an upper respiratory infection and presents as a symmetrical and predominantly motor weakness and a less marked sensory impairment (chapter XVII)

Hypotonia due to disease of the myoneural junction :

Myasthenia gravis : The basic abnormality appears to be a block in neuromuscular transmission mediated by acetylcholine.

- a) *Transient myasthenia gravis* : Transient myasthenia gravis occurs in newborn infants whose mothers have had myasthenia gravis. The clinical disease begins a few hours to several days after birth and lasts for a week or two up to several months. When treated with anticholinesterase drugs, the symptoms improve or even subside.
- b) *Congenital myasthenia gravis* : This occurs in infants whose mothers do not have myasthenia gravis, and the symptoms persist throughout childhood. Prostigmine produces symptomatic improvement which is not complete.

Hypotonia due to primary disease of muscle :

Benign congenital hypotonia : These infants evidence muscular weakness and generalized hypotonia from birth. Tendon reflexes are present in some cases and absent in others. With time, symptoms improve spontaneously and no intellectual impairment is noted. These patients usually sit and walk later than the average. Muscle biopsy reveals no abnormality.

Universal hypoplasia of muscles : The infant is hypotonic at birth and the muscular weakness, although it improves slightly with time, persists throughout life. Deep tendon reflexes are usually present. The muscle mass in these patients is smaller than normal.

Muscle biopsy reveals no definite abnormality, and electrical reactions of the muscles are normal. Effective therapy is unknown.

Muscular dystrophy : Infants with congenital muscular dystrophy exhibit hypotonia and weakness from birth; there is weakness of all the voluntary muscles including the diaphragm. Muscle biopsy is characteristic.

Myotonic dystrophy : This is a familial disease characterized by progressive atrophy and weakness of distal muscles of the extremities, the muscles of the face, jaw and neck, progressive baldness and testicular atrophy. Symptoms suggestive of hypothyroidism often occur and the incidence of cataracts, both in patients and relatives, is high.

When myotonic dystrophy is manifest in infancy, there are hypotonia, poor sucking ability, feeding problems, and delayed progression of motor development. Mental retardation of variable degree becomes obvious as the infant grows older. The electromyographic pattern of myotonia can be detected as early as 9 months of age. Clinically myotonia is not usually detected before the child is 3 to 6 years of age. It is characterized by slow contraction and relaxation of muscle before a warm-up period; progressive improvement in function follows repetition of the movements.

Abnormal findings in muscle biopsies are not obvious.

Polymyositis : It is a rare and progressive disease in which there is both weakness and hypotonia. Muscle biopsy is characteristic of chronic polymyositis.

Diagnosis needs the interpretation of the clinical picture and the use of specific diagnostic tests as :

1. Muscle biopsy which could differentiate between myelopathic or neural atrophy and a primary myopathy. The histologic picture of myelopathic or

neural atrophy can be indicative of Werdnig - Hoffman's disease, congenital or infantile poliomyelitis, or peripheral polyneuropathy.

Patients with hypotonia and a histologic diagnosis of primary myopathy will include children with infantile muscular dystrophy, dystrophica myotonica, etc. Patients who are weak with a small muscle mass, but with no family history of muscle disease and in which the cerebrospinal fluid, nerve conduction times and muscle biopsy show no abnormality, are cases of «benign congenital hypotonia».

2. Electromyography and the determination of nerve conduction times can help in differentiation of different types of hypotonia.
3. Serum enzyme determination : elevated SGOT, SGPT, serum aldolase or serum LDH may occur in children with muscular dystrophy and with polymyositis. The earliest and most consistently elevated values in muscle dystrophy are those of aldolase and creatine kinase.

Children with hypotonia secondary to myelopathic or neurogenic atrophy or with dystrophic myotonia are likely not to have elevated concentrations of these serum enzymes.

PROGRESSIVE MUSCULAR DYSTROPHY

Progressive muscular dystrophy is a primary muscle disease of unknown etiology, characterized by progressive weakness and atrophy of the skeletal muscles with increasing disability and deformity. Muscular atrophy occurs in all forms, but pseudohypertrophy appears in one form. The disease is three times commoner in males than in females.

Pathology : Muscles are pale and fibrous in all types. Fatty infiltration is evident in the pseudohypertrophic type. Microscopically, muscle fibers vary in diameter and there is fragmentation of fibrils and hyaline and granular degeneration. Late in the disease, connective tissue replaces most of the muscle mass. The myocardium may show similar but less marked changes.

Clinical forms : All clinical forms of muscular dystrophy may be considered variations of a single disease, differing only in the muscle groups affected, the age at onset and rate of progression.

Pseudohypertrophic form (Duchenne type) : This is the most common form in childhood. The onset is usually before the fifth year of life and few patients live after the second decade.

The first manifestation usually appears in infancy as difficulty in standing or walking. There is gradual increasing weakness of the legs and waddling gait due to weakness of the gluteal muscles. There is also progressive weakness of the muscles of the shoulder girdle. This is evident from slipping of the arms upwards through the examiner's hands on trying to lift the child from the axillae.

The way the patient rises from a sitting position «climbing-up the legs» is characteristic. He turns on his side, flexes his knees and hips, and with his arms extended raises his trunk to assume a position of kneeling. The feet are brought forward and the legs extended at the knees. Then by bringing the hands successively to the shins, knees and thighs, he pushes his body to the upright position. On standing, there is severe lordosis with protrusion of the abdomen forward. Winging of the scapulae may be noted.

Muscles are usually involved symmetrically. Pseudohypertrophy is observed most frequently in the infraspinatus, supraspinatus, deltoids and triceps and calf muscles. Atrophy is usually first observed in the pectoralis major. As the disease progresses there is atrophy of muscles of the upper arm, gluteus and the anterior thigh muscles. Late in the disease all muscles of the legs, spine, pelvis and shoulder girdle are atrophic. Contractures and skeletal deformities may result. Tendon reflexes are normal early in the disease but become hypoactive or disappear with progression of the disease.

In late stages of the disease cardiomegaly and heart failure may be noted. One third of the cases are accompanied by mental deficiency.

Facioscapulohumeral form (Landouzy and Dejerine type) : The onset is usually between six and twenty years. The muscles first affected are those of the face and the shoulder girdle. There is inability to raise the arms above the head and the face is expressionless and masklike. The condition progresses slowly and over a period of years spreads to muscles of the pelvis and legs.

Limb-girdle muscular dystrophy: The onset of this type usually occurs in adolescence or early adult life.

- a) *Juvenile scapulohumeral muscular dystrophy of Erb* : The muscles of the shoulder girdle are first affected, winging of the scapulas and difficulty of elevating the arms above the head occurs.
- b) *Atrophic pelvifemoral dystrophy of Leyden-Moebius* : In this type the pelvic girdle and thigh muscles are first affected.

Diagnosis : The symmetrical and proximal distribution of muscular weakness, pseudohypertrophy, slow progression and absence of sensory changes and the occurrence of the disease in other members of the family are

important points in the diagnosis. Differential diagnosis of this condition includes polyneuritis and spinal muscular atrophy.

Prognosis : The disease is progressive.

Treatment : There is no specific therapy. Exercise is encouraged. Orthopedic and surgical correction of contractures may be resorted to.

CRANIOSYNOSTOSIS

Premature bony closure of the sutures of the skull results in deformities of the head and often damage of the brain and deterioration of vision. Genetic factors are responsible for some cases, while other cases are associated with vitamin D-resistant rickets, hypophosphatasia and idiopathic hypercalcemia.

ACHONDROPLASIA

Achondroplasia is a genetic defect of cartilage. The long bones of the extremities are markedly affected than the vertebrae and the head. The results in a disproportionate type of dwarfism.

Pathology : There is a disturbance of endochondral ossification caused by inability of the epiphyseal plate to produce a sufficient amount of columnar cartilage. The result is deficient growth of bones of endochondral formation.

Clinical manifestations : Characteristically there is short extremities with a head and trunk approximating normal size. The limbs are curved and their epiphyseal junctions enlarged. The forehead is prominent and the bridge of the nose is flattened. The mandible projects forwards. The thoracic kyphosis and the lumbar lordosis are usually accentuated.

Diagnosis : The thickness of the bones and their irregular epiphyseal ends as seen in the x-ray make the diagnosis possible even in newborns. The bones of the extremities are short and broad and show a mushroom-like broadening of the ends of the shafts.

Treatment : No specific treatment is known.

MORQUIO'S DISEASE

It is a genetically controlled disease. The neck is short. The spine and the chest become severely deformed. Fusion of cervical vertebrae and platybasia may occur. The thorax is short and broad with increased anteroposterior diameter and protruded sternum. Thoracic kyphosis is exaggerated. The abdomen is protruded. The arms are relatively long and reach the knees. There is genu valgum and flat feet. The joints are enlarged.

The condition is progressive as regards the deformity.

No specific treatment is available. Orthopedic treatment may prevent or correct the deformity.

OSTEOGENESIS IMPERFECTA

Osteogenesis imperfecta is a defect of the mesenchyme and of some of its derivatives «sclerae, bones and ligaments». It is characterized by increased fragility of bones. Osteoblastic activity of bones is defective. There are two forms :

Osteogenesis imperfecta congenita : in which fractures may occur early in utero, and the infant is born with deformed extremities. Fractures may also occur during delivery. The skull has wide membranes between the bones. Eyes are prominent and sclerae are blue. The chest and the spine are deformed. Many children with the severe form die soon after birth. Those who survive may have fractures of the extremities with very mild trauma. Callus forms rapidly but is replaced by weak bone. Serum levels of calcium and phosphorus are within normal ranges.

Osteogenesis imperfecta tarda : The child in this type appears normal at birth. Fractures usually do not occur until after the first year of life. Usually it is a milder form and the fractures cease with puberty. The bones of the extremities are long and slender. Blue sclerae is a common finding. Deafness is a late manifestation. The flaccidity of the ligaments and muscles result in repeated dislocations.

Prognosis : Many children with osteogenesis imperfecta congenita are stillborn or die soon after birth. Those who survive usually become severely deformed. Children with osteogenesis imperfecta tarda may also become deformed but they live longer.

Treatment : Orthopedic management may help by doing multiple osteotomies and threading the bones on a long nail which may need to be replaced by a longer one later on.

ACUTE INFECTIOUS ARTHRITIS

Acute infectious arthritis is usually preceded by an infection in other sites of the body. The common causative organisms are staphylococcus, streptococcus, pneumococcus and less commonly gonococcus, meningococcus, Hemophilus influenza, typhoid bacillus or one of the salmonella group of organisms. Big joints are more commonly affected. Clinically, the onset is sudden and is ushered by fever and local swelling with severe pain. Marked limitation of movements appear rapidly. If untreated, dislocation may take place. X-ray reveals widening of the joint spaces.

Treatment : Prompt systemic treatment with penicillin or one of the broad-spectrum antibiotics should be started immediately. Surgical drainage may be needed if the response is not rapid.

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INBORN ERRORS OF METABOLISM

Inborn errors of metabolism are hereditary defects, due to genetically determined absence of specific enzymes involved in the metabolic pathways. At present, at least over 100 of these have been discovered.

There are many mechanisms by which an enzymatic block produce clinically detectable disease :

- (1) Failure of production of biologically active end product, e.g. agammaglobulinemia and albinism.
- (2) Accumulation of precursor substances and intermediate metabolites before the site of enzymatic block. If these are toxic or biologically active, specific dysfunction results, e.g., galactosemia, phenylketonuria and congenital adrenal hyperplasia.
- (3) Abnormality or absence of an enzymatically regulated renal tubular transport mechanism may lead to, reabsorptive failure e.g. cystinuria and De Toni Fanconi Syndrome or excretory failure, e.g., primary renal tubular tubular acidosis.

Genetic abnormality, always leads to biochemical abnormality even without evidence of clinical disorder, depending upon the patterns of inheritance ("recessive" and "dominant" "penetrance" and "expressivity" - Autosomal and Sex linked).

Most of these conditions are rare autosomal recessive traits. However, the development of inexpensive screening procedures and the increased potential for treatment, have made them an important group of pediatric diseases. Some of the well known and more common syndromes are described below, others are described elsewhere in this book - e.g., hemoglobinopathies and coagulation defects in chapter XIV and phenylketonuria in chapter XVII.

Classification :

I. ERRORS IN PROTEIN METABOLISM

- A) Defective synthesis of plasma proteins :

- i) Deficiency of clotting factors e.g. congenital fibrinogenemia, hemophilia . . . etc. (see Chapter XIV).
 - ii) Defects of immunoproteins e.g. agammaglobulinemia.
 - iii) Other plasma proteins e.g. — Analbuminemia.
 — Haptoglobin deficiency. — Abeta-lipoproteinemia.
 — Ceruloplasmin deficiency (Wilson's disease).
 — Alpha-antitrypsin protein deficiency.
- B) Defective Hemoglobin Synthesis :**
 Hemoglobinopathies e.g. Thalassemia and sickle cell disease (chapter XIV).
- C) Defects of proteins of other tissues**
 Duchenne muscular dystrophy (X-linked) (Chapter XX) Xeroderma pigmentosum.
- D) Defects of Metabolism and transport of aminoacids :**
 Phenylketonuria, alcaptonuria, homocystinuria, hyperglycinuria, . . . Maple syrup urine disease (leucine, isoleucine and valine), Hartnup disease, Fanconi syndrome, cystinuria, cystinosis . . . etc.

II. ERRORS IN CARBOHYDRATE METABOLISM :

- A) — Defect in carbohydrate absorption e.g.
 - Malabsorption of lactose. — Renal glucosuria.
 - Malabsorption of glucose and galactose. — Lactosuria.
 - Malabsorption of sucrose and isomaltose.
- B) — Defects in monosaccharide metabolism e.g. Galactosemia, fructosemia ... etc.
- C) — Defects in glycogen metabolism e.g. glycogen storage disease.
- D) — Defects in mucopolysaccharides e.g. Hurler's disease (Chapter XVII)
Morquio's disease (Chapter XX).

III ERROR IN LIPID METABOLISM:

- A) — Hyperlipidemias e.g. cholesterolemia, skin xanthomatosis.
- B) Defects in steroid metabolism e.g. congenital adrenal hyperplasia.
- C) — The lipidosis e.g. Gaucher's disease, Niemann-pick disease and Tay-Sachs disease.

IV. ERRORS IN PIGMENT METABOLISM :

- A) — Porphyrin metabolism e.g. hepatic and erythropoietic porphyria.
- B) — Methemoglobinemias.
- C) — Primary hemochromatosis.
- D) — Crigler Najjar syndrome.

ERRORS IN PROTEIN METABOLISM

Defects in Plasma Proteins

Albuminemia : Congenital absence of albumin. No treatment is usually required because most cases were asymptomatic or exhibited only slight edema.

Haptoglobin deficiency : Haptoglobin is an alpha-2-globulin which binds free hemoglobin. Haptoglobin deficiency has been reported in March hemoglobinuria and also in asymptomatic persons.

Abetalipoproteinemia : Abetalipoproteinemia is an autosomal recessive defect in the synthesis of beta-lipoprotein. It is characterized by acanthocytosis and retinitis pigmentosa in early adulthood.

Analphalipoproteinemia (Tangier disease) : Congenital absence of alpha lipoproteins, leads to moderate reduction of cholesterol and phospholipids and storage of large amounts of cholesterol esters in reticuloendothelial tissues particularly the tonsils which becomes large with distinctive orange colour. Hepatosplenomegaly and lymphadenopathy may be present.

Ceruloplasmin deficiency : Hepatolenticular degeneration (Wilson's disease) is a recessively inherited disorder due to defect in the synthesis of ceruloplasmin, leading to abnormal accumulation of copper within the body.

Manifestations : Neurologic symptoms due to involvement of the basal ganglia, in the form of dysarthria, dysphagia, emotional lability, incoordination and involuntary movements. Pericorneal pigmentation, appearing as a narrow greengray zone overlying the outer margin of the iris (Kayser-Fleischer ring). Renal tubular dysfunction may also occur leading to aminoaciduria, phosphaturia and glucosuria.

Diagnosis is confirmed by the demonstration of low plasma ceruloplasmin 14 mg% (normal range 16-32 mg/160 ml.).

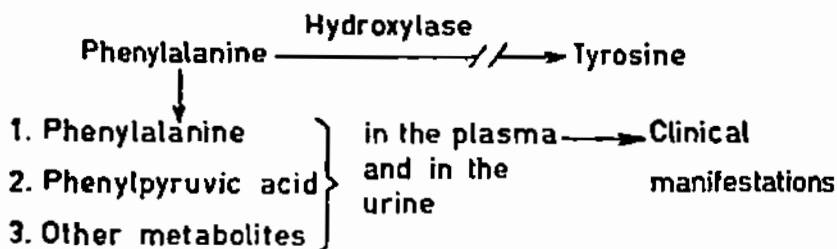
Treatment is by copper chelating agents e.g. penicillamine.

Alpha₁ - antitrypsin protein deficiency : Alpha₁ - antitrypsin is a normally circulating protein with in vitro antitryptic activity. It is synthesized in the liver. Deficiency of this protein is described in children with neonatal hepatitis and in adults with either hepatic cirrhosis or fibrosis. It has been reported to be deficient in cases with emphysema as it may inhibit bacterial proteinase which would otherwise destroy alveolar architecture.

Defects in Amino acid Metabolism

Aminopathies : are disorders due to defects in enzymes responsible for steps in the catabolism of aminoacids. They are characterized by elevated levels in plasma of the involved amino-acids, with overflow into the urine of the amino-acid or related metabolite. Examples of this group are :

Phenylketonuria (PKU) : Phenylketonuria (see also chapter XVII) is due to absence of activity of the hepatic enzyme, phenylalanine hydroxylase which converts phenylalanine to tyrosine, thus phenylalanine accumulates and is transaminated to Phenylpyruvic acid which then can be converted to other metabolites. Both phenylalanine and phenylpyruvic acid plus other metabolites are excreted in the urine (Fig 43.)



Fig, 43 : Phenylalanine hydroxylase enzyme deficiency

Restriction of dietary phenylalanine to maintain blood levels between 5 and 10 mg/dl and provision of adequate supply of tyrosine is essential for at least the first five years of life.

Albinism : Albinism is an inborn error in the formation of the pigment melanin in the melanosomes of the melanocytes. Generalized albinism is inherited as autosomal recessive trait. Melanin is formed from the amino acid Tyrosine.

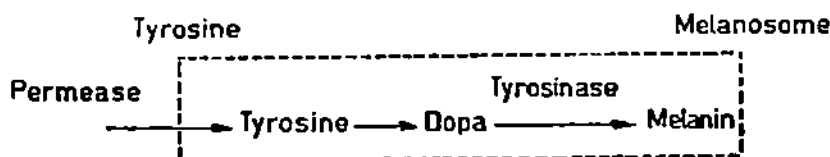


Fig. 44 : Melanin formation

Thus albinism could result from inactivity of tyrosinase enzyme (Tyrosinase negative variety) and this is the commonest variety or due to failure of the transport of tyrosine into the melanosome (Tyrosinase positive variety).

Albinos are characterized by extremely fair skin, fine silky hair, depigmented iris and numerous ocular abnormalities like, squint, nystagmus and loss of visual acuity.

Alkaptonuria : Alkaptonuria is, rare autosomal recessive defect, of phenylalanine-tyrosine metabolism due to defective activity of homogentisic acid oxidase. This results in accumulation in body and excretion of homogentisic acid.

The disease is usually detected in early infancy as the affected infant shows staining of the diaper black due to excess homogentisic acid which darkens on standing. In later life tissues become blackened particularly sclera, cheeks, nose, ears due to deposition of polymers of homogentisic acid. Later still arthropathy develops. No treatment is required.

Maple syrup urine disease : Is an autosomal recessive defect in the metabolism of the three chain branched amino acids, valine, leucine and isoleucine characterized by : (1) Urine with odor of maple syrup. (2) Gross mental retardation. (3) Progressively downhill course in first year of life. (4) Branched-chain-amino aciduria. (5) Branched-chain ketonuria.

Treatment consists of early restriction of these three amino acids.

Hartnup disease : Hartnup disease is characterized by; photosensitivity with development of pellagra-like skin lesions on exposure to

sunlight, occasional fully reversible (spontaneously or with treatment) cerebellar ataxia and consistent gross renal aminoaciduria (transport defect). Plasma amino acids are normal except tryptophan which is characteristically low due to defective intestinal absorption in addition to urinary loss. Large doses of nicotinamide may cause sustained remission of neurologic and cutaneous manifestation.

Fanconi Syndrome : De Toni-Fanconi syndrome (refractory rickets associated with multiple defects of the renal tubules) is discussed in chapter VII.

Cystinosis : (Lignac's syndrome) . It is essentially similar to Fanconi syndrome with the addition that cystine crystals are found all over the body.

ERRORS IN CARBOHYDRATE METABOLISM

Defects in Absorption of Carbohydrates :

Absorption of monosaccharides takes place in the small intestine, and digestion of disaccharides involves at least two steps—absorption into mucosal cells and splitting within the cells by the specific disaccharidase (lactase for lactose, sucrase for sucrose and isomaltase or isomaltose).

Congenital disaccharidase deficiency e.g. lactase, sucrase and isomaltase deficiency are rare inborn errors of metabolism.

Symptoms characteristically start after the ingestion of the disaccharide concerned e.g. lactose (milk) in lactase deficiency (lactose intolerance). Watery diarrhea, abdominal distension, vomiting are the characteristic symptoms, and the diagnosis is confirmed by demonstration of low stool pH and reducing substances in the stools and finally by peroral intestinal biopsy for histochemical studies.

Treatment consists of avoidance of the concerned disaccharide in the diet e.g. lactose free formula in primary lactose intolerance.

Defects in Monosaccharide metabolism :

Galactosemia (See also chapter XVII) When galactose is absorbed it is initially phosphorylated into galactose-1-phosphate by the enzyme

galactokinase in the liver. Galactose-1-phosphate is metabolized to glucose-1-phosphate in the presence of galactose-1-phosphate uridyl transferase enzyme.

Galactosemia is abnormal elevation in the blood galactose due to enzymatic defect in its metabolism. Two types are known : Galactose transferase defect and galactokinase defect, the latter is rare and relatively benign.

Clinical manifestations : Infants start, to be ill soon after initiation of milk feeding, the earliest manifestations include, restlessness, feeding difficulty, vomiting, jaundice, hepatosplenomegaly followed by nuclear cataract and mental retardation if the diagnosis is delayed, beyond the first month of life, manifestations of hepatic failure may also occur.

— *Diagnosis* is confirmed by the following laboratory findings:

1. Galactosuria in milk-fed infants, reduces Benedict's solution but not test tape.
2. Raised blood galactose "total blood sugar high" but glucose level is characteristically low.
3. Abnormal galactose tolerance test; seldom used as it precipitate hypoglycemic attack.
4. Definite diagnosis can be made by cytochemical study of RBCs for the enzymatic defect.
5. Generalized aminoaciduria is usually present.

— *Treatment :* Galactose free diet and surgical correction of the cataract.

Galactosemia due galactokinase defect is characterized by galactosemia, galactosuria and cataract without mental retardation or aminoaciduria.

Defects in glycogen metabolism (Glycogen storage diseases) :

Glycogen is a branched polysaccharide, composed of glucose units linked together by alpha 1-4 bonds. The branching links however, are formed by alpha 1-6 glucosidic bonds.

Both muscle and liver can form glycogen from glucose, this process involves the activity of glycogen synthetase which leads to formation of a linear chain with 1-4 glucosidic bonds, followed by the activation of another enzyme called amylo - 1,4 - - - 1,6 - transglucosidase (branching enzyme) which dislodges appropriate terminal chain segments and re-attaches them in the 1,6 position.

Both liver and muscle can degrade glycogen to glucose-1-phosphate and this

involves the activation of phosphorylase enzyme which break off 1-4 glucoside links in terminal chains but not the points of branching which requires another enzyme amylo-1,6 glucosidase (debranching enzyme).

The liver is peculiar to have glucose-6-phosphatase which frees glucose from G-6-P. There are many types of glycogenosis due to different specific enzymatic defects in the above pathway. The more common types are described briefly below.

TYPE I : HEPATORENAL GLYCOGENOSIS (VON JIERK'S SYNDROME)

Type I glycogenosis, is the commonest variety. It is due to deficiency of glucose 6-phosphatase. Manifestations starts at birth or in early infancy. There is abdominal enlargement with huge hepatomegaly, no splenomegaly, palpable kidneys, retardation of growth, and a doll-like appearance manifestations of hypoglycemia may be present.

Laboratory manifestations include : Hyperglycemia, raised blood glycogen impaired hyperglycemic response to epinephrin and glucagon, hyperlipemia and hyperlactic acidemia. Liver biopsy reveals abnormal accumulation of glycogen in the liver cells.

TYPE II: GENERALIZED GLYCOGENOSIS (POMPE'S DISEASE)

It is due to deficiency of the lysosomal alpha-1,4-glucosidase enzyme it is characterized by heavy glycogen deposition of many tissues particularly the heart, liver and muscles. Manifestations include, cardiomegaly with early heart failure often during neonatal period, muscular weakness and hypotonia, hepatomegaly and occasionally macroglossia. It is usually fatal within the first few months of life. Laboratory tests mentioned in type I are usually within normal range and the diagnosis is supported by demonstration of glycogen deposition in muscle and liver biopsy. The demonstration of the enzymatic defect is definitely diagnostic. The electrocardiogram shows shortened PR interval and widened Q.R.S. complex.

TYPE III : DEBRANCHING ENZYME DEFICIENCY (CORI'S DISEASES)

This type involves the liver, striated muscle and red blood cells symptomatology of hepatic involvement is similar to those of type I but more mild. In addition there is variable degree of muscle weakness and hypotonia due to muscular involvement. Laboratory evaluation shows partial reduction in the glycemic response to epinephrin and glucagon. The red cell glycogen content is strikingly elevated.

TYPE IV BRANCHING ENZYME DEFICIENCY (ANDERSON DISEASE)

Amvlo 1.4 - 1.6 - transglucosidase is characterized by deposition of abnormal glycogen (with decreased branching) in the liver, muscles, spleen and nervous system. Clinically characterized by growth retardation hepatosplenomegaly, cirrhosis and ascites. It is invariably fatal in the first few years of life. Hypoglycemia, ketosis and acidosis are absent in this type.

TYPE V : MUSCLE PHOSPHORYLASE DEFICIENCY (McARDLE'S SYNDROME)

This disorder is limited to the skeletal muscles which show abnormal accumulation of glycogen due to failure of degradation. The disease is characterized by: muscular weakness, pain after mild exercise and in severe cases myoglobi-nuria. Diagnosis is confined by the absence of hyperlacticacidemia after epinephrine and by specific enzymatic assay.

TYPE VI : LIVER PHOSPHORYLASE DEFICIENCY (HER'S DISEASE)

Clinically similar to type I however, the symptoms and signs are mild and can only be diagnosed by specific enzymic assay.

A. SAMIR KASSEM

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