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A REVIEW

ON

"An Assortment of Some Treatable Causes of Mental Subnormality"

Submitted for partial fulfilment
of the M.Sc. Degree in Childhood
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BY

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INTRODUCTION

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Mental subnormality is a problem frequantly encountered by : pediatricians neurologists and psychiatrists Increasingly, children with mental subnormality have become of concern to psychiatists, social workers and other health professionals as well.

This widening area of involvment reflects greater recognition of the many aspects of mental subnormality that pertain to the child, family and community.

Commonly associated issues include behavioural and emotional problems of the mentally subnormal, the stresses such a child places on the family, and the different kinds of remediation to be considered for the child. It is, hence, not only important problem to the affected persons, their families, and health professionals, but also to society at large.

AIM OF THE WORK

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The subject of mental subnormality is a multifacet problem, that involves all commounity services. The mentally subnormal individual needs extra care and special educational program to achieve such a state that they can care for themselves. This certainly takes much effort, time and money. Not only, they are not productive economically but also the house holding expendature of families with a subnormal individual is increased by about 40$ / week (Alm et al.,1986, Chetwynd, 1985, Buckle, 1984) which is definitely a great financial load on the family and hence the society. Regardless the drawbacks on the emotional balance of the family, the parents and sibilings.

Concerning the legal viewpoint of the problem, it is well known that such retarded individuals are easily suggestable and led. They could be abused and turned to be criminals. The law of almost all countries does not punish them, which means that the society has to protect them from being abused.

The subnormals are not only the medical professional concern, but the whole society concern, for the sake of its own wellfare. The prevalence of mental subnormality of any population is at least 3% (Nelson,1987) meaning that it is at least 1,350,000 individual in Egypt according to the national survey in 1984. In the study done by the center of criminology and sociological research 1970, about the prevalence of mental subnormality in primary schools in Cairo, Giza, and Kaliobia it is found to be 8.7% (Samia Ahmed, 1987). Hence refering to national survey 1984 the number of school age mentally retarded persons will be about 554,494 individual. Since this problem is accumulative, then at least a similar number is added each 5 years.

Unless we study this problem, mental subnormality in our society and plan for reducing and controlling it, we will definitely face a drastic situation. And the first step in studying a problem is collecting data about it and supplying them, even the few information to the agencies and professionals who care and deal with mental subnormality. It is hoped that this work may share a little in this concern.

DEFINITION

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Despite the work that has been done on the subject of mental subnormality, it is still confusing. This may be attributed primarily to the perplexity of the problem of mental retardation which defeats simple coceptualization.

Mental deficiency is used interchangeably with mental retardation. However, the World Health Organization has recommended the use of the term mental subnormality. There are other nomenclature which are in common use at different areas; such as feeble-mindness in Great Britain, oligopherenia in USSR, Scandinavians and amentia; which is recently used to refer to a terminal stage of degenerative illness (Kaplan, 1985).

Definition:

In this review, the term "Mental Subnormality" is used in place of the earlier term "Mental Deficiency" as the Mental Health Act of 1959 has superseded the Mental Deficiency Act of 1927, and new definitions have been imposed by the legal authority (Vernon,1962).

The twentieth century has witnessed a number of significant changes in the definition of mental subnormality. The most recent definitions reflect a growing awareness of the negative consequence that may be

involved in mislabeling an individual.

Doll's Definition:(1941)

For many years the standard definition for mental subnormality was that of Edgar Doll. In his words; "Six criteria by statement or implication have been generally considered essential for an adequate definition and concept."

There are: (1) Social incompetence

(2) due to mental subnormality

(3) which has been developmentally arrested

(4) which appeears at/before maturity

(5) is constitutional in origin

(6) and is essentially incurable(Doll,1941)

This early definition resembles the one that is commonly used today except for two important differences: Doll theorized a causal link between the mental subnormality and social incompetence. Today, social incompetence is not viewed as a necessary by-product or result of mental subnormality. With proper training, many mentally subnormal individuals can function efficiently and well in their societies. In another word, if a person scores low I.Q. tests but has adequate social adaptation skills, many professionals will not consider him subnormal at all.

The second difference is that Doll beleived that the condition was incurable. With special eduacation and training, the I.Q. scores can be increased;i.e.,the level of the mental functioning does not necessarily remain stable, particularly for those individuals who are only mildly or moderately subnormal.

Grossman's A.A.M.D. Definition: (1973)

The definition that is currently accepted by most authorities is the one that has been adopted by the American Association of Mental Deficiency (AAMD), the major organization for professionals on the field of mental subnormality.

First presented by Heber in 1961, it was later revised by Grossman to read "Mental subnormality refers to significantly subaverage general intellectual functioning existing concurrently with deficits in adaptive behaviour, and manifested during the developmental period".(Grossman,1973)

Clarke and Clarke's Definition: (1974):

Mental retardation has been defined as general intellectual functioning below the range of normal, beginning during the first 16 years of life and associated with impairment of maturation, learning and social adjustment.

Maturation refers to the rate of development of self-help skills in infancy and early childhood. Learning is the capacity to acquire new information and social adjustment refers to the indivisual's ability to adapt within the community to activities of adult life, including those at work and within home(Joel Herskowitz and N.Paul Rosman,1982).

Thus in order to be classified as mentally subnormal, a person must be well below average in both measured intelligence and adaptive behaviour.

1-Adaptive behaviour: It is an important element of the AAMD definition, and much more weight is given to its role in determining whether or not a person is subnormal. Thus a child can conceivably score low on a standard intelligence test but has adequate adaptive skills. Such adaptive skills refer to the person's effectiveness in social skills, communications and daily living skills and how well the person meets the standards of personal independance and social responsibility expected of his or her age by his or her cultural group. useful scales are Vineland Adaptive Behaviour Scale and American Association Of Mental Deficiency Adaptive Behaviour Scale. The adaptive behaviour skills are age and situation specific and involve more than being to survive "on the street"(DSM

III R,1987).

2-Intellectual functioning:

The phrase "subnormal general intellectual functioning" in the AAMD definition refers to performance in the standardized test of intelligence that is more than two standard deviations below the mean. For the commonly used tests such as the Stanford-Binet or Revised Wechsler-Intelligence Scale for Children (WISC-R), and Kaufman Assessment Battery For Children, a score of 68 or 69 or below, now calssifies a child as subnormal (DSM III R, 1987).

Social System Definition:

There is a related viewpoint that is consistent with the trend towards acknowledging the harmful effect of labelling a person subnormal. The sociologist Jane Mercer (1973) posits that it is the individual's social system that determines whether or not he is subnormal. Most mentally subnormal children, particularly the higher functioning one, do not officially become subnormal until they enter school, a social system that has a certain set of expectations that some children do not meet. Such children may not perform in a subaverage way within their own neighbourhood.(Mercer,1973)

Behavioural Definition:

Some professionals espouse a definition that reflects a learning-theory orientation. Bijou Sidney (1966), suggests that "a subnormal individual is one who has limited repertory of behaviour shaped by events that constitute his history"

A subnormal behaviour is a function of observable social, physical and biological conditions, all with the status of independent variables. The behavioural definition carries with it the implication that some apparently subnormal children can be considered "normal" when the consequences of their behaviour are appropriately arranged so that their thinking and actions more accurately reflect their mental abilities (Bijou Sidney, 1966).

Conclusively, the definition of mental subnormality requires more than the demonstration of an intellectual inferiority or defect. It involves both the degree and character of the defect that results in a wholy or partly inadequate independent social adjustment. Moreover, this inadequecy must be demonstrated in the environment in which the individual is expected to live.

EPIDEMIOLOGY

It is important to recognize that almost 3% of normal population falls 2 standard deviations below the mean on any intelligence test(Nelson,1987). The figure is much higher than most prevalence studies have revealed, though it would include the large number of people of limited intelligence whenever come to attention of any specialized agency for the mentally handicapped(Kendell,1988).

Of more value is the field surveys which have combined intelligence test scores with other social and educational criteria. The classic study of this kind was conducted by E.O.Lwis,1929. This study revealed:-

1- A similar result to Kaplen,1983 close to the figure 0.8% near to the figure by Okasha,1988, which represents the severely mentally retarded.

2- Higher incidence in rural area than in urban one. This was explained by Innes et al.,1968, by that persons of normal I.Q. tend to move to cities while limited I.Q. or retarded persons remain in their rural societies.

3- For each severely retarded individual there are 4 moderately and 15 mildly retarded persons. Innes et al,1968, found that the incidence of severely and moderately mental retarded is constant, aproximatly 0.37% while the incidence of mild retardation is considerably

varient. They explained that by the effect of social and educational services provided by the community which do influence the mild retardation, yet do not benifit either the moderate or severe mental retardation.

4- Variable incidence with age, owing to principally to the need to adapt to the changing environmental circumstances. It increases during school years and reaches its peak by 10 to 14 years. The incidences then decreases in late adolescence when the scholastic demands are no longer an obstacle to function adequacy (Kendell,1988, Nelson,1987, Kaplan,1983).

Davie et al.1972 found a close correlation between overcrowding, poverty, irregular unskilled employment and educational backwardness, which draw the attention to the importance of the socioeconomic view of mental subnormality. Counting on the fact that 60 to 70% of mentally retarded are of mild degree and can benifit from environmental, social, educational and medical services prevalence is much influenced.

There is a marginal increase of mental retardation among males to females 1.5 to 1. Benrose,1972 has claimed that this would be explained on the grounds that males intelligence is more widely distributed about the mean than females. It is also probable that mentally retarded males

are more likely utilise services than females, who often can be maintained at home for a longer period with less social distress than men..

Socio-Cultural Approach

The child who is born with normal hereditary equipment can still be reduced to imbecility by environmental causes such as birth trauma, nutritional defeciency during childhood, education,..etc. Such cases represent about 5%. It was seen that sibilings reared apart have been found to show a markedly lower correlation coefficient than sibilings reared together, mainly due to the different environment (Tredgold, 1947). It has also been found that a large majority of the pupils of special schools and inmates of institutions come from lower strata. Against this fact, is that the backward children of the wealthy are placed in private schools and homes, and their number is relatively small because of the smaller size of the family in the better educated classes. (Slater and Roth, 1979).

In the USA, the overwhelming majority of the mentally retarded come from the lowest socio-economic group. The exact statistics are not available, but the estimates of the the frequency of mental retardation in this segment of the population range between 10% to 30% as contrasted with 3% in the total population (Kaplan, 1983)

Due to such low socio-economic state, many medical problems arise; the mother is frequently malnourished and

is likely to have little if any prenatal care; consequently, pre-toxemic and toxemic state are seen. The diet lacks the necessary minimum of vitamins and minerals.

Maternal infections are treated with delay or not at all. Also, uncontrolled diabetes of the mother, prematurity, all these factors resulting from a low socio-economic state, will bring about brain damage (Pasamanick,1963).

After birth, the baby may never have regular post-natal care; routine check-ups, immunizations, and may suffer from many medical conditions that if were treated in their course, would have been without mental insult.

Several studies about malnutrition and mental retardation cleared the relationship between the mental retardation and substandard diet. (Lloyd,1976), such as chronic protein depletion in infants and young children which causes irreversible mental retardation of mild to moderate degree (Cravioto,1968).

As the frequency of backwardness and mentally defectives are commoner in the lower economic and cultural states of home, the question raised, could the low or limited intelligence of one or both parents be responsible for the low social state rather than itself being the

direct cause of mental retardation?

In a study done by Dennis, 1976 changes in the I.Q. of about 16 points over a period of 6 years were observed after the removal from adverse environmental conditions: such as cruelty and neglect, which consequently provide less love, less attention, less stimulation, and less encouragement for the children in their initial attempts at exploration and self expression, as well as providing bad nutrition, such phenomenon was called "pseudo-feeble mindnes" (Clark, Clark, Reinman 1958).

The preliminary results of the study conducted by Herber and Garber 1970 at the University of Wisconsin indicate that children of retarded parents can develop intellectually along normal lines if given an intensive enrichment program (Herber and Garber, 1970).

CLASSIFICATION

CLASSIFICATION

There are two popular ways in which the subnormals are classified: by the degree of severity and by the cause of subnormality. Each of these has its own advantages and disadvantages, and depending upon the orientation of the persons or the group of professions; the system of classification chosen, e.g., behavioural, educational or medical. It is not uncommon for children to be classified by both methods.

(A) Classification by Severity:

One of the oldest systems; although practical, is to classify subnormals into feeble-minded, imbecils and idiots. This subdivision, originally devised for administrative use only, gained value by being linked with the mental age and intelligence quotient as assertained by intelligence tests(Slater and Roth, 1979).

(1) Idiots:

I.Q. is below 20; persons in whose cases, there exists mental defectiveness of such a degree that they are unable to guard themselves against common physical dangers.

(2) Imbecils:

I.Q. is between 20-50; persons in those cases, mental defectiveness, though not amounting to idiocy, yet

is so pronounced that they are incapable of managing themselves and their affairs, in the case of children of being taught to do so.

(3) Feeble-minded:

I.Q. is between 50-70; persons, though their mental defectiveness does not amount to imbecility, yet require care, supervision and control for their own protection, or for the protection of others, or, as in the case of children, appear to be permanently incapable of receiving proper benefit from instruction in ordinary school.

Although this classification is useful, the division is arbitrary because the gradation from one level to the next is continuous.

Recently, 1973, the most generally accepted approach to classification is to consider subnormality along a continuum of degree to which the individual's intelligence is lowered.

The classification of the AAMD and the one used primarily by educators present two of the most common of these systems.

(1) AAMD System:

Most professionals agree to that , the most useful classification based on the severity is that of the AAMD.

This is because the terms used; mild, moderate, severe and profound retardation, do not convey the degree of negative stereotyping that earlier description (idiot, imbecil and feeble-minded) has implied. They can apply universaly to many other traits. Additionally, they are words that are relatively descriptive of the functioning of the child.

The DSM 111-R 1987 adopted this system classifying the defectiveness into four types as follows:

317.00..Mild mental retardation I.Q.:50-55 to 70

318.00..Moderate mental retardation I.Q.:35-40 to 50-55

318.10..Severe mental retardation I.Q.:20-25 to 35-40

318.20..Profound mental retardation I.Q.:below 20-25

There is also a fifth subtype;

319.00..nspecified mental retardation; which should be used when there is a strong presumption of mental retardation but the individual is intestable by standard intelligence tests.

Also the Egyptian Diagnostic Manual of Psychiatric Disorder 1979, used this system with the addition of two other categories, namely:

01.0...Borderline mental retardation I.Q.: 68 to 83

01.1...Mild mental retardation I.Q.: 52 to 62

01.2...Moderate mental retardation I.Q.: 36 to 51

01.3...Sever mental retardation I.Q.: 20 to 35

01.4...Profound mental retardation I.Q.: below 20

01.5...Unspecified mental retardation : reserved for patients whose intellectual functions can not be evaluated precisely but who are recognised clearly as subnormal.

In the international classification of mental diseases 9 (ICD9) the classification of mental retardation is as follows:

317.0...mild mental retardation

318.0...moderate mental retardation

318.1...severe mental retardation.

318.2...profound mental retardation.

319.0...unspecified mental retardation.

In the draft for field trial of ICD10 by the World Health Organization division of mental health, mental retardation is clasified as:

F70...mild mental retardation	I.Q.50-69	9-12years.
F71...moderate mental retardation	I.Q.35-49	6-9 years.
F72...severe mental retardation	I.Q.20-34	3-6 years.
F73...Profound mental reteradation	I.Q. < 20	<3 years.

F79...Unspecified mental retardation.

(2) Educator's System:

While not officially sanctioned by any official organization, these categories: educable, trainable and custodial retards have survived over the years among educators because they are particularly oriented towards describing the educational needs of retarded children.

In general, educable retards (EMR) have been considered as those who can be taught the basic academic subjects. Whereas the program for trainable retards (TMR) concentrates more on functional academics with emphasis on self-help and vocational skills. Custodial retards are those who require special care, usually within an institution, and until recently, these children were not educated within the public school system(Kirk and Jonhnson,1951, Kirk,1964)

A disadvantage of this system of classification is that some educators have at times taken the categories too literally with the result that some children labelled as trainable retards were denied access to learning academic subject matter within their intellectual reach. Intelligence test scores are not so reliable and valid that they can be used to determine entirely diferent educational objectives for one child with an I.Q. of 51; classified as educable, and the other with an I.Q. of 49; classified as trainable.

Mental retardation and functional capacity

Severity	mild	moderate	severe
I.Q.	50-75	25-50	<25
Educability	yes	no	no
Trainability	yes	yes	no
Independent living	often	with supervision	no,custodial residential care
Routine self-care	yes	yes	limited or none
Vocational capability	often	sheltered workshop	limited or none

(Joel herskowitz and N.Paul Rosman, 1982)

(B) Classification by cause:

Classification of mental subnormality according to causes is very difficult. Moreover, it has several serious disadvantages. First, its utility has limited value for some, particularly, special educators, since knowledge of the cause is not of much help in the determination of an educational program for the child. Mental subnormality, either idiopathic or of known causes, does not always differ in the behavioural characteristics.

Second, the diagnosis of brain injury is not as accurate as popular opinion would imply. (Cruickshank and Paul, 1971) Only the most obvious cases can be diagnosed with certainity. The neurological procedures are still too crude to be reliable indicators of many cases of brain damage.

One of the oldest approaches to classify the mentally subnormal involves grouping them on the broad basis of whether or not they owe their condition to brain damage.

At one time it was popualr to refer to exogenous and endogenous causes. Exogenous mental subnormality referred to cases in which the subnormality was due to brain injury, whereas endogenous mental subnormality was used to indicate either hereditary or environmetal factors. Today, the same

basic differrentiation is made between injury to the brain on the one hand and hereditary social influences on the other, but the term "organic" or simply "brain injury" or "brain damage" has replaced the term exogenous, while the term "cultural-familial" has been used instead of endogenous. Cultural denotes the possible influence of social factors (e.g. poor environment) or sometimes called idiopathic factors and familial implies possible genetic factors (Slater and Roth,1979)

Only in about 1-15% of cases of mental subnormality can the cause be determined with some degree of certainity, because the less severe the degree of subnormality, the less likely it is that a case will be identified, no matter what is, e.g.,genetic abnormality, chromosomal disturbance, brain damage, environmental deprivation..etc. Its influence will be so subtle that it is hard to detect.

On the other hand, the fact that vast majority; 85% of the mentally subnormal fail into the mild classification means that very little can be said about the etiology of most cases. When the cause of a child's subnormality is unknown, it is likely to be referred to as cultural-familial retardation (kaplan, 1985,1983).

In AAMD terminology the phrase "psychological disadvantage" rather than "cultural-familial" is used in referring to children whose retardation is of unknown origin. While this term does not do much more and pinpoint definite causation of mental subnormality, it more clearly distinguished the genetic contribution from social determinants of mental subnormality (Kaplan, 1983, 85).

AETIOLOGY

AETIOLOGY

According to the researcher's opinion

(1) Metabolic Disorders:

- Defects in amino acid metabolism.
- Defects in carbohydrate metabolism.
- Defects in lipid metabolism.
- Miscelaneous metabolic disorders.

(2) Genetic Abnormalities:

- Abnormalities of autosomes.
- Abnormalities of sex chromosomes.
- Autosomal dominant disorders.
- Recessive or unknown genetic disorders.

(3) Prenatal Factors:

- Maternal and fetal infections (intrauterine infections).
- Fetal irradiation.
- Prematurity.
- Seasonal and geographical variations.
- Prenatal nutrition.
- Fetal alcohol syndrom.
- Socio-economic factors.
- Prenatal emotional stress.

METABOLIC DISORDERS

(i) Defects in Amino Acid Metabolism:

- Phenyl-ketonuria. see next chapter treatable causes
- Maple syrup urine disease (Menke's disease).see next chapter treatable causes
- Hartnup disease.
- Cystinuria.
- Urea cycle disorders:
  * Citrolinuria.
  * Hyperammonemia; types 1,11.
  * Argino-succinic aciduria.
  * Hyperarginemia.
  * Hyperxornithinemia.
- Hyperglycinemia.
- Histidinemia.
- Malabsorption of methionine.
- Oasthonse disease.
- Homocystinemia.
- Cystathioninemia.
- Hyperprolinemia.
- Tyrosinemia.
- Richner Hanhart syndrome.
- Hyperlysinemia.
- Pseudo-hypertrophic muscular dystrophy.

(ii) Defects in Carbohydrate Metabolism:

- Galactosemia. see next chapter treatable causes
- Glycogen storage diseases (glycogenoses).
- Mucopolysaccharidosis:
  - *Hurler syndrome: mucopolysaccharidosis type 1.
  - *Hunter syndrome: mucopolysaccharidosis type 11.
  - *Sanflipo syndrome: mucopolysaccharidosis type 111.
- Idiopathic hypoglycemia. see next chapter treatable causes

(iii) Defects in Lipid Metabolism:

A) Metachromatic leukodystrophy (sulphatide lipidosis).

B) Progressive leukoencephalopathies.

-Schilder' disease.

-Krabbe' disease.

-Pelizaenes Merzbacher disease.

C) Degeneration of cerebral grey mattar (neuronal storage disease):

-Tay Sach's disease.

-Sandhoff disease.

-Generalised gangliosidosis (GM.gangliosidosis type 1)

-Juvenile GM1 gangliosidosis (GM1 gangliosidosis type 2)

-Juvenile GM2 gangliosidosis (GM2 gangliosidosis type 3)

-Late infantile and juvenile cerebromacular degeneration

1) Bielschowsky syndrome.

2) Spielmeyer Vogt or Batten's disease.

3) Kuf's disease.

- Niemann Pick disease.

- Gaucher's disease.

(iv) Defects in Calcium Metabilism:

- Pseudo-hyperparathyroidism.

- Idiopathic hypercalcemia.

- Lowe syndrome.

(v) Miscellaneous Metabolic Disorders:

-Hypothyroidism. see next chapter treatable causes

GENETIC ABNORMALITIES

(i) Abnormalities of Autosomes:

a) Aneuploidies: 21-trisomy (mongolism)

18-trisomy

13-trisomy

22-trisomy

b) Structural aberrations (deletions):

- chromosomes No.4, 5.
- chromosome No. 7.
- chromosome No. 18.
- chromosomes of the D-group 13.
- ring chromosome 14.
- ring chromosome 15.
- ring chromosome 17.
- chromosomes of the F-group.
- chromosomes of the G-group.

(ii) Abnormalities of Sex Chromospmes:

- Klinefelter's syndrome.
- Klinefelter variants.
- Turner's syndrome.
- Turner-like syndrome.
- Triple X syndrome.
- XXXX and XXXXX females.
- X-linked mental retardation.
- Fragile X syndrome.
- Martin Bell Renpenning syndrome.
- A new syndrome.
- Borjeson, Forssman and Lehmann syndrome.
- Terminal deletion of Y chromosome.

(iii) Autosomal Dominant Disorders:

- Dystrophia myotonia.
- Tuberous sclerosis (Epiloia)
- Neurofibromatosis (Von Recklinghausen's disease).
- Huntington's chorea.
- Sturge Weber disease.
- Von Hippll Lindau disease.
- Arachnodactyly (Marfan's syndrome).
- Achondroplasia (chondrodystrophy).
- Cranio synostosis.
  * Apert syndrome.
  * Crouzon's disease.
- Treacher Callins syndrome.
- Uveal colobomata, cleft lip and palate and mental retardation.
- Hypertelorism.

(iv) Recessive or Unknown Genetic Disorders:

-Anencephaly.
-Porencephaly.
-Agyria and Pachygyria.
-Agenesis of corpus callosum.
-Laurence Moon Biedl syndrome.
-Prader Willi syndrome.
-Hydranencephaly.
-Microcephaly.
-Ataxia telaniectasia
-Carpenter syndrome
-Cohen syndrome.
-Norrie's disease.

-Menkes Kinky hair syndrome.

-Xeroderma pigmentosum.

-Sjogren and Larsson syndrom.

-Goldenhar syndrome.

-Branchial dysplasia and mental deficiency.

-Keratoconus pesticus circumscriptus and mental retardation.

- Congenital universal alopecia and mental deficiency.

- Mental retardation, short stature.

- Schinzel Giedion syndrome.

- Hydrocephaly see next chapter treatable causes.

-Cockayne's syndrome

-Marden Walker syndrome

DEFECTS IN AMINO ACID METABOLISM

(1) Hartnup Disease:

This is a rare disorder, named after the family in which it was detected. It is transmitted by a single recessive autosomal gene. The metabolic defect involves defective intestinal absorption and renal tubular reabsorption of tryptophan.

The biochemical findings include:

1- Massive amino aciduria.

2- Normal concentration of plasma amino acids, except for tryptophan. This means that there are faulty tubular reabsorption and impaired intestinal mucosal absorption of tryptophan. As a result, nicotinic acid synthesis is decreased

3- Increased excretion of indican and its indoxyl derivatives.

The cutaneous photosensetivity is the main character of this disorder. The unprotected skin becomes rough and with further exposure to sun it becomes red and pellagra-like rash develops. Episodic cerebellar ataxia may be seen together with mental deficiency. Large doses of nicotinamide may help improving the neurologic manifistation but not the mental retardation (Nelson,1987).

(2) Hyperglycinemia:

There are two variants of this disorder; ketotic and non-ketotic hyperglycinemia. In the ketotic hyperglycinemia, there are episods of severe ketosis and acidosis, hyperglycinemia is secondary to elevated levels of several amino acids in blood. Clinically, there are seizures, mental retardation, vomiting, dehydration, ketosis and acidosis. (Sorcano et al,1967)

The second variety; the non-ketotic hyperglycinemia, which is inherited as an autosomal recessive traits, results from a genetic deficiency of the glycine cleavege enzyme system. Clinically, manifistations appear few days after birth, in the form of poor feeding, difficulty in suckling, failure to thrive, deep coma and death. In mild cases who survive, the child suffers from mental retardation, convulsions and spasticity.

In both forms there are severe hypergylcinemia and hyperglycinuria. The non-ketotic form is differentiated from the ketotic one by the high ratio between glycine in cerebrospinal fluid and glycine in blood (Nelson,1987).

(3) Histidinemia:

This condition is due to deficiency in the histidinase enzyme, which is normally present in the liver and skin. It is transmitted as an autosomal recessive trait. This

enzyme is responsible for the conversion of histidine into urocanic acid and its deficiency results in increased levels of histidine in blood and urine. There are also other metabolites that are found in urine; namely imidazole pyruvic, imidazole lactic and imidazole acetic acids. Imidazole pyruvic acid reacts with ferric chloride as does phenylpyruvic, misdiagnosing a histidinemic case as one of phenylketonuria during screening tests. Clinically, the persons with histidinemia suffer from impaired speech, retarded growth and some have mental retardation (Nelson,1987 and Barbara K,1987).

(4) Cystinuria:

This term refers to at least three closely related disorders that are inherited in an autosomal recessive manner. These are: cystinosis, sulfide oxidase deficiency and -mercaptolactate cysteine disulfiduria. The defect involves an absent or nonfunctioning transport system of a group of amino acids: cystine, arginie and ornithine which are excreted in massive amounts in urine. Renal calculi result from cysteine as it is the least soluble amino acid. (Nelson,1987)

Mental retardation in cases of cystinuria were recorded by Berry (1956) in sibilings of cases of atypical osteogenesis imperfecta.

(5) Homocyteinemia:

Homocysteine is an intermediary compound of methionine degradation which is normally remethylated to methionine. It is ordinarily not detected in plasma or urine but defects at different enzymatic steps can produce homocyteinemia and homocysteinuria. The classic form is due to deficiency of the enzyme cystathionine synthetase which is an autosomal recessive condition. Its prevalence is 1/200,000 live births.

At birth the infant is normal but with non-specific manifistations such as failure to thrive and developmental delay. At three years of age, ocular manifistations such as ectopia lentis, severe myopia, astigmatism, glucoma and others together with progressive mental retardation, skeletal abnormalities resemble Marfan's syndrome. (Nelson,1987*Kaplan,1983)

(6) Cystathioninemia:

Cystathionine is an intermediary metabolite of methionine degradation by the cystathioninase enzyme into homoserine and cysteine. This enzyme needs vitamin B'6 as a co-factor.

The condition is inherited in an autosomal recessive manner. In addition to cystathioninemia there is massive cystathioninuria. (Nelson,1987*Kaplan,1983)

(7) Hyperprolinemia:

Two distinct types of hyperprolinemia are known, in which excessive amounts of proline are present in both blood and urine. The first is due to a defect in proline oxidase and the second is due to a defect in proline dehydrogenase. Both seem to be inherited as autosomal recessive conditions and show mild mental retardation. (Nelson, 1987)

(8) Tyrosinemia:

This condition is due to the absence of the soluble fraction of tyrosine transaminase. The biochemical findings resulting are high tyrosine in blood and para-hydroxyphenyl pyruvic acid in urine.

It is an autosomal recessive condition. There are, apart from the mental retardation, other congenital malformations.

(9) Richner Hanhart Syndrome:

This autosomal recessive disorder results in mental retardation, plasma and plantar punctate hyperkeratosis and herpetiform corneal ulcers. Patients have both tyrosinemia and tyrosinuria.

(10) Hyperlysinemia:

This is a rare autosomal recessive disorder of which only 20 patients have been reported. It is due to deficiency in the putative enzyme complex lysine ketoglutarate reductase saccharopine dehydrogenase system. There are severe mental and physical retardation, joint laxity and convulsions. Biochemical findings are hyperlysinemia, saccharopinemia, lysinuria, saccharopinuria and homocitrulline and homoarginine in body fluids. (Nelson,1987).

(11) Pseudohypertrophic Muscular Dystrophy (Duchenne type):

In its classic form, it occurs only in boys. A history of sex-linked inheritance is obtained in about 50% of cases. A mild mental defect is a commonly associated abnormality in the Duchenne form of muscular dystrophy. The mean I.Q. of these children is about 20 points below the normal mean and a frank mental defect is present in about 25% of cases. (Dubowitz,1965)

DEFECTS IN CARBOHYDRATE METABOLISM

(1) Glycogen Storage Disease (GSD):

A variety of disorders result from derangements of synthesis or degradation of glycogen or of its subsequent utilation.

Lewis (1962) mentioned the one type associated with mental subnormality that was named after him: Lewis aglycogenesis, now called GSDO. It is the form in which the basic defect is inability to synthesize glycogen in adequate amounts due to absence of activity of the enzyme glycogen synthetase.

The glycogen synthetase activity is deficient in the liver but normal in muscles and both the red and white blood cells. Glycogen concentration is low; less than 2% but not absent in the liver, and normal in the muscles. This differential involvement of tissues reflects the fact that different lsozymes of glycogen synthetase exist in various tissues.

Clinically, early morning convulsions associated with hypoglycemia are typical symptoms. There is an associated hyperketonemia. The hypoglycemic convulsions and mental retardation can be avoided if the patient is given frequent meals rich in protein. (Nelson,1987)

No evidence of heterozygosity was demonstrated in the parents but presumptively it is an autosomal recessive condition (Lowis,1963). In a study of 2 families by Lewis 1963 and Parr 1965, the prognosis has not been good. In the first family, one child was significantly mentally subnormal, while in the second family all four children had died.

(2) Mucopolysaccaridosis:

Mucopolysaccaridosis comprise a group of diseases which have in common, disorders in the metabolism of mucopolysaccharides and which are separated by genetic, clinical and biochemical characteristics.

a) Hurler's syndrome:

- mucopolysaccharidosis type 1 (MPS 1).
- gargoylism, dysostosis multiplex,
- lipochondrodystrophy.

This disorder is a metabolic disturbance which affects both skeletal and soft tissues. Although the metabolic disturbance is present at birth, yet most of the manifistations develop slowly in the post-natal live (Strauss,1948).

There is hepatosplenomegaly which is responsible for the abdominal enlargement, as well as dwarfism, peculiar facial features that raise the name gargoylism, include confluent eyebrows, thick lips, large tongue and coarse features. Hypertolorism and hydrocephaly are some times present. These facial features could be differentiated from cretinism by X-ray examination. The radiological findings include elongated sella turcica, breaking of the thoracic spines in the lateral view, kyphosis, club-shaped lower ribs, thickening of long bones and mis-shaped metacarpal bones and phalanges. (Kaplan,1983)

Benda (1952, Jervis (1950), Reilly and Lindsoy (1948) have reviewed the syndrome in detail. The disorder is genetically determined and inherited as an autosomal recessive traits. The basic metabolic disturbance result in accumulation of abnormal intracellular material which affects the cells and the structure of many organs. Substances such as dermatoid sulfate and heparitein sulfate are found in urine and tissues as well as increased level of gangliosides in the brain. There is also decrese activity of -galactosidase (Kaplan,1985).

b) Hunter syndrome:

= mucopolysacchridosis type II (MPS II)

This syndrome is characterised by physical and biochemical resemblance to Hurler syndrome but with a slower course, milder mental retardation and no corneal opacities. It affects males only and is transmitted as a sex linkd recessive trait (Kaplan,1985).

c) Sanflippo syndrome:

= mucopolysaccharidosis type III (MPS III).

This syndrome is inherited as an autosomal recessive trait and is characterised by less severe somatic alteration but severe mental retardation. Heparitin sulfate is found in urine and tissues in large amounts. There is decreased activity of -galactosidase (Kaplan,1983).

d) Lesch Nyhan syndrome:

The syndrome affects males and is sex-linked recessive. It is characterised by elevated uric acid in blood due to deficiency in hypoxanthino-quanine-phosphoribosyl-transferase. There is also severe mental retardation and self-mutilating behaviour that often leads to permenant tissue destruction.

N.B.: Allopurinol is prescriced for improvement of the behaviour only and not the mental retardation.

e) Mucopolysaccharidosis type VII:

=Beta-glucouronidase deficiency.

This mucopolysaccharidosis was first described by Sly et al (1973) in an infant with short stature, skeletal deformities, hepatosplenomegaly and mental subnormality. A profound dificiency of beta-glucourinidase was identified.

Recently, a child with MPS VII has been evaluated by Hoyme et al (1981), who exhibited some features; which were previously unrecognised as part of the syndrome: presentation in the neonatal period, progressive joint contructures and hydrocephaly. This supports the concept that at least two forms of MPS VII exist; an early onset type and another form that presents in the second decade of life.

This disorder is most likely to be associted with moderate mental subnormality which does not progress over time. Repeated urine screening by the acid albumin turbidity test demonestrated grossly raised acid mucopolysaccharides (one hundred times the normal value).

DEFECTS IN LIPID METABOLISM

(A)Metachromatic Leukodystrophy (Sulphatide Lipodosis)

The disease is a heriditary condition in which sulphatide deposites, cerebroside sulfuric acid esters, occur not only in relation to the devastated myeline of the central and peripheral nervous systems, but also in some systemic organs, notably the kidneys and the gall bladder. The metabolic lesion in this disorder appears to be caused by a decrease in the activity of a sulfuric acid esterase. The studies of Austin and colleagues (1963-1965 a) showed a deficiency in arylsulfatase activity in the brain and other tissues obtained from patients with metachromatic leukodystrophy (Austin et al,1963-1965a).

A consecutive series has recently been reported by Schutta and colleagues (1966). In 12 sibships, all without parental consanguinity, there was a total of 18 affected and 20 unaffected children. These findings are suggestive of autosomal recessive inheritance (Schutta et al,1966).

The disease may manifest at any time between early infancy and adulthood (Moser,1972). Impairment of motor function is listed as one of the earliest signs that appear in children. Also involved, are speech and mental development (Hagberg et al,1962).

Further course of the disease is characterised by hypotonia, ataxia, coarse tremors, paralysis of ocular muscles and nystagmus. Impairment of vision occurs in most children after optic nerve atrophy. The final stage is one of decerebrate rigidity, blindness and deafness.

(B)Progressive Leukoencephalopathies:

This group of disorders consists of several clinical syndromes, characterised by a degeneration of the cerebral white matter, with the onset varing from infancy to adulthood and even old age. The three variations of the disorder are not always distinguishable from each other, and their classification is based primarily on the time of onset and the duration of illness.

1.Schilder's Disease:

Diffuse sclerosis may occur at any age but is most common in late childhood. Schilder's disease may occur sporadically. The neurologic findings are extremely variable; cortical blindness, optic neuritis, spastic hemiplegia, paraparesis, cortical deafness, aphasia and seizures have been described in the early phase. Late manifestations include dementia and coma. Little is known about the aetiology of the disease, the finding of raised IgG in the cerebrospinal fluid in such cases raises the possibility that an autoimmune process plays an important role (Walton,1977).

2.Krabbe's Disease:

Cerebroside lipidosis, or globoid leukodystrophy, is transmitted on an autosomal recessive basis. Chemical study of white matter discloses an increased ratio of cerebroside (ceramide galactose) to sulfatide (ceramide galactose sulfate), but usually there is no absolute increae in the quantity of cerebroside (Austin,1963). These changes are thought to be secondary to an inherited defect in cerebroside metabolism, with deficiency of galactocerebroside-b-galactosidase activity (Suzuki,1971).

The illness becomes evident in early infancy with progressive rigidity, hyper-reflexia, swallowing difficulties and failure of normal motor and intellectual development. The parents of a child with proved Krabbe's disease should be advised that there is a 25% chance that any subsequently born child may be affected (Nelson,1987).

3.Pelizaeus-Merzbacher Disease:

It is one of a group of diseases named as the Sudanophilic leukodystrophies. They drive their name from accumulation in the white matter of breakdown products of myelin, especially neutral fats, which stain positively with Sudan stains (Norman,1966).

It is transmitted by sex-linked recessive inheritance. The onset is in infancy with nystagmus and head nodding followed by progressive ataxia, spasticity and choreoathetosis. Progression is slow, with survival into adulthood (Norman et al,1966).

Degeneration of Cerebral Gray Matter:

(Neuronal Storage Diseases)

1-Tay-Sach's disease:

Infantile cerebromuscular degeneration is by far the most common of the gangliosidosis. It is most frequently met with among children of Eastern European Jewish. It is transmitted on an autosomal recessive basis. The basic defect is virtual absence of the enzyme hexosaminidase from all body tissues which results in marked accumulation of GM2 gliosides in all neurones, including those in the peripheral autonomic nervous system. Neuronal degeneration and gliosis are marked in infants who survive for several years (Kaplan,1983).

2-Sandhoff disease:

It is also transmitted on an autosomal recessive basis, but it occurs in non-jewish children. The defect is absence of the enzyme hexo-amidase A and B. The enzymatic defect leads to the accumulation of GM ganglioside and globoside. The outcome is the same as Tay-Sach's disease (Kaplan,1983).

3-Generalised gangliosidosis:

(GM1, gangliosidosis type 1)

It is transmitted on an autosomal recessive basis. The defect is absence of B-galactoside A,B and C. The disorder starts in utero or in early infancy. There are 2 forms. Type I, also known as pseudo-Hurler's disease,

and type II. In type II, progressive mental retardation, often with convulsions, begins at about 8-16 months of age and a cherry red spot is usually present but bony abnormalities are present and there is no enlargement of the liver or spleen as in type I (Kaplan,1983).

4-Juvenile GM1 gangliosidosis:

(GM1 gangliosidosis type 2)

It is transmitted on an autosomal ressive basis. The defect is absence of b galactosidase B and C. This is a more slowly progressive disorder, characterized by the onset of pschomotor deterioration at about one year of age and progresing to spastic quadroplegia with a fatal outcome betwen 3 and 10 years of age (Kaplan,1983).

5-Juvenile GM2 gangliosidosis:

(GM2 gangliosidosis type 3)

It is transmitted on an autosomal recessive basis. The defect is partial deficiency of hexo-amidase A. It starts between 2-6 years of age leading to mental deterioration, ataxia, spasticity and seizures (Kaplan,1983).

6-Late infantile and juvenile cerebromācular degeneration:

This group of disorders represent a variety of disorders in which there is progressive mental deterioration and loss of visual function. They are all transmitted by an autosomal recessive gene. They differ as regards the age of onset (Kaplan,1985).

The onset is between ages 1 and 3 years in the late infantile form (Bielschowsky syndrome) and is usually between 5 and 7 years in the more common juvenile for (Spielmeyer Vogt and Batten's disease). In the rare adult variety (Kuf's disease) the onset is after the age of 15 year.

All these disorders should be suspected in a child with the combination of progressive visual loss, seizures and mental deterioration (Kaplan,1985).

7-Niemann-Pick Disease:

This disorder is transmitted on an autosomal recessive basis and is characterised by storage of sphingomyelin in the cells of the reticulo-endothelial system: liver and spleen and some times in neurones. It is due to reduced activity of a sphingomeylin. Clinically, there are developmental arrest, mental regression, hepato-splenomegaly; hence abdominal enlargement, and anemia. A cherry red spot similar to that in Tay-Sach's disease as well as spasticity are also present. There is no known treatment (Nelson,1987, Kaplan,1985).

8-Gaucher's Disease:

This rare disease is usually due to an autosomal recessive gene. There is storage of cereroside in the cells of the reticulo-endothelial system and neurones. It is due to deficiency of enzymes, mainly glucocerebrosidase. There are two forms: The infantile one is characterised by progressive mental deterioration, developmental arrest, hepato-spleno-megaly and abdominal enlargement. It is usually fatal before the end of the first year of life, The juvenile form is chronic and of insidious onset, before the age of 10 years and with less or no CNS involvement, but physical handicaps is a prominant feature (Nelson,1987).

DEFECTS IN CALCIUM METABOLISM

Pseudohypoparathyroidism:

(Albright's Hereditary Osteodystrophy)

In this syndrome, in contrast with the situation in idiopathic hypothyroidism, parathyroid glands are normal or hyperplastic histologically, and they can synthesis and secrete parathormone. The primary defect is a failure of the end organ, particularly the kidney and skeleton, to respond to parathormone.Administration of parathormone fails to raise the serum level of calcium or to lower the level of phosphorus (Frame et al,1972).

Mental retardation is common. The disorder has been regarded as X-linked dominant, but females appear to be more severely affected than males.

Idiopathic Hypercalcemia:

This syndrome comprises hypercalcemia. "elfin" facies, mental retardation, hypertension and nephrocalcinosis in its most severe form.

The disease represents chronic vitamin D intoxication resulting from variable individual tolerance to the sterol. It appears that vitamin D in excess of the individual's tolerance produces a variety of aberrations in form

(vascular, growth and mental retardation). The nature and extent of the lesions produced and their reversibility depend on the time of exposure to the agent. Early severe damage may cause permanent morphologic changes which remain after recovery from hypercalcemia.

Lowe Syndrome:

This rare affliction is chracterised by mental retardation, glaucoma, organic aciduria, amino-aciduria and diminished renal production of ammonia. Some patients have metabolic acidosis and rickets. Large doses of vitamin D are ineffective unless calcium and sodium supplements are also provided. It is inherited in a sex-linked partially dominant pattern (Lowe et al,1952).

MISCELLANEOUS

KERNICTERUS

(Bilirubin Encephalopathy)

This is a neurologic syndrome resulting from the deposition of unconjugated bilirubin in the basal ganglia, cerebellum and brain stem, frequently resulting in cerebral palsy, mental retardation and hearing defect. Erythroblastosis fetalis is the most common cause of non-physiologic jaundice. Other factors such as neonatal sepsis, glucose-6-phosphate dehydrogenase deficiency, prematurity, vitamin K administration, sulfonamide, salicylates, some antibiotics, caffeine and sodium benzoate may all result in indirect hyperbilirubinaemia (Kaplan,1983).

It seldom develops unless the blood level of indirect bilirubin exceeds 20 mg/dl. Jaundice usually begins shortly after birth and becomes progressively more extensive, leading to hepatosplenomegaly, apathy, neurologiacl signs in the form of rigidity, inactivity, high pitch or feeble cry and poor Moro's reflex (Kaplan,1983).

In exceptional circumstances, kernicterus in premature infants with serum bilirubin concentration as low as 9-12 mg/dl has been associated with an apparently cumulative effect of a number of factors. These are: prematurity, hemolysis, asphyxia, acidosis, increased non-estrified fatty acids (NEFA), hyperosmolarity, cold stress, decreased serum albumin, hypoglycemia, infection and male sex (Brow ,1973).

Reliable estimates of the frequency of the clinical syndrome are not available because of the wide spectrum of manifistations. Overt neurological signs have a grave prognoss; 75% or more of such infants die, and 80% of the affected survivors have bilateral choreo-athetosis with involuntary muscle spasm.

ABNORMALITIES OF AUTOSOMES

A)Aneuploidy:

The degree of mental retardation is usually more severe in autosomal aberrations, while it is milder in sex-linked chromosome aberrations.

1-Mongolism:

(Down's Syndrome)

The most common and best known chromosomal syndrome is 21-trisomy. Its causes still remain obscure, despite a plethora of theories and hypotheses, it may be due to either one of the following three chromosomal abnormalities:

a. Approximately 92.5% of all children with Down's syndrome have primary trisomy 21 (three 21 chromosomes). A non-disjunction during miosis, occurring for yet unknown reasons, is held responssible.

b. 4.5% have a traslocation Down's syndrome, where there is a fusion of two chromosomes, mostly 21 and 15. Unlike trisomy 21, it is usually inherited, and the translocation may be found in unaffected parents and siblings (Kaplan, 1983).

c. 2.7% have mosaicism, where a non-disjunction occurs

after fertilisation in any cell division.Both normal and trisomic cells are found in various tissues (Girand et al,1975).

Two per cent of all children with Down's syndrome have a G/G type of translocation, most of these are 21q/21q. About 4% of these are familial; one parent is found to be a balanced translocation carrier. The remaining 96% are presumably de novo translocations in that the chromosomes of the parents are normal (Garver et al,1982).

Biochemical studies in Down's syndrome have revealed increased levels of galactose-1-phosphate uridyl transferase, and of acid and alkaline phosphatase, elevated activity of glucose-6-phosphate dehydrogenase and 5-nucleotidase, and diminished blood serotonine levels. Those abnormalities were found only in the trisomic type of the syndrome. The enzyme levels were in the high normal range in the translocation type. Biochemical findings suggest that the surplus genetic material in Mongolism results in a derangement of genetic homeostasis involving many genes or gene complexes (Kaplan,1983)

There is an agreement that one of the major predisposing factors is the age of the mother. The incidence for mothers younger than 25 years is 1/2,000,

whereas it is 1/100 for mothers between 40-44 years old. For mothers of 45 years, it is 1/50.

A recent study in Manitoba has reported almost a 70% increase in Down's syndrome live births to mothers aging 35 years and over, but no change for under 35 years in the period 1970-1974 compared to 1965-1969 (Evans et al,1978).

Also in New York State, the standardised rate of Down's syndrome in live births to women of 35 years of age and over, reported on birth cerificates, increased 30% in 1970 and later years compared to rates in 1965 and 1969 (Hook and Cross,1981).

There has been recent renewal of interest in the possibility that older fathers might be at higher risk of producing babies with Down's syndrome. There appears to be an increased risk of 20-30% of Down's syndrome associated with older fathers; more than 50 years independant of maternal age effect (Erickson et al,1981).

To compare the risk associated with mothers of the age of 40 and over, it is about 0.13% higher than that of those under 40. When recurrence is considered, two possible explanations for an increase in the risk of a second child with regular Down's syndrome; an inherited predisposition to non-disjunction and the occurrence of trisomy 21 in mosaicism in one of the parents (Hamerton et al,1961).

In cases of translocation, the ratio of the number of sibs found affected to the number expected is much influenced by the age of mothers at the birth of the index patient.

Young mothers with children with Down's syndrome, but rarely older mothers, will have a high risk of a second affected child because either they or their parents have a chromosome abnormality (Carter et al,1961).

With de novo 21q/21q translocation, the risk of reccurrence of Down's syndrome is persumed to be low probably less than 1/100 (Schmidt et al,1977). However, after the birth of a child with a de novo 21q/21q translocation Down's syndrome, there can be a significant risk of a second affected child, even when the cytogenic studies of the parents were normal (Graver et al,1982).

G trisomy has been observed with a relatively high frequency among abortuses, and these have recently been shown by banding studies to be mainly 21 trisomies (Nelson,1987).

Mental retardation is the overriding feature of Down's syndrome. The majority of patients belong to the moderately and severely retarded groups, with only a minority having an I.Q. 50. Mental development seems to

progress normally from birth to 6 months of age. I.Q. scores gradually decrease from near normal at 1 year to about 30 at older ages. It could be the infantile tests that do not reveal the full extent of the defect which becomes manifest when more sofisticated tests are used in early childhood (Kaplan,1985 and 1983).

Life expectancy used to be 12 years, with the advent of antibiotics few young patients succumb to infections, but most of them do not live beyond the age of 40, when they already have many signs of senescetence.

2-18-Trisomy Syndrome:

(E Syndrome,Edward Syndome)

This is the second most common autosomal aberration. Its frequency is 1/500 live births. There is proponderance of women, 80%; the sex ratio being one male to four females. As with 21-trisomy, late maternal age is etiologically important. X-ray irradiation of gonads before conception has been suggested as a causative factor (Kaplan,1983).

The syndrome has been of sporadic occurrance, it usually leads to death in early infancy, the oldest known patient being 15 years of age. Trisomy 18-syndrome, results in a characteristic pattern of multiple congenital

anomalies, of which, apparent mental retardation with moderate hypertonicity, low set malformed ears, small mandible, flextion deformity of the fingers with the index finger overlying the third finger, constitute the most prominent clinical abnormalities (Smith et al,1982).

3-13 Trisomy Syndrome:

(D Syndrome, Patan Syndrome, Holoprosencephaly)

The incidence of this syndrome is in the range of 1 in 5,000 or less. Most patients die in the first year of life, at least one is known to be alive at the age of 10. There is no significant difference in the sex ratio and there is an elevation of the average maternal age (Nelson,1987).

Translocations of chromosomes 13 have been more frequently reported than those of number 18 (Nelson,1987).

Trisomy 13 is characterised by rudimentary olfactory lobe, low set ears, cleft palate and lip, sloping forehead, single transverse palmar crease, polydactyly and abnormal dermal patterns. The patients are mentally retarded and often have minor motor seizures and apneic spells (Kaplan,1983).

4-22 Trisomy Syndrome:

Trisomy 22 is a rare clinical syndrome which has now begun to merge. It occurs in a lesser frequency than 21 trisomy which may be due to a lesser susceptibility to non-disjunction of chromosome 22 compared to 21.

Trisomy 22 characteristics are menatl and growth retardation, microcephaly, micrognathia, preauricular skin tags, appendages and/or sinus, low set and/or malformed ears, cleft palate, congenital heart disease and malformed lower extremeties (Nelson,1987).

B) Deletion:

1-Chromosomes Nos 4 and 5:

(4p- and 5p- Syndromes)

The best known syndrome is cri-du-chat syndrome (5p-). It is so named because the cry of affected infants resembles that of a kitten and is characterised by high pitch and tense phonation. This typical cry tends to disappear in late infancy. Most cases arise sporadically, but a few reports of reciprocal translocation in a parent have been recorded. Ring chromosomes with loss of material from both ends also produce the same syndrome (Nelson,1987).

The small deletion of the mid portion of the 5p15 band is considered to be the phenotypically relevant segment in the syndrome (Niebuhr,1978).

Patients with (4p-) are much more retarded and severely malformed and do not have the typical cry (Nelson,1987).

There is a case reported by H.Rivera et al to be a de novo chromosomal deletion. The clinical picture was fairly typical of the cri-du-chat, but on cytogenetic analysis on peripheral blood lymphocytes of the case, the karyotype was interpreted as 46,XY, inv(5), del(qtu->q22::p15->q22) (inversion of centric segment and deletion of the p15 band; also two precentric breaks, one located at the proximal edge of p15 and the other at q22)(H.Rivera,et al,1987).

2-Chromosome No 7:

(Partial Monosomy 7q Syndrome)

Several patients have been reported with interstitial deletions of the mid portion of the long arm of chromosome number 7. All the patients so far reported, have been females which raise the possibility of lethality in males.

Although the affected patients have been all mentally retarded and have had several abnormalities in common, such as epilepsy, hypo- or hyper-tonia, early swallowing and feeding problems and large mouth, their facial features and general appearance are not sufficiently distinctive to constitute an easily recognisable clinical syndrome.

Several of those patients have been described as having an abnormal cry which may be correlated with the q31 segment which was involved in all these cases (Abuelo et al,1982).

3-Chromosome No.18:

(18p- and 18q- Syndrome)

Deletion of chromosome No.18 takes three forms:

-loss of the entire short arm; 18p-,

-loss of part of the long arm; 18q-, and

-deletion of both ends to form a ring; r(18).

Patients with 18p- are phenotypically extremely variable. A few have been severely affected. With arhinenencephaly, cyclopia or cleft lip and palate, but most have only minor congenital anomalies and are only moderately retarded. It may resemble Turner's syndrome.

On the other hand, children with 18q- are severely retarded and have more characteristic malformations as microcephaly, ophthalmologic defects, carp-shaped mouth, apparent protruding mandible, atretic ear canal and super-numery ribs. Children with a ring chromosome 18 have phenotypic features of both short and long arm deletion.

The syndrome 18p- is the only structural abnormality of the chromosome in which late maternal age appears to be important (Nelson,1987).

4-Chromosomes of the D group:

Loss of a part of the long arm of a D chromosome has been reported in a few patients. The phenotypic similarities are such that involvement of the same chromosome 13q- is suspected. Severe mental retardation is present with failure to thrive (Nelson,1987).

Ring chromosome 13 has been reported frequently and is characterised both by multiple external malformations of a fairly characteristic pattern and by mental retardation (Surano et al,1971).

5-Ring chromosome 14:

The major features of the ring chromosome 14 syndrome, which has been described in 6 girls, include severe mental retardation, a disorder of skin manifestations, seizures and dysmorphic features as flat occiput, epicanthal folds, downward slanting eyes, flat nasal bridge, up-turned most ribs, short neck and large low set ears (Schmidt et al,1981).

Ring 14 chromosome cases have been all described in severely mentally retarded females and so far one case has been reported in males. It is believed and concluded that the ring chromosome must be a de novo structural rearangement (Riley et al,1981).

Scattered vitiliginous spots over the legs, buttocks and abdomen, as well as multiple hyper-pigmented spots in conjunction with psychomotor delay and severe refractory seizures, are characteristic of tuberous sclerosis. However, the dysmorphic features of the ring chromosome 14 syndrome are not found in patients with tuberous sclerosis, and may alert the pediatrician to this particular chromosome abnormality (Schmidt et al,1981).

6-Ring Chromosome 15:

In the two reports of ring chromosome 15 (Fujita et al,1978 and Wisniewiski et al,1980) there were only slight mental retardation with short stature.

7-Ring Chromosome 17:

This is a new emerging syndrome. The patients have mental retardation, short stature, low weight, hypo-tonia, micro-cephaly, seizures, hydrocephalus and abnormal dermatoglyphs. The variation in clinical findings among these patients may be explained by a difference in the break points on chromosome 17. Transmission of a ring chromosome 17 from father to son was also described (Carpenter et al,1981).

8-Chromosomes of the F group:

Deletion compatible with life may often be too small to be identified unless a ring is formed. F group aberrations were first reported only in studies of aborted material and patients with blood dyscrasias. A few patients with severe mental retardation and F group deletion have now been described (Nelson,1987).

9-Chromosomes of the G group:

Two syndromes are begining to emerge. Common clinical signs are retarded development, hyper-tonia, epicanthic folds, large and low set ears, broad and prominent nasal bridge, high arched palate, micrognathia and micro-cephaly or dolichocephaly.

Patients with r(22) appear to be more severely retarded than those with r(21), but the formers have fewer physical signs. Also differences in dermatoglyphics have been noted (Nelson,1987).

ABNORMALITIES OF SEX CHROMOSOMES

1-Klinefelter's Syndrome:

Approximately 1 in 750 newborn male has an XXY complement. Accordingly, Klinefelter's syndrome is slightly more common than Down's syndrome. The incidence is about 1% among the mentally retarded, preferentially among patients with I.Q. above 50 (Nelson,1987).

The karyotype usually shows an XXY pattern; there is a darkly stained Barr chromatin body on the nuclear membrane of the cells. This is a female nucleus pattern dependant on having a double set of X chromosome, i.e.,XX, one of which is genetically active and the other is inactive and constitutes the nuclear sex chromatin body or Barr's body (Kaplan,1983).

The chromosomal aberration may result from meiotic non-disjunction of an X chromosome during paternal gametogenesis or from mitotic non-disjunction in the zygote. Increased maternal age is a predisposing factor to meiotic non-disjunction and hence to this syndrome (Nelson,1987). Some patients have a mosaic pattern with less marked features. At puberty there is testicular atrophy and signs of feminisation. The degree of mental retardation may vary from mild to severe, but many patients have normal intelligence. Patients of superior intelligence are on the record (Slater and Roth,1979).

2-Variants of Klinefelter's Syndrome:

When the number of X chromosomes exceeds two, the clinical manifestations are more severe, the degree of mental retardation and the impairment of virilisation are greater. Indeed, the rare XXXXY variant is sufficiently distinctive to be detected in childhood. Affected patients are severely retarded. Defects suggestive of Down's syndrome are common. The mosaic patterns XXXY/XXXXY, XXXY/XXXXY/XXXXXY and XXXY/XXXXY/XXXXYY have also been observed. Patients with XXXY syndrome or with mosaic patterns with only XXX chromosomes tend to have less extensive changes (Nelson,1987).

3-Turner's Syndrome:

(Ovarian dysgenesis)

Patients with Turner's syndrome have a single X chromosome. They have a 46,XO chromosomal constitution, the X chromosome is more often maternal than paternal, but unlike the situation in Klinefelter's syndrome, maternal age does not influence the occurrence of Turner's syndrome. Most cases probably arise from non-disjunction or anaphase lag in the zygote.

The XO disorder occurs in about 1 in 3,000 live born females. It appears that the majority (95%) of all XO conception is aborted. A large prospective study found evidence for a seasonal pattern, two thirds of all births with non-disjunction occurring between May and October.

Mosaicism (XO/XX) among patients with Turner's syndrome constitutes 25% of cases; a proportion higher than with any other aneploid state. Other types of mosaics, such as iso-chromosome for the long arm, deletion of the short arm and rings of the X chromosome are much less common (Nelson,1987).

XO chromosomal constitution is associated with female bodily sex, inadequate genital development and sterility, not usually with mental retardation (Slater and Roth,1979).

4-Turner-like Syndrome:

The term "male Turner syndrome" has been applied to males who resemble females with Turner's syndrome in respect to certain anomalies which occur in both conditions. These boys have a normal karyotype; 46,XY. Moreover, this syndrome occurs in girls with normal karyotypes of 46,XX. The phenotype differs from that of a true Turner's syndrome in the following aspects:

1-Mental retardation is much more common.

2-The cardiac defect is most often a pulmonary valve stenosis or atrial septal defect,whereas coarctation of aorta is rare; the reverse situation is seen in the true Turner's syndrome.

3-There is a wide spectrum of gonadal defects varying from severe deficiency to apparently normal sexual development.

The disorder is heterogenous, counselling is therefore difficult (Nelson,1987).

5-Triple X Syndrome:

The XXX chromosomal constitution is the most frequent X chromosomal abnormality in females, occurring in almost 1 in 1000 live born females. Affected infants are usually not recognised. Past experience with XXX females has been biased, since most patients were found among the institutionalised mentally retarded. Affected adult females have been found, however, who are completely normal including having normal fertility. Of a group of nine triple X females, identified at birth, only one was clearly retarded at a year of age (Nelson,1987).

6-XXXX andXXXXX Females:

About 17 females with XXXX and six with XXXXX chromosomes have been described. All were mentally retarded, except for one of the XXXX girls.

Commonly associated defects are epicanthal folds, hyper-tolerism, clinodactyli, simian crease, radio-ulnar synostosis and congenital heart disease (Nelson,1987).

7-X-linked Mental Retardation:

It has long been known that there are more men than women affected by non-specific mental retardation. Davidson (1973) first suggested that X-linked genes should be considered in the aetiology of non-specific mental retardation as a whole, but it was Turner and Turner (1974) who stressed the importance of this.

In 1969 Lubs described the presence of a marker-X-chromosome in affected males who belong to a family whose pedigree indicated X-linked mental retardation.

Sutherland (1977) showed that this marker was in fact a fragile site occurring at band q27 or q28 of the X chromosome. Further studies showed that not all males with what is apparently X-linked mental retardation have this fragile site on the X-chromosome. Also, it must be stressed that the absence of the fragile site does not exclude X-linkage (Berry,1981).

There appears to be at least three distinct forms of X-linked mental retardation that occur within families and may or may not be allelic, that is to say, variants at the same locus (Berry,1981):

1-Boys with the marker X-chromosome do not have dysmorphic features and were originally described as being of average height, with head circumference tending to be above the mean, large lower jaws and blue eyes. A specific recent finding is macro-orchidism. Mental retardation ranges from severe to mild (Turner et al,1980).

2-Members of families who do not show the marker X-chromosome, have clinical features which can only be distinguished from the above by the absence of macro-orchidism.

3-A separate syndrome, in which affected individuals tend to have micro-cephaly and small testes are more severely retarded and do not show the marker X-chromosome (Fox et al,1980).

These findings are in contrast with those of Jacobs' (1979) who studied six X-linked families, in three of these, all the affected males had the fragile site but none had testicular enlargement, and the one family with testicular enlargement had no fragile site. However, in these six families, testicular size was not established with the orchidometer.

Recent studies in British Clumbia (Herbts et al,1980) gave an incidence of at least 1.83 in 1,000 males for X-linked non-specific mental retardation. So, this may be second only to Down's syndrome prevelence.

7-Fragile X Syndrome:

The fragile X syndrome had recently been recognised to be a common cause of mental retardation. It included a chromosomal fragile site at Xq27 or Xq28 and macro-orchidism (Carpenter,1982). The fact that the syndrome of mental retardation with macro-orchidism and of mental retardation with marker chromosome of fragile site Xq27-28 were one and the same, was established by Turner et al (1978), Sutherland and Ashforth (1979) and Howard-Peeble and Stoddard (1979).

From the male excess they estimated that X-linked inheritance could account for one fifth of non-specific mental retardation in male subjects. The frequency of X-linked mental retardation was estimated to be about 1.83 per 1,000 male subjects and the marker X-chromosome was considered to account for half of these (0.92 per 1,000 male subjects) (Townes,1982).

However, the delineation of mental deficiency in fragile X syndrome has not been easy, since different results have been reported by various investigators. Gustavon et al (1981) concluded that only 25% of males were severely retarded and the majority (75%) have an I.Q. between 50-70. On the other hand, Frijns (1984) found that 95% of male had an I.Q. below 50.

Lubs (1969) initially proposed three possible explanations to account for the association of marker X-chrmosome and mental retardation:

1-A recessive allele closely linked to the secondary constriction.

2-An effect of the secondary constriction itself.

3-A variable deletion at the site of constriction during pregnancy.

There was no suggestion from the data of Carpenter et al (1982) that the increasing age of the female increases the frequency of the fragile X syndrome although others as Jacobs et al (1980) have noted such an effect.

There are reports of males with fragile X but with no macro-orchidism (Turner et al,1980 and Martin et al,1980). Also, there may be another mental retardation syndrome associated with macro-orchidism without the expression of the fragile X-chromosome (Carpenter et al,1982 and Webb et al,1982).

In the investigation done by Webb et al (1982) the most important result was finding a range of intellectual capacity in female carriers of the fra.(x)(q27) with the most extreme being severely retarded.

Gerald (1980) suggested that the severity of expression of mental retardation in those females might depend directly on the cellular expression of such abnormality. Veenema et al (1987) through studying the cytogenic and clinical data has proved that the more the cellular expression of fra.(x) in tissues the more severe the picture is. The expression of the fragile site on the X chromosome has been shown to be highly dependent on the culture conditions (Sutherland,1977). A part from slightly alkaline pH optimum and a few serum content, the main factor necessary for the expression of the fragile site is culture medium deficiency of folic acid and thymidine. Also, the folic acid antagonist methotrexate (MTX) enhances the expression (Tommerup et al,1981).

8-Martin-Bell-Renpenning Syndrome:

This is a defined disorder which includes severely retarded males of normal appearance and normal stature. They have no physical, motor or behaviour abnormalities. They often have rather long faces and large ears. It has also been reported that enlarged testes, occurring in both pre and post-pubertal males, are also an associated feature of the syndrome (Turner et al,1975).

All subjects with Renpenning syndrome carried a fragile X q27-28 chromosome in more than 4% of their blood lymphocytes. A female age effect was observed and one possible carrier of Renpenning syndrome exhibited the fragile X in 10% of her lymphocytes but was also mentally retarded (Froops and Webb,1981).

9-X-linked Hypogonadism,Gynaecomastia,Mental Retardation: Short Stature and Obesity:A New Syndrome:

This syndrome is consistent with an X-linked recessive trait, with little variability in its expression. The major findings are most likely the result of a developmental anomaly of the central nervous system with involvement of the hypothalamus. The endocrine evaluation and the histologic findings of the testes are consistent with partial hypogonadotropic hypogonadism and exclude the possibility of primary testicular failure (Vasquez et al,1979).

10-Borjeson,Forssman and Lehmann Syndrome:

The major findings distinguishing this syndrome from the previous one include:

1-The severe degree of mental retardation and the protracted seizure disorder observed in all the affected males.

2-The moderate degree of mental retardation observed also in three female members of the kindred.

3-The relatively early death of two of the retarded males.

4-The peculiar facies;with excessive subcutaneous fat on the face,narrow palpebral fissures and large ears.

5-The endocrine abnormalities including dwarfism, hyalinisation of the seminiferous tubules and a low urinary 17-ketosteroids.

The authers suggested that this syndrome is transmitted by an X-linked recessive mutant gene. But the pattern of inheritence, however, as suggested by Vasquez (1979) appears to be X-linked dominant for mental retardation.

11-Partial X Chromosome Duplication:

A mentally retarded male patient with a structurally abnormal X chromosome is reported; the karyotype being 46, dir dup.(X)(p11.2->p21.2)Y. In the normal mother a similar X chromosome duplication was found which was preferentially inactivated.

The findings indicated that recombination took place at maternal meiosis (Nielsen and Langkjaer,1982). The functional disomy of active X chromosome material may explain the clinical picture in the repoted patient with X duplication and a normal Y chromosome.

12-Terminal Deletion of Y Chromosome:

A child with a terminal deletion of the long arm of the Y chromosome (Yq-) presented with marked live do reticulosis, snub nose, micro-cephaly, short stature and other dysmorphic features. He was profoundly mentally retarded (Podruch et al,1962).

Most of the patients with (Yq-) have been reported as having dysmorphic features, mental retardation and short stature. In only one of these, was the Yq- familial. There is no information in the newborn surveys whether the small Y chromosome was a familial inheritant variation (Yq-variant) or a true terminal deletion of the long arm of a Y chromosome (Yq-)(Podruch et al,1982).

AUTOSOMAL DOMINANT DISORDERS

These anomalies are determined by single dominant genes of variable expressivity and penetrance, that vary in frequency. The clinical picture varies greatly and mild forms, with minimal signs and mild mental retardation, are often seen. In addition to cerebral defects, ectodermal, visceral and skeletal anomalies are involved.

1-Dystrophia Myotonica:

This illness is transmitted on an autosomal dominant basis and is characterised by wasting and weakness of muscles of the extremities, face, jaw and neck, all symptoms usually appear in young adults, but developmental delay is noted later in infancy; including mental retardation, which ranges from moderate to severe (Dubowitz,1965).

2-Tuberous Sclerosis (Epiloia):

This disorder, a major cause of mental defect and of intractable convulsions, is inherited as a dominant trait, with wide variation in expression, probably due to the irregularity of the abnormal gene or to the influence of additional modifying gene(Kaplan,1983).

The skin lesion consists of sebaceous adenomata, red on the face and brownish white on the rest of the body. Vitiligo patches and depigmented navi often offer the first diagnostic lead (Kaplen,1983 and Gold and Freeman,1965).

Convulsions are the most common clinical sign of brain involvement and occur in more than 90% of patients. Mental defects, varying from mild to severe, are present in 60-70% of patients. Behaviour disorders, especially hyperactivity and destructiveness are also met with (Nelson,1987). Among defectives, not more than about 0.5% suffer from epiloia (Slater and Roth,1979).

3-Neurofibromatosis:

(Von Recklinghausen' Disease)

It is transmitted as an autosomal dominant trait, the main features of this disorder are small brown patches distributed over the entire body, along the course of the subcutaneous and autonomic nerves as well as nerve trunks. Sensory nerves are usually more affected than other nerves. The skin involvement is in the form of Cafe au Lait spots, of irrigularly shapped areas of increased skin pigmentation and it constitutes a hallmark of the disease.

Epilepsy is seen in about 10% of cases. Mental retardation is also seen. Mild impairment of intellectual fnctions is common, but severe mental defect rarely occurs (Kaplan,1983).

4-Huntington's Chorea:

This is a dominant inherited degeneration of the basal ganglia, especially of the caudate nucleus, manifesting clinically by dementia, irrigular dancing gait and choreiform movements.

The onset is usually in middle age. However, Jervis (1963) has described four cases with onset in childhood. Apearing so early, the condition leads to an intellectual deficit resembling defect rather than dementia (Slater and Roth,1979). Jervis (1963) draws attention to the absence of choreic movements and the occurrance of epilepsy in childhood cases.

5-Encephalofacial Angiomatosis:

(Sturge-Weber Disease)

It occurs sporadically without known hereditary factors. It is believed to be due to an irregularly dominant gene, but the exact manner of hereditary mechanism is not yet clear (Kaplan,1983).

In its classical form, the syndrome includes a facial navus in the distribution of the trigeminal nerve, buphthalmos, hemiparesis of the contralateral extremities, convulsions and mental retardation. The convulsions and the mental retardation are due to intra-cranial angiomata which often become calcified and may be radiologically demonestrated (Peterman et al,1958).

6-Retino-cerebellar Angiomatosis:

(Lindau's Disease)

This disease is characterised by retinal angiomata associated with hemangioblastoma of the cerebellum and frequently with such other tumours as hemangioma of the

spinal cord, hypernephroma and cystadenoma of multiple visceral organs. Dominant inheretence has been demonestrated in several families (Nelson,1987). The clinical picture includes mental retardation and cerebellar signs (Kaplan,1983).

7-Archnodactyly:

(Marfan's Syndrome)

The disorder is considered a "general mesodermal dystrophy". It is an inheretable disorder, probably transmitted by a single dominant gene of variable expressivity.

It involves changes in many parts of the body, chiefly in the skeletal, cardiovascular and ocular structures. The patients are tall, have long extremities with long spider-like fingers and toes, colobomas, bilateral lens dislocation and also have cardiac anomalies. The mentality is normal in the majority of instances, but when it is retarded, it is usually mild (Nelson,1987 and Kaplan,1983)

8-Achondroplasia:

(Chondrodystrophy)

A disorder of cartilage which begins in prenatal life and leads to specific type of dwarfism. The long bones are most severely affected, so that the disproportionate dwarfism becomes manifest with growth.

Genetic factors play a leading role, most pedigrees suggesting a dominant mode of transmission. Sporadic cases

occur frequently and they should be attributed to new mutations. Advanced parental age, probably paternal, has been considered a possible factor. Males and females are equally affected. Mental subnormality, if present, is of mild degree (Nelson,1987).

9-Craniosynostosis:

This group of disorders includes several conditions characterised by premature closure of cranial sutures, skull deformities and brain damage due to increased intra-cranial pressure.

The cause of most cases of craniosynostosis is still unknown, but a dominant mode of inheretence was reported in some instances, with familial tendency to the same type of anomaly. Since not all the cranial sutures are necessarily involved, the shape of the skull may vary greatly, where the normal growth is inhibited in a direction perpendicular to the obliterated suture line, and compensatory growth takes place in other directions. So, one may get:

1-Elongated cranium dolichocephaly which is the commonest.

2-Broad skull (brachycephaly).

3-Pointed skull (acrocephaly).

4-Craniofacial dystosis (Crouzon's Disease).

Several facial and orbital deformities may be associatd with the various forms of craniosynostosis (Kaplan,1983).

10-Treacher-Collins Syndrome:

This syndrome has a wide variability of expression. The common signs are anti-mongoloid slant of the palpebral fissures, mandibular hypoplasia, lower lid colobomata and pre-auricular tags. Mental deficiency has been reported in only 5% of cases (Smith,1976). The syndrome is a mendelian dominant disorder.

11-Uveal Colobomata, Cleft Lip and Palate and Mental Retardation:

An autosomal dominantly inhereted uveal coloboma, associated eye defects and cleft palate and lips occurring in 12 subjects over 3 generations has been reported by Kingston et al (1982).

Considerable variability in expression of the gene is apparent, uveal colobomata being the most constant feature. Mental retardation is a variable feature of the syndrome.

This family as one member had mild mental retardation and was in an institution, three others had mild mental retardation with schooling problems.

Genetic factors may operate through intracellular regulatory mechanisms which influence cell differentiation and fusion processes. The mode of genetic influence remains unclear, but it is likely that RNA transcription and translocation play a part (Kingston et al,1982).

12-Hypertolerism:

This condition is characterised by an abnormally long distance between the eyes and an apparent broadening of the root of the nose is a non-specific sign and not a disease entity. It is often associated with mental retardation and may be combined with other congenital defects (Nelson,1987 and Kaplan,1983).

Familial occurrence of the disorder indicates a dominant mode of inheretence in most cases, but some cases with a recessive mechanism have been reported (Kaplan,1983).

The mentality ranges from normal to moderately retarded. Some retarded patients with the anomaly have hyper-amino-acid-uria. Convulsions may occur (Kaplan,1983).

AUTOSOMAL RECESSIVE DISORDERS

1-Goldenhar Syndrome:

The distinguishing features of this syndrome include dermoid, lipodermoid or lipomas of the eyes, colobomata of the upper eyelids and vertebral abnormalities.

In this syndrome, mental deficiency and club feet are found in approximately 20% of cases. This syndrome is usualy sporadic, only two cases of autosomal recessive inheretence have been reported (Krause,1970).

2-Branchial Dyspalasia, Mental Deficiency, Club Feet and Inguinal Hernias:

A distinct, probably autosomal recessive, disorder was ascetained in a boy and his sister (Lambert et al,1982). The common features were signs of abnormal development of the first and second branchial arches, mental deficiency, club feet and inguinal hernias. In addition, the boy had hypospadius and the girl had ventricular septal defect.

The association of these anomalies and their suggested mode of inheretence do not seem to correspond to any well known syndrome. Familial occurrence in 2 children of both sexes of unaffected consanguineous parents, the lack of exposure to teratogenic factors and the normal karyotypes indicate an autosomal recessive mode of inheretence (Lambert et al,1982).

3-Keratoconus Posticus Circumscriptus, Cleft Lip and Palate, Genitourinary Abnormalities, Short Stature and Mental Retardation:

Young et al (1982) described 2 sibs in each of whom keratoconus circumscriptus is associated with multiple abnormalities. These include short stature, mental retardation, cleft lip and palate and vertebral anomalies. No former reports of an identical condition have been traced. The findings in these children may represent a previously unrecognised malformation syndrome showing probable autosomal recessive inheretence.

4-Congenital Universal Alopecia, Mental defect and Micro-cephaly:

Pfeiffer et al (1982) reported a brother and sister who had congenital universal atrichosis, micro-cephaly and mental retardation. Mental retardation was severe. Autosomal recessive inheretence is suggested.

5-Mental Retardation, Contractures of the Hands and Genital Anomalies:

Two teen-age XY brothers with mental retardation, short stature, obesity, genital anomalies and contractures of their hands are described by Urban et al (1979). They had generalised osteoporosis and a history of frequent fractures. Their endocrinologic evaluation was normal except for mild glucose intolerance and delayed but normal puberty.

Although these brothers are similar to individuals with Prader-Willi syndrome (PWS), their unusual hand contractures, clinically significant osteoporosis and lack of hypotonia indicate that they represent a different entity. Their mental retardation is milder, however, and their osteoporosis is more severe (Dunn,1968). Inheretence in this family must be either autosomal recessive or X-linked recessive (Urban et al,1979).

6-Cohen Syndrome:

This is a new syndrome with hypotonia, obesity, mental retardation and anomalies of the face, mouth, eyes and limbs. The affected subjects have the opposite palpebral fissure slant, mottled retinae hyper-extensibility of joints (Cohen et al,1973).

7-Schizel-Giedion Syndrome:

Schinzel and Giedion (1978) and Donnai and Harris (1979) have together a total of 3 infants with a syndrome characterised by mid-face retraction, hypertrichosis, multiple skeletal anomalies and cardiac and renal malformations. Two patients who survived beyond the neonatal period also had seizures together with profound mental and physical retardation. Another infant has been recently evaluated by Kelly et al (1982) who is believed to be another example of this newly described syndrome. The evidence may be interpreted as indicating the Schinzel-Giedion syndrome to be a single gene autosomal recessive disorder (Kelley et al,1982).

8-Marden-Walker Syndrome:

This syndrome is characterised by blepharo-phimosis (short narrow palpebral fissures) and congenital contructures. These affect the knees, hips, elbows and ankles and remain stable or slightly improve with time. The blepharo-phimosis is associated with an immobile facies, micro-gnathia and low set ears (Marden and Walker,1966).

mental retardation has been present in all cases reported with delayed milestones of development and marked delay in language development (no speech had been acquired by 5 or nearly 7 years, although hearing was normal, in the longest survivors) (Howard et al,1981).

The evidence for autosomal recessive inheretence previously rested on the male first cousins (related both on the maternal and paternal sides) and the sib pair cases described by Howard et al (1981) strengthens the case for autosomal recessive inheretence.

9-Cockayne's Syndrome:

In 1936 Cockayne described 2 sibs with dwarfism, progressive mental retardation and erythrematous dermatitis, who went on to develop old facial appearance and visual failure associated with retinal pigmentation.

Later reports have confirmed that this is a syndrome inhereted in an autosomal recessive manner, although there are fewer than 40 cases reported (Proops et al,1981). Parental consanguinity has been described in 4 cases and the family described by Proop et al (1981) is the seventh reported case of Cockayne's syndrome occurring in sibs, which strongly supports autosomal recessive inheretence.

10-Spondylo-epiphyseal Dysplasia Tarda:

Spondylo-epiphyseal dysplasia tarda (SEDT) is a skeletal disorder which usually presents clinically in late childhood as a short trunk type dwarfism, due to progrssive involvement of the spine and epiphyses. Inheretence is almost always X-linked recessive, although autosomal recessive and autosomal dominant inheretence have been reported (Spranger and Langer,1974).

Yet a new variant of spondylo-epiphyseal dysplasia tarda with mild to moderate mental retardation is described in three daughters born to healthy consanguineous parents. The mode of inheretence is compatible with that of an autosomal recessive disorder (Kohn G. et al,1987).

The identification of this variant is important, as it enables more precise councelling in families in which sporadic cases with this form of representation are found.

DEVELOPMANTAL ANOMALIES DUE TO RECESSIVE OR UNKNOWN MECHANISMS

1-Anencephaly:

The cause of this lethal anomaly is unknown, but it is believed to be a hereditary polygenic disorder. Its incidence ranges between 0.05% and 0.37%. The anencephalic fetus usually succumbs during delivery or shortly thereafter (Kaplan,1983).

A mother who has had one anencephalic fetus has a recurrence risk of one of the closure defects of the neural tube of about 10% for each subsequent pregnancy (Nelson,1987).

2-Hydranencephaly:

This condition, which is of unknown cause, is defined as a congenital absence of the cerebral hemispheres. The cerebrum is replaced by a large fluid filled cavity. Failure of development of the cerebral arteries and destruction of the brain by severe intra-uterine infection have been suggested as possible aetiological factors (Nelson,1987).

The hydranencephalic infant may look remarkably normal at birth. However, the infant does not have visual following and later in infancy there is complete failure of motor and intellectual development. Seizures may occur (Hamby et al,1950).

The diagnosis is achieved by pneumo-encephalo-gram and trans-illumination of the head.

The prognosis is hopeless. Early institutionalisation is indicated.

3-Porencephaly:

This disorder is characterised by cystic formation in the cerebral hemispheres, communicating sometimes with the ventricular system or subarachnoid space. The clinical picture depends on the amount of the remaining functional cortical tissue. The patients who survive early childhood are usually bedridden, have bilateral hemiplegia and present with total amentia (Kaplan,1983).

4-Microcephaly:

Microcephaly is a purely descriptive term, covering a variety of disorders whose main clinical feature is a small sized head more than three SDs below the normal (Nelson,1987). Developmental abnormalities and destructive processes affecting the brain during the fetal and early infantile periods may lead to this defect.

The more important known causes listed by Nelson (1987) are :

i-Defects in brain development:

1)Hereditary (recessive) microcephaly.

2)Mongolism and other autosomal trisomy syndromes.

3)Fetal ionising irradiation.

4)Maternal phenylketonuria.

5)Seckel's dwarfism.

6)Cornelia de Lange syndrome.

7)Rubinstein-Toybi syndrome.

8)Smith-Lemi-Opitz syndrome.

The clinical picture varies but is generally with milder mental retardation than the acquired microcephaly. There is a small and bird-like face with the under-sized but relatively well developed body. A minority, with motor functions defects, shows severe retardation and the-rest shows moderate retardation (Kaplan,1983).

ii-Intra-uterine infections:

1)Congenital rubella.

2)Cytomegalovirus infection.

3)Congenital toxoplasmosis.

4)Congenital syphilis.

5)Neonatal herpes virus infection.

The frequency of such condition is far greater than that of inherited microcephaly. Usually there is a specific abnormal indicative to the causative agent e.g. cataract, micro-ophthalmia, deafness, cardiac abnormalities or hepato-spleno-megaly.

iii-Perinatal and postnatal disorders:

1)Intra-uterine or neonatal anoxia.

2)Severe malnutrition in early infancy.

3)Episodes of cardiac arrest.

4)Uncontrolled seizures.

5-Agyria and Pachygyria:

In both conditions the convulsions of the brain are absent or mal-developed. Both anomalies are associated with a severe degree of mental retardation (Kaplan,1983).

6-Agenesis of Corpus Callosum:

This is a developmental anomaly in which the major fibre tracts that connect the 2 cerebral hemispheres are absent. Rarely, partial agenesis of the corpus callosum is transmitted by recessive inheritence: most cases are of unknown aetiology (Nelson,1987).

The extent of clinical picture varies with the extent of the associated brain anomalies.

Commonly, the condition presents with major, minor or focal seizures, mental retardation of varying severity, abnormal head enlargement and often with hypertelorism.

Pneumo-encephalo-gram shows several characteristic features of which the marked separation of the lateral ventricles is one (Kaplan,1983).

7-Laurence-Moon-Biedle Syndrome:

This disorder usually follows an autosomal recessive mode of transmission, but some sex-linked tendency may be suspected from a hiegher frtequency in males than in females. The main features include mental retardation, retinitis pigmentosa, obesity, hypogonadism, polydactyly and deaf mutism (Kaplan,1983).

8-Ataxia-Telangiectasia:

This is a complex disorder in which a specific immunologic dysfunction is associated with progressive cerebellar degeneration, telangiectasis of bulbar conjuctiva and skin as well as an increased likehood of malignancy. The disease is transmitted on an autosomal recessive basis.

Mild mental retardation is seen during late stages of the illness. Death usually occurs in adolescence or early childhood as a result of pulmonary failure, infection or malignancy (Nelson,1987).

9-Norrie's Disease:

This is a disease characterised by blindness shortly after birth, persistant hyperplastic primary vitreous, corneal opacity, cataract and phthisis bulbi. Mental retardation is present with deafness and central nervous system changes. It is transmitted on an X-linked recessive basis (Nelson,1987).

10-Menkes-KinkyHair Syndrome:

This sex-linked recessive disorder is caused by defective absorption of copper and decreased levels of ceruloplasmin and copper in plasma, There is also a diminished content of mitochondrial copper-containing enzyme; cytochrome oxidase. Severe cerebral degeneration leads to profound developmental retardation within the first few months of life and may be accompanied by myoclonic seizures. Most infants die within the first year (Nelson,1987).

11-Carpenter's Syndrome:

This condition is characterised by acrocephaly, a peculiar facies, brachysyndactyly of the fingers, preaxial polydactyly and syndactyly of the toes, hypogonadism, obesity and mental retardation. It is transmitted on an autosomal recessive basis (Nelson,1987).

12-Sjogren and Larsson Syndrome:

In 1957 Sjogren and Larsson described in detail the syndrome of congenital ichthyosis, progressive spacticity and mental retardation. There is also shortened life span, speech defect and changes in the fundus oculi (Thiele,1974). It is transmitted as an autosomal recessive trait. Mental retardation is either profound or moderate (Nelson,1987).

13-Xeroderma Pigmentosum:

This rare disease is transmitted in a simple recessive manner. It is characterised by a lack of one of the enzymes responsible for the repair-replication of the DNA molecule (Nelson,1967).

It is characterised by large freckles and areas of cutaneous atrophy, keratosis, photophobia and conjuctivitis. Multiple skin cancers may occur and lead to early death. Mental retardation is also present.

14-Prader-Willi Syndrome:

This syndrome of unknown cause is characterised by mental retardation, muscular hypotonia, obesity, short stature and hypogonadism. It is frequently associated with a cytogenetic abnormality involving chromosome 15 (Wisniewski et al,1980). A new case of this syndrome with the karyotype 45,XX,-15,+19,-der(19),t(15;19)(q12;q13) is rported by Moric-Petrovic et al (1981). This case further dmonstrates the heterogenity of chromosome 15 aberrations wich may be associated with the syndrome and gives some suport to the hypothesis that the presence of a lesion in 15q may be the underlying common factor of significance in this syndrome.

It is postulated that a single hypothalamic defect might account for all the abnormalities (Urban et al,1979). Recurrence risk is about 1.6%.

PRENATAL FACTORS

1-Maternal and Fetal Infections:

(Intra-uterine infections)

A great deal of evidence is accumulating that events early in pregnancy affect the outcome greatly. A review of the effect of the intra-uterine infection on fetal growth and development in the human population was made by Lechtig et al,(1979).

Studies of infection by cytomegalovirus has indicated a 20-100% presence of microcephaly. In 10 to 70% of these cases of cytomegalovirus, mental subnormalitity was detected generally at one year of age or later .

Convulsions and mental subnormality have been observed in fetal infection by Western equine encephalitis virus , coxackie B virus and poliovirus.

It has been shown that more than half the cases of congenital syphilis were clinically normal at birth and only began to show signs of mental subnormality at 15-20 years of age .

From 21 cases of miningitis due to gram negative bacteria acquired in utero, 33% showed mental retardation(Lectig et al,1979).

Eichenwald (1967) reported mental subnormality and

neurological alterations in 90% of a group of 116 cases of fetal infection by toxoplasma, observed until the age of 5 years. Similar results have been notified by others.

Approximately 13.3% of all cases of mental subnormality which occur in the USA are due to intra-uterine infection produced by cytomegalovirus, rubella and toxoplasmosis (Lechtig et al,1979).

An obviously important factor that influences the effect of intra-uterine infection is the identity of the infectious agent itself. Also, the gestational age at which injury occurs is of importance in determining the magnitude of the damage as well as its nature and reversibility.

The infection is more dangerous if it occurred during the first months of pregnancy, since at this stage many human organs, including the brain are in the hyperplastic phase of growth .

Another factor is the severity of the infection, defined by the extension involved, duration and locality of the lesion. Factors that modify the fetal physiological status such as nutrition, are also important. The magnitude and efficiency of the host immune response as well as maternal mechanisms of defence may also influence

the effect of intra-uterine infection (Lecthig et al,1979).

2-Fetal Irradiations:

It has been well known for many years that pelvic irradiation of pregnant women especially during the first trimester, may lead to serious fetal injuries. The most common clinical manifestation of fetal injuries is micro-cephaly, with its associated mental defect.

The effect of the atomic bomb in Hiroshima and Nagasaki on the offspring of women who were in the first trimester of their pregnancy was quite similar to that following therapeutic irradiation (Plummes,1952). The observation confirmed the high incidence of micro-cephaly with mental subnormality, and of the congenital anomalies. These results were confirmed by Miller (1972).

There is no doubt that there is a high incidence of injurious mutant genes, after the atomic blast, producing fetal abnormalities in subsequent pregnancies.

However, Neel and co-workers (1953) studied children conceived of subsequent to the blast but found no significant increase in congenital malformations. This was also emphasized by Miller (1969) as no effect could be demonstrated among the 75,000 first generation offspring exmined.

3-Prematurity:

Although it is true that premature infants, and particularly small premature infants, contribute very little in terms of numbers to the total population, it seems to be a mistake to emphasize this aspect of the situation. Emphasis should be placed in stead on the percentage with physical and mental handicaps. There is an inverse relation between birth weight and the incidence of neuro-psychologic handicaps. Infants of very low birth weight are born with brain damage, and this high incidence of damage is not found in any other prenatally affected, or prenatally determined conditions that occur in significant numbers, with the exception of mongolism (Kaplan,1985).

Recent evidence suggests that, in as many as half of premature infants the defect found may be developmental in origin and unlikely to be affected by improvement in prenatal care of mothers or postnatal care of infants (Kaplan,1983).

4-Seasonal and Geographic Variations:

The relation between the season of birth and the inteligence has been studied by many investigators, and the reports of Dixtein's large scale studies were at hand. In eleven of these studies the lowest I.Q. occurred in

persons born in Winter, and in four studies it was lowest in those born in Autumn. In the only one study that was an exception to such a pattern only 337 cases were involved. However, there was found an excess of birth of mentally retarded children in Winter months (Knobloch and Pasamanick,1962).

To explain this finding they postulated that adverse factors were acting in the eighth to the twelfth week of pregnancy, the period when the molecular organisation of the cortex is taking place.The increase in temprature during the Summer months, acting perhaps by decreasing protein intake, or more directly on the adrenocortical-pituitary-hypothalamic axis, was responsible for the difference (Knobloch and Passamanick,1962).

They found, also, that the incidence of complications of pregnancy was significantly higher for infants born in the Winter months, and that the complications, largely involved in this seasonal differential were the same ones previously noted to be associated with neuro-psychiatric disability, namely bleeding and toxaemia of pregnancy. It may be also related to the socio-economic status (Knoblock and Pasamanick,1962).

5-Prenatal Malnutrition:

There is evidence of protein's effect in altering the percentage of abnormalities during pregnancy. Proteins and vitamin supplementation of the diet decreased the incidnce of toxaemia of pregnancy and premature separation of the placenta. It was also found that when the diet was supplemented by protein and vitamins, the prematurity rate was 3-0%, 4-8% if protein only, 5-6% if vitamins alone were given, and 6-4% in absence of any dietary supplementation.

Also, prematurity has a very definite relation to the pregravid nutritional state of the mother, and to the weight gain during pregnancy.

It appears also, that a protein deficiency imposes handicaps on the synthesis of steroid hormones by the maternal organism (Knobloch and Pasamanick,1962).

Studies also showed that early postnatal caloric and protein deficiencies affect growth and may produce irreversible mental changes. In rats, it produces reduction in the number of brain cells as a result of deficient cell division, while malnutrition introduced after 21 days decreases the cell size without affecting the numbers; and that change is reversible.

Winnick and Rosso (1979) conducted a study in Chile and found a similar phenomenon in children died due to insufficient diet. Seventy per cent of the survivors had

significantly reduced head circumference,50% had a limited capacity to adapt to their environment and suffered from mild to severe mental retardation.

6-Fetal Alcohol Syndrome:

High levels of alcohol ingestion during pregnancy can be damaging to emberionic and fetal development. A pattern of malformation identified as fetal alcohol syndrome by Jones and colleagues (1973) is now established. Mental deficiency of varying degrees is the most debilitating characteristic of this syndrome.

The characteristics of the fetal alcohol syndrome include the following:

1-Persistant growth deficiency for length, weight and brain of prenatal onset.

2-Facial abnormalities, including short palpebral fissures, epicanthal folds, maxillary hypoplasia, micrognathia and thin upper lip.

3-Cardiac defects, primarily septal defects.

4-Minor joints and limb abnormalities, including restriction of movement and altered palmar crease pattern.

5-Delayed development and mental deficiency varying from borderline to severe (Palmer et al,1974).

The severity of dysmorphogenesis varies from the severely affected with full manifestations of fetal alcohol syndrome to the mildly affected with only a few indications of the syndrome.

Intellectual development is significantly related to dysmorphogenesis, the most severely dysmorphic children also, have the greatest intellectual handicaps. However, there is still considerable variability of I.Q. scores even for children with the same phenotypic categorisation. Although a significant relationship is demonstrated between structure and function in the fetal alcohol syndrome, one is not fully predictable from the other. This relationship may also be important in term of the early provision of enrichment experiences, for affecetd children, so that optimal mental development and functioning can be obtained (Streissguth et al,1978).

7-Socio-economic Factors:

There is a higher incidence of neuropsychiatric disabilities in the lower socio-economic groups. The important complications of pregnancy (bleeding and toxaemia) increased as the socio-economic status decreased, being 5% in the white upper economic fifth, 10% in the lower economic fifth and 15% in the non-white group

(Knobloch and Pasamanick,1960).

8-Antenatal Hypoxia:

In a study done by Naeye and Peters (1987), it was found that antenatal disorders and conditions that can produce subacute or chronic fetal hypoxia correlate with low I.Q. values.

Causes of antenatal and neonatal hypoxia can be enlisted as follows:

a)Acute hypoxia:

i.Post-term delivery.

ii.Vaginal bleeding during delivery.

iii.Placenta previa.

iv.Abruptio placenta.

v.Intrapartum maternal shock.

vi.Tight knot of the umbilical cord.

vii.Umbilical cord tied around the neck.

viii.Umbilical cord prolapse.

ix.Labour taking more than 20 hours.

x.Persistant high uterine tone during labour.

xi.Tumultuous labour.

b)Chronic hypoxia:

i.Anaemia: decreased maternal gestational haemoglobin level and fetal blood loss

(Naeye and Tafari,1983).

ii.Low utero-placental blood flow; third trimester hypotension (diastolic blood pressure < 60mmHg). (Grunberger et al,1979) and third trimester hypertension (diastolic blood pressure > 94 mmHg) (Gallery et al,1979).

iii.Muliple births; where there is reduced utero-placental blood flow per capita.

iv.Cigarette smoking (Lehtovirta and Forss,1978).

c)Other causes:

i.Neonatal respiratory distress syndrome (Pelman et al,1984).

ii.Neonatal apneic episodes (Palman and Valpe,1985).

Both conditions lead to cerebral ischemia.

However, the mechanisms that produce chronic hypoxia may not be widely understood.

Taking socio-hereditary and demographic influences into consideration, antenatal disorders and factors that can produce chronic hypoxia correlate with low I.Q. scores whereas disorders that can produce acute hypoxia do not have this correlation. This raises the possibility that chronic fetal hypoxia can impair children's long term

cognitive performance. Only 2% of the children had I.Q. scores between 60-70 and 6% had scores under 60. Through the study of Naeye and Peter, only 2% of I.Q. in the CPS;collaborative perinatal study; are due to all fetal and perinatal hypoxia-producing factors combined. This effect is so small that it would be very difficult to measure any over-all improvement in the I.Q. scores that might have resulted from advance's in obstetric and neonatal management that have been taking place.

TREATABLE CAUSES

TREATABLE CAUSES

(1) Phenylketonuria:

This condition is transmitted as a simple recessive autosomal Mendelian trait. Its frequency in the United States is 1/10,000 to 1/20,000 of births and is 1% among institutionalized defectives. The incidence of the gene in the population is 0.5% to 1.0% as Meister (1958) has indicated.

Phenylalanine is an essential amino acid. Dietary phenylalanine not utilised for protein synthesis is normally degraded via the tyrosine pathway. Deficiency of the enzyme phenylalanine hydroxylase, or of its co-factor tetrahydrobiopterin (BH4) is responsible for this disorder. As a result, phenylalanine accumulates in body fluids and is transmitted to phenylpyruvic acid which can be converted into other metabolites. (Nelson 1987).

This defect gives rise to several abnormal biochemical findings:

1) Elevated phenylalanine in the blood, about 10 to 25 times the normal; as well as in the cerebrospinal fluid.
2) Execretion of abnormal metabolites in urine; phenylpyruvic acid, - hydroxyphenylacetic acid and phenylalanine; as 30 to times the normal.
3) Related disturbances in tryptophan and tyrosine metabolism, leading to marked decrease in serum

serotonine and lower than normal blood levels of epinephrine and norepinephrine. This is the main characteristic feature of phenylketonuria that is due to deficiency of the co-factor tetrahydrobiopeterine (BH4). (Kaplan,1983).

Recently, two other types of phenylalaninemia were discovered. One is due to a deficiency of an enzyme, dehydropterdine reductase and the other is due to the deficiency of a co-factor biopterine . Both of the two disorders carry a high risk of fatality. (Kaplan,1983)

The exact mechanism of brain damage in phenylketonurea is still unknown. Some researchers think that an increase in blood concentration of a single amino acid interferes with the transport of all amino acids, causing a decrease in the intracellular amino acids, concentraction available for protien synthesis and consequently subnormal development of the brain (Nelson 1987).

The affected infant is normal at birth, and although it may develop a normal intelligence, yet, it is rarity. The mental retardation may develop gradually and not become evident till few months of age. It is estimated that the untreated children lose 50 points in I.Q. by the end of the first year of their life. It ends by severe mental retardation and institutionalised care is then required.

The clinical picture begins with vomiting, which is severe enough to misdiagnose the condition as pyloric stenosis.

The child is hyperactive, with purposeless movements rhythmic rocky and athetosis. The child is blonder than normal sibilings, with fair skin and blue eyes. This is manily due to decreased melanine. The unusual odour of phenylacetic is described as musty, mousy or wolf-like. Fifty per cent of the affected children have abnormal EEG, which improves by treatment. Twenty-five per cent of the patients have seizures. There is no neurological manifistations except in phenylketonuria due to deficiency of the co-factor tetrahydrobiopterine (BH4).

Other abnormalities, such as microcephaly, prominent maxilla, widely spaced teeth, enamel hypoplasia and growth retardtion are often met with (Nelson,1987).

Any children with transient phenylalanineamia, which is considered as an independent entity or a partial or arrested form of phenylketonuria caused by the influence of modifying genes. Such children do not develop mental retardation nor execrete phenylpyruvic acid in urine, and should not be put on such a resticted dietary treatment (Kaplan,1983).

It is worth noting that phenylketonuria mothers unless put under dietary treatment even preconceptionally, they will have a higher risk of spontaneous abortion than the general population. Their enfants as well will suffer many abnormalities; 92% of them will be mentally retarded, 37% will be microcephalic, 40% will have growth retardation, 12% with congenital anomalies (Hanley,1987).

For screening purpose, there are two main tests; ferric chloride test and Guthrie test. The ferric chloride test depends on the reaction of phenylpyruvic acid in urine with the reagent; ferric chloride, resulting in a vivid green colour. This test has some limitations. It is not a specific test for PKU, as it gives positive results with other amino acidurias such as maple syrup urine disease, tyrosinosis and histidinemia. Secondly; it only becomes positive at 6 weeks of age which deprives the infant of early diagnosis (Kaplan,1983).

The second commonly used screening test is Guthire's test, which measures the phenylalanine level in blood through biological procedures. It requires only few drops of capillary blood, if the phenylalanine level in the blood of the neoborn is more than 0.24 mmol/l, the Guthrie test becomes positive. The test sample is 3-7 days after birth, and following a protein meal (J.Alm et al.1986)

With positive Guthrie test plasma level of phenylalanine and tyrosine should be measured. The former will be about 20mg/dl while the latter remains normal (Nelson,1987). In tyrosinemia there is elevated level of serum tyrosine and sometims methionine, in histidinemia there are elevated level of histidine in plasma and urine. Also, imidazole pyruvic, imidazole lactic and imidazole acetic acids are found in urine in large amounts (Kaplan,1983).

(2) Maple Syrup Urine Disease(Manke's Disease):

This is an inborn error of metabolism, transmitted by a rare single autosomal ressive gene. It is named after the sweet odor of maple syrup found in body fluids, specially urine. The biochemical defects interfere with the decarboxylation of branched chain aminoacids; valine, leucine and isoleucine (Kaplan,1983).

The process of decarboxylation of these aminoacids is accomplished by a complex enzyme system using thiamine pyrophosphate as co-enzyme. As a result, accumulation of those aminoacids and their respective intermediate metabolites which are organic acids, in the blood causes metabolic acidosis which occurs during the first days of life; and an over flow of aminoaciduria (Nelson,1987).

The pathological changes include small brain, thin cerebral cortex, poorly demylinated subcortical U fibers, but the exact nature of the brain damage is still not clear (Kaplan,1983).

There are variants of the clinical picture; the classical one and the most severe appears in apparantely normal infants. In the neonatal period poor feeding, vomiting, lethargy, coma and if the condition is not treated death occurs or survivors sufer severe mental

retardation. The distingushed odour of urine of maple syrup raise the suspicion of the disease.

A progressive neurologic manifestation of hypertonicity which may alternate with periods of flacidity, muscular rigidity, severe opithotonus or convulsions, this neurologic picture may be misdiagnosed as generalised sepsis or meningitis. Hypoglycemia is a common finding, although this hypoglycemic state is not improved by correction of blood glucose.

A group of variants of the condition are described:

1) Intermittent Maple Syrup Urine Disease:

The disorder is generally transmitted as an autosomal recessive trait. Children who are apparently health but during stresses such as infection or surgery develop a complete picture are victims of such variant. The activity of the decarboxylase enzyme, although higher than that of the classic disease, yet is only 8-16% of the normal. (Nelson,1987)

2) Mild (Intermediate) Maple Syrup Urine Disease:

A milder form of the classic disease. There is moderate mental retardation. The decarboxylase enzyme activity is only 2-8% of the normal.

3) Thiamine Responsive Form:

In this disorder, the defect is at the binding site of the enzyme for the co-factor; thiamine pyrophosphate which is involved in the oxidative decarboxylation of all the -keto acids. This form responds to treatment with thiamine hydrochloride.

(3) Urea Cycle Disorders:

Catabolism of amino acids results in the production of free amonia, which is highly toxic to the central nervous system. Amonia is detoxified to urea through a series of reactions known as the Krebs Hemseleit or urea cycle. Five enzymes are required to accomplish this process; carbamyl phosphate synthetase (CPS), ornithine transcarbamylase (OTC), argininosuccinate synthetase (AS), argininosuccinate lyase (AL) and arginase. Individual deficencies of those enzymes have been observed and resulted in mental retardation (Efron,1966)

The overall prevalence of urea cycle defects is 1/80,000 live births, and are the most common genetic causes of hyperammonemia in infants. (Nelson,1987)

Regardless the cause of hypeammonemia, the clinical manifistation is similar and is mosly related to brain dysfuntion. The infant is normal at birth, then a few days after starting a protein diet, manifistations appear.

These are: refusal to eat, vomiting, tachypnea, lethargy, deep coma, convulsons, hepatosplenomegaly and mental retardation.

Individual causes:

1) Hyperammonemia Type I:

This condition is due to dificiency in the enzyme carbamylphosphate synthetase (CPS), which is responsible for the conversion of ornithine to citrulline; the initial step of urea cycle. The disorder is inherited as an autosomal recessive trait. The enzyme is normally found in the liver and intestine. (Nelson,1987)

2) Hyperammonemia Type II:

This is due to deficiency in the enzyme ornithine transcarbamylase (CTC). It is an X linked dominant disorder; The homozygous males are more sevely affected than the hetrozygous females, who may be mildy affected or asymptomatic carrier. The condition is diagnosed by a protein diet load. It is differentiated from hyperammonemia type I due to CPS deficiency by the increased level of orotic acid in urine. The enzyme is normally present in the liver. (Nelson,1987*Kaplan,1983)

3) Citrullinemia:

This is due to deficiency in argininosuccinate

synthetase enzyme (AS), which is responsible for the conversion of citrulline to arginiosuccenic acid. It is inherited as an autosomal recessive trait. Citrulline' level in blood, cerebrospinal fluid and urine are elevated. (Nelson,1987*Kaplen,1985)

4) Argininosuccenic Aciduria:

This is due to deficiency in the enzyme argininosuccinate lyase (AL). It is inherited as autosomal recessive trait. The enzyme is normally found in erythrocytes, liver and cultured fibroblasts. The prevalence of this disorder in the United States is 1/70,000. It is the second most common disorder. (Nelson,1987) This disorder shows a high level of arginine in blood, urine and cerebrospinal fluid. (Nelson,1987)

The laboratory studies show no specific findings when hyperammonemia is due to disorder of the urea cycle. The infant with hyperammonemia are often diagnosed as having a generalized infection and may succumb to the disease without correct diagnosis. It is therefore, imperative that plasma level of ammonia be measured in all infants whose clinical picture can not be explained by an obvious infection. The plasma ammonia is usually above 400 ug/dl; the upper limits of normal is 35-60 ug/dl. The blood urea nitrogen is usually low (Nelson,1987).

A) Citrullinemia; ageninosuccinic acid synthetase deficiency:

There is marked elevation of plasma level of citrullin. The assay of the enzyme argininosuccinic acid synthetase activity which is normally present in cultured fibroplast is confirmatory test. High levels of citrullin in urine and cerebrospinal fluid are present.

B- Argininosuccinic aciduria; argininosuccinate lyase deficiency:

There are: hyperammonemia, nonspecific increase in plasma level of glutamine, alanine and moderate increase of citrulline (less than that of citrullinemia) and marked increase in plasma levels of argininosuccinic acid which is also found in large amounts in urine and in C.S.F.

C- Hyperargininemia; arginase deficiency:

There are high level of plasma arginine, and high urinary levels of argine and of oratic acid. Assaying arginase activity in erythrocytes is conformatory.

(4) Galactosemia:

It is first detected in 1965 by Kalckar and associates, and consists of inability to convert galactose. This results in abnormal elevation of the concentration of galactose in blood. There are three different enzymatic defects known: Galactokinase, galactose-1-phosphate uridyl transferase and uridyl diphosphogalactose-4-epimerase.

In the commoner form: the classic galactosemia, which is almost always accompanied with mental subnormality, there is almost complete absence of galactose-1-phosphate uridyl transferase activity. The enzyme is absent from the liver and the red blood corpuscles, the latter fact being helpful in substantiating the diagnosis in early infancy. (Kaplan,1983)

The clinical manifestations begin after a few days of milk feeding and include jaundice, diarrhoea, failure to thrive and hepatomegaly. Untreated cases show progressive mental retardation, cataract, hepatic insufficiency and occassional hypoglycemic convulsions. The incidence of this disorder is about 1 in 50,000 (Segal, Rutman and Frimpter,1979)

Galactosemia due to deficiency of the enzyme galactokinase which catalises the initial phosphorylation of galactose. So, ingestion of galactose leads to increased concentrations of galactose in both blood and urine. Mental subnormality has not prviously been reported in association with galactokinase deficiecy. Segal et al (1979) reported two cases which are severely subnormal in addition to having the one main manifistation of galactokinase deficiency cataract.

The findings in these patients suggest that not enough information is at the hand to dissociate mental subnormality conclusively from galactokinase deficiency. The incidence of this disorder is 1 in 40,000.

Galactosemia due to deficiency of uridyl diphosphogalactose-4-epimerase has two forms. Depending on the tissue distribution, the condition can be either completely asymptomatic or clinically identical with the classic galactosemia. In the former type, the enzyme tissue activity is enough to explain the normal tolerance for galactose and also the absence of any clinical manifistation other than galactosemia.(Neson,1987 and Garibaleli RL et al.1983).

From the work of Donnell and his co-workers (1960), the relationship between the age at onset of treatment to eventual I.Q. seems clearer in galactosemia than in phenyl-ketonuria and early treatment in this disorder is in fact essential for survival. However, galactosemia should be suspected in any infant with failure to thrive (Donnel et al,1964). Masia (1960) beleives that there is a better chance of escaping mental subnormality in galactosemia than in phenyketonuria.

(5)Hypoglycemia:

The brain depends on a normal supply of glucose for its energy needs. Recurrent or prolonged hypoglycemia, particularly in the neonate during a period of critical central nervous system development, will result in brain damage, manifested by mental retardation and seizures. The mechanism of brain damage in humans is unknown but in an experiment done by Pagliara et al (1973) on neoborn rats, it was shown that hypoglycemia will result in decreased brain growth, decreased neuronal protein content and decreased myelination. Under normal circumstances, blood glucose concentration in children is maintained between remarkably narrow limits by homeostatic mechanisms regulating glucose production and utilisation(Pagliara et al, 1973)

All tissues utilise glucose as a source of energy but the central nervous system and formed elements of blood have an obligatory glucose requirement. During extended fasting, the brain is able to metabolise ketone bodies; aceto-acetate and beta-hydroxybutyrate, for up to two-thirds of its energy requirement. Red blood corpuscles, leukocytes, platelets and the peripheral nervous system oxidise glucose to pyruvates and lactates which undergo reconversion to glucose in the liver (Pagliara et al 1973).

Glycogen stores in adults provide glucose for 6-12 hours of fasting, while in infants and children, they only provide glucose for 4-6 hours. This appears to be due to both the smaller glycogen stores and the increased demands from the proportionately larger infant brain. Glycogen stores supply glucose through the process of glycogenolysis which takes place in the liver. After depletion of hepatic glycogen, gluconeogenesis starts and this represents 50% of the glucose supply during fasting and depends on amino acids. Other sources of glucose during fasting are lactates 30% and glycerol 10%. Protein break down for providing amino acids should be tightly controlled and limited as protein is required for body structure and essential functions. In addition, the protein mass in infants and children relative to total body mass is smaller than in adults (Stephen La Franchi,1987).

The criteria of Cornblath and Schwartz,1966 for hypoglycemia have been widely used for the last 20 years; their lower blood glucose level for premature infants in th first 3 days of life is 30 mg/dL and for infants thereafter 40mg/dL. Concerns have been raised however, that what may be statistically correct may not be physiologically correct, and that these levels may put some premature and

full term infants at risk for brain damage from untreated hypoglycemia. In a comparitive study by Saxon (1984) who compared the criteria of Cornblath and Schwartz: 30 mg/dL to considering the lower blood glucose to be 40 mg/dL, the percentage of neanates with hypoglycemia increased from 8.1% to 20.6% (Saxon,1984).

The clinical symptoms and signs of hypoglycemia can be divided into 2 main categories: those resulting from lack of glucose for the C.N.S.metabolism and those resulting from increased epinephrine secretion in response to hypoglycemia. Hypoglycemia in the neonate may manifest relatively non-specific symptoms such as feeding difficulties, flappiness, cyanosis or apnea, in addition to the more specific signs such as pallor jitterness, convulsions or coma. Also, electrencephalogram shows decreased voltage and diffuse slowing (Stephen La Franchi,1987).

Symptoms of C.N.S. depression due to hypoglycemia:

1-Mental confusion.

2-Irritability.

3-Visual disturbance, acute cortical blindness.

4-Bizarre or psychotic behaviour.

5-Headache.

6-Convulsions.

7-Coma.

Symptoms due to increased epinephrine production:

1-Tremors or jitteriness

2-Pallor.

3-Sweating.

4-Tachcardia.

5-Tingling sensation.

6-Weekness.

7-Anxiety.

8-Hunger.

The causes of hypoglycemia in general are classified into:

1-Failure to receive or absorb nutrients; which is an unusual cause.

2-Decreased production or release of hepatic glycogen.

3-Limited substrate for gluconeogenesis, as undernourished infants are more likely to have limited amino acid and glycerol substrates.

4-Decreased alternate fuel production.

5-Increased utilisation of glucoe e.g. hyperinsulinism, massive non-pancreatic tumours and hypothermia.

The likely cause of hypoglycemia varies with the age of presentation and with the transient or permanent nature of hypoglycemia (Stephen La Franchi,1987).

I-Neonatal Transient Hypoglycemia:

(1)Premature and small for gestational age infants:

These are at increased risk for developing hypoglycemia due to the larger brain in relation to body weight that results in high obligatory glucose requirements, reduced hepatic glycogen stores that become depleted rapidly, immature enzyme system and decreased subcutaneous fat (Stephen LA Franchi,1987).

(2)Transient hyperinsulinism:

Infants of diabetic mothers develop pancreatic beta cell hyperplasia.

Infants with erythroplastosis fetalis have hypoglycemia secondary to beta cell hyperplasia; whose cause is unknown (Urbach et al,1986).

Other causes such as malposition of the umbilical artery catheter and rapid discontinuation of concentrated I.V. glucose transfusion.

(3)Fetal distress:

Asphyxia (Cobbin and Leonard,1984).

Toxemia (Pildes et al,1973).

Hypothermia.

Cyanotic heart disease.

Chronic hypoxia (Gass et al,1975).

II-Neonatal Persistant Hypoglycemia:

(1)Hepatic enzyme deficiency:

These are relatively rare disorders, involving decreased storage or breakdown of glycogen or decreased gluconeogenisis. These enzyme deficiencies are suspected in infants who present with hypoglycemia and hepatomegaly; which is due increased lipid and accumulated glycogen. There is usually a positive family history of unexplained deaths in infancy. They are inherited in an autosomal recessive manner (Stephen La Franchi,1987).

(2)Defects in glyconeogenesis:

Glucose-6-phosphatase defeciency is the most severe form of the glycogen storage diseases, as both gluconeogenisis and glycogenolysis are blocked. The accumulated glucose-6-phosphate is converted to lactic acid, producing lactic acidosis. These patients do not show glycemic response to glucagon or infusions ofgalacose, fractose, alanine or glycerol (Pagliara,1973).

Fructose-1,6-diphosphatase deficiency tends to present later in infancy and to be less severe than glucose-6-phosphatase deficiency. Ketosis is more pronounced and a glycemic response is seen with glucagon and galactose but not with fructose, alanine or glycerol (Pagliara,1973).

(3)Defects in glycogenolysis:

Amylo-1,6-glycosidase difeciency and defects in the phosphorylase enzyme system tends to be relatively mild, and hypoglycemia and ketosis may only develop during prolonged fasting.

Glycogen synthetase deficiency; which usually presents in the neonatal period with severe hypoglycemia. Ketosis is present but lactic acidosis is absent.

(4)-Defects in fatty acid oxidation and ketogenesis:

Hypoglycemia with hepatomegaly and associated myopathy or cardiomyopathy without ketosis or acidosis should raise the suspicion of a defect in fatty acid oxidation or ketogenesis. Carnitine serves as a carrier for long chain fatty acid oxidation, hence carnitine deficiency interferes with the use of fatty acids as alternate fuels and probably also limits substrate for gluconeogenesis. Carnitine therapy has proved helpful in some patients. A similar clinical presentation is seen with deficiencies of long-, medium-, and short-chain fatty acid acyl Co-A-dehydrogenase. Carnitine is not helpful in these cases (Slonim et al,1985).

(5)-Endocrine deficiency:

Hypopituitarism or isolated GH deficiency: congenital hypopituitarism, that presents in infancy and includes GH and ACTH deficiency, will predispose the affected infants to hypoglycemia. Since both GH and cortisol stimulate hepatic gluconeogenesis: GH stimulates protein synthesis and fat breakdown while cortisol stimulates protein breakdown, hypoglycemia should be expected. The clinical tipoffs to hypopituitarism include congenital midline defects such as midline cleft lip and palate.

Primary adrenocortical insufficiency; Inadequate adrenal cortisol secretion will also predispose to ketotic hypoglycemia. This may result from congenital or aquired Addison's disease, congenital adrenal hyperplasia (Slonim et al,1985) or glucocorticoid deficiency from ACTH unresponsiveness (Soltesz et al,1985).

Other hormone deficiencies; such as glucagone deficiency and adrenal medullary unresponsiveness.

Hyperinsulinism; is the most common cause of intractable hypoglycemia. It is associated with either neisdioplastosis or beta cell hyperplasia. The hypoglycemic symptoms are usually present since the first few hours of life (Aynsley Green,1981). The infant's mother often had gestational diabetes whose diagnosis was missed and treatment delayed.

III- Childhood Hypoglycemia:

(1)-Hepatic disease:

Any disorder that interfers with hepatic function may result in decreased glycogen stores and abnormal gluconeogenesis. Severe hypoglycemia may be a feature of fulminant infections, hepatitis or Reye's disease (Glasgon et al,1973). Hence, adequate administration is an important part of the supportive management in these disorders.

Certain drugs also predispose to hypoglycemia, salicylates for example, may cause hepatic enzyme disfunction and hypoglycemia. Propranolol administration, although its effect is beta blockage, may inhibit glucagon secretion and result in hypoglycemia (Seltzer,1972).

(2)-Ketotic (idiopathic)Hypoglycemia:

It is the most common form of hypoglycemia in childhood. The age of onset is usually between 1-5 years, with a peak around 18 months. Hypoglycemia typically occurs after a longer than usual fast, 12-15 hours, or with decreased caloric intake as with an intercurrent illness or vomiting. This is often described as the "Sunday morning

fits" which occurs when the family members sleep in and the infant or child misses breakfast.

Children with this condition may be underweight for height, with decreased muscle mass, a history of being small for gestational age or having transient neonatal hypoglycemia. Some evidence supports the decreased availability of gluconeogenesis substrate; alanine. Other evidence suggests that decreased epinephrine secretion in response to hypoglycemia is the underlying mechanism (Christensea,1980).

(3)-Endocrine deficiency:

-Hypopituitarism or isolated GH deficiency

-Primary adrenal insufficiency.

-Hyperinsulinism; due to islet cell adenoma, exogenous insulin or oral hypoglycemic agents.

-Non-pancreatic tumours; which produce insulin-like substance (Mark et al,1980), for example, massive retroperitoneal tumours which manifest excessive glucose uptake.

(4)-Reactive hypoglycemia:

A wide variety of symptoms, particularly behaviour or personality changes following ingestion of certain food, and the symptoms are relieved by ingestion of food or infusion of glucose (Stephen La Franchi,1987).

(6)Hypothyroidism:

The thyroid hormones increase oxygen consumption, stimulate protein synthesis, influence growth and differentiation and affect carbohydrate, lipid and vitamin metabolism. The thyroid is regulated by the thyroid stimulating hormone (TSH), a glycoprotein produced and secretd by the anterior lobe of the pituitary gland. It is measured in blood by specific radio-immune assays. Its synthesis and release are stimulated by thyrotropin releasing hormone (TRH), which is synthesised in the hypothalamus and secreted into the pituitary. TRH is found in other parts of the brain besides the hypothalamus, and in other organs. Aside of its endocrine function, it seems to serve as a neuro-transmitter (Nelson,1987).

Further control of the level of circulating thyroid hormones occurs in the periphery. In many non-thyroidal illnesses, extra-thyroidal production of T3 decreases; factors which inhibit thyroxin-5-deiodinase include fasting, chronic malnutrition, acute illness and certan drugs.

The decreased level of T3 results in decreased rates of oxygen consumption, substrate utilisation and of other catabolic processes.

From the work of Fisher and others(1981), a useful concept has evolved that thyroid axis maturation occurs in three partially overlapped phases, and that the fetal hypothalamic-pituitary-thyroid system develops independantly of maternal influence as T3, T4 and TSH do not cross the placnta. By 10-12 weeks of gestation the fetal thyroid is able to concentrate iodine and synthesis iodothyronine. Around mid-gestation the integrity of the hypothalamic-pituitary portal system is established and functional maturation of the thyroid axis can occur, but in man, this process is not completed until after birth(Fisher,1981).

Fetal serum T4 increases progressively to approximately 1-5 ug/dl at term. Fetal levels of T3 are below measurable levels before 30 weeks and then gradually rise to about 50 ng/dl at term. At birth there is acute release of TSH which produces a dramatic rise in the level of T3 to approximately 300 ng/dl in about 4 hours. This seems to be largely derived from increased peripheral conversion of T4 to T3. Levels decline during the first week of life to about 200 ng/dl (Wilson,1985, Kaplan,1983, Fisher,1981).

These remarkable mechanisms which spare thyroid hormone effect in the fetus and then ampilify it immediately after birth, suggest one reason why early post-natal hormone replacement is so effective. The other major factor is probably the late brain growth spunt in the human compared to other species, which permits the critical period for treatment to extend into the early post-natal weeks. (Wilson,1985, Kaplan,1983, Fisher,1981).

Hypothyroidism is the resultant of deficient production of thyroid hormones.

Etiological Classification of Hypothyroidism:

I.Deficiency of TRH:

1-isolated.

2-multiple hypothalamic deficiencies

(idiopathic hypopituitarism)

II.Deficiency of TSH:

1-isolated.

2-multiple pituitary deficiencies

(craniopharyngioma)

III.Deficiency of thyroid hormone:

1-aplastic, hypoplastic or ectopic thyroid:

i.developmental defects:thyroid dysgenesis.

ii.maternal radio-iodine therapy.

iii.maternal auto-immune disease.

2-defective synthesis of thyroid hormones

(goitrous hypothyroidism)

i.trapping defect.

ii.organification defect:

absent peroxidase.

defective binding of peroxidase,

inactive bound peroxidase,

pendred syndrome.

iii.iodo-tyrosine coupling defect.

iv.iodoglobulin synthesis defect.

3-iodine deficiency (endemic cretinism).

4-damage of thyroid:

i.auto-immune disease(lymphatic thyroiditis).

ii.cystinosis.

iii.neonatal goitre;

eg,iodides, propylthiouracil,methimazol.

iv.iatrogenic:

thyroidectomy.

drugs (iodides,propylthiouracil,

methimazole,para-amino salicylic acid).

neck irradiation (eg.Hodgkin's disease).

IV.End organ defect:

1-TSH unresponsiveness.

i.defective TSH receptors.

ii.defective G unit.

iii.type I pseudohypoparathyroidism.

iv.maternal TSH binding inhibition.

2-Thyroid hormone unresponsiveness:

i.autosomal recessive.

ii.autosomal dominant(Nelson,1987).

Clinically there are two types of hypothyroidism; congenital and juvenile.

I-Cogenital Hypothyroidism:

Screening showed that it is much more common than was believed. Retrospective studies had suggested an incidence of perminent primary hypothyroidism around 1/7,000 (Alm et al,1978), but screening gave a true rate of 1/3,500 to 1/4,50 in many parts of America, Europe and Asia (Fisha et al,1979).

This wide discripancy is at least in part due to neonatal identification of children in whom the diagnosis would previously have been acquired hypothyroidism of early post-natal onset.

1.Thyroid dysgenesis:

May take the form of hypoplasia or aplasia. It is the most common among congenital hypothyroidism, comprising 80-90% of the cases. Little is known about the factors that interfere with the normal development of the thyroid gland. About 1/3 of cases have no detectable thyroid tissue and the remaining 2/3 have an ectopic or dysplastic gland (Branes,1985).

2.Maternal radio-iodin therapy:

When administered during pregnancy is hazardous to the fetal thyroid. A pregnancy test should be carried out before prescribing I131 for any woman in the child-bearing period.

3.Thyrotropin deficiency:

This could be isolated TSH deficiency or as a part of pan-hypopituitarism (e.g.hypoglycemia, micro-genitalia, persistant jaundice).

4.Thyrotropin unresponsiveness:

In such a condition, the ability of the thyroid gland to respond to TSH is impaired due to deficient activity of guanine-nucliotide-binding regulatory unit (Codaocioni et al,1980).

5.Thyroid hormone unresponsiveness:

An increasing number of patients are being found, who are resistant to the action of endogenous and exogenous T3 and T4. Most of them have goitre and clearly elevated levels of T3, T4, free T4 which led to the diagnosis of Grave's disease although they are clinically euthyroid.

The fibroblasts of the affected patients have defective receptors' affinity for T3. The resistance to thyroid hormones appears to vary among different tissues and a variable expression has been observed within families. Both autosomal recessive and autosomal dominant modes of inheritance have been described, suggesting hetrogenity (Menezes-Fereira et al,1984).

6.Defective synthesis of thyroxine:

The congenital hypothyroidism in such patients is due to a defect in the biosynthesis of thyroid hormones. Goitre is a character, and it is termed goitrous hypothyroidism or goitrous cretinism. It is detected in 1/30,000 - 1/50,000 live birth in neonatal screening program. It is genetically determined in an autosomal recessive manner. The defect could be in:

a-Iodine trapping.

b-Iodine organification.

c-Coupling.

d-Deiodinase.

e-Thyroglobin synthesis(Nelson,1987).

Clinical Picture:

The condition is twice as common in girls as in boys. The established diagnosis of congenital hypothyroidism can be reached during the early weeks of life if the initial but less characteristic manifistations are recognised.

The child is significantlly heavier at birth, with prolonged physiological jaundice, feeding difficulties and respiratory difficulties due to large tongue (apneic episodes, noisy respiration and nasal obstruction), long hours of sleep, little cry, poor appetite, conistipation, abdominal enlargement, umbilical hernia, hypothermia (35°C,

skin manifestations (dry, scaly, little prespiration and carotenemia), bradycardia, cardiomegaly, murmurs, anemia that is refractory to treatment, physical retardation and mental retardation. Physical retardation may take the form of stunted growth, short extremeties, delayed closure of fontanelles, delayed dentition, short and broad hands and fingers, delayed sitting and standing and delayed sexual maturation(Smith D.W. et al,1975), if ever.

Mental prognosis in congenital hypothyroidism is variable, ranging all the way from gross mental subnormality to a superior level of I.Q. in the 120s (Money,1956). In order to explain this vast range, one must call hypothetically on the following variables:

1. The family stock and what the I.Q. might have been if not impaired by the thyroid defect.
2. The data of thyroid failure, perhaps in utero, and its relation to developmentally critical periods in CNS morphogenesis.
3. The completeness and suddeness of thyroid failure versus the insidious onset.
4. The duration of thyroid deficit prior to it correction by thyroid substitute therapy.
5. The continuous adequacy of thyroid substitute therapy.

Money stated that the prognosis for I.Q. is better the later the onset of thyroid failure, and the fewer the signs of neurologic impairment, the earlier the onset the therapy, and the more consistently the therapy is maintained at an adequate level (Money,1956).

The mental subnormality of cretinism is not the only cognitional, and higher central nervous system defects concomitent with the thyroid deficit may be present. There are also:

i.Congenital hearing impairment, particularly for perception of higher frequencies (Pendred's syndrome) (Fraser et al,1960).

ii.Taste blindness for the bitter taste of phenyl-thiocarbamide (Shepard,1961).

II-Juvenile Hypothyroidism:

Acquired Hypothyroidism.

The development of hypothyroidism in a child who was previously euthyroid may be due to a wide variety of defects. A congenitally hypoplastic thyroid gland may furnish amounts of hormone sufficient for the first few years, but the deficiency may become manifest when rapid growth of the baby increases the demand on the gland.

Accordingly, all etiologic causes of congenital hypothyroidism must be considered.

-Complete or subtotal thyroidectomy for thyrotoxicosis or cancer.

-Removal of ectopically placed thyroid tissue, especialy a lingual thyroid which is misdiagnosed as a thyroglossalduct cyst.

-Chronic infectious processes or medications.

-Lymphocytic thyroiditis.

The clinical manifistation depends upon the age of the child at the onset of, as well as the extent of the dysfunction (Nelson,1987).

Neurologically, there is hypotonia, pseudohypertonia and rarely hypertrophy (Kocher-Dobre-Semelaigne syndrome) (Najjar,1974).

Endemic Goitre and Endemic Cretinism:

The association between deficiency of iodine and the prevalence of goitre and/or cretinism has been recognised for over half a century. If iodine deficiency is moderate; the demand can be satisfied by increased efficiency in synthesis of thyroid hormones. In areas where iodine deficiency is severe, decompensation and hypothyroidism may result (Nelson,1987).

Endemic cretinism has been recognised for centuries and only in geographic association with endemic goitre. There are two very different yet overlapping syndromes;

1-Nervous Syndrome:

The child shows ataxia, spasticity, deaf-mutisim, mental retardation but is with normal stature and little or no impairment of thyroid function. Recent evidence from Papua New Guinea strongly suggests that in the nervous type a deficiency of iodine throughtout fetal life has damaged the developing nervous system quite apart from its role in the synthesis of thyroid hormones; the damage occuring in the first trimester of pregnancy even before the fetal thyroid has developed(Nelson,1987).

2-Myxeodematous Syndrome:

The child shows marked delay in growth and sexual development, mental retardation and myxeodema. No neurologic abnormalities or deafness is observed. The iodine deficiency occurs in late fetal life of post-natally (Nelson,1987).

7-Hydrocephalus:

The term hydrocephalus is applied to conditions where enlargement of the ventricular system results from an imbalance between production and absorption of the cerebro-spinal fluid (CSF). It is almost due to interference with the circulation and absorption of the CSF, rarely it is due to over-production of the fluid. Two anatomic types of hydrocephalus are distinguished:

1)Obstructive hydrocephalus: Where there is interference with circulation of the CSF within the ventricular system itself, resulting in enlargement of the ventricular system proximal to the site of obstruction.

2)Communicating hydrocephalus: Where the interference with absorption of the CSF is due to either to occlusion of the subarachnoid cisterns around the brain stem or to obstruction of subarachnoid spaces over the convexities of the brain. The CSF pathways inside the ventricular system are open, up to the spinal subarachnoid spaces. Hence, the entire ventricular system becomes uniformly distended(Nelson,1987).

* Causes of obstructive hydrocephalus:

1)Congenital aqueductal stenosis; which is the most common cause. It is transmitted as an X-linked

recessive trait. It is usually combined with mental retardation and the characteristic aplasia of the thumb abductor muscles (Jansen,1975).

Edward et al,1961).

However, the pattern of this genetically determined condition is broader and more hetrogenous both with respect to form of inheritence and type of abnormality (Fernell et al,1987).

2)Acquired aqueductal stenosis: Occurring after infections.

3)Congenital aneurysm of the vein of Galen.

4)Posterior fossa subdural hematoma; which is common as a result of birth injuries, especially in preterm infants who suffer from a high risk of periventricular hemorrhage and intraveventricular hemorrhage (Volpe,1981) and its manifistation is a function of the severity of hemorrhage (Catto-Smith et al,1985).

5)Dandy-Walker malformation: where there is atresia of the foramina of Luschka and Magendie.

6)Midline brain tumours.

* Causes of communicating hydrocephalus are of unknown aetiology. The following are examples:

1)Arnold-Chiari malformation.

2)After infections: meningitis, toxoplasmosis, cytomegalovirus.

3)Secondary to subarachnoid hemorrhage.

4)Secondary to excessive production of CSF e.g. cases of papiloma of the choroid plexus.

5)Diseases of connective tissue e.g. Hurler syndrome and achondroplasia.

6)Vitamin A intoxication.

The incidence of congenital hydrocephalus varies in different populations, especially the type associated with meningiomyelocoele. It is about 0.1%. Aqueduct stenosis is found in about one third of all hydrocephalic children (Nelson,1987).

The clinical manifestations of hydrocephalus depend on the time of onset and the severity of the imbalance between CSF production and resorptive capacity. Abnormal enlargement of the head is a common feature; serial measurement of head circumference is essential for early diagnosis as well as for assecing the rate of prognosis.

Dilatation of the 4th ventricle, demonstrated by occipitl trans-lumination of the skull, is another feature. The anterior fontanelle is large and bulging with palpable separation of the cranial sutures which leads to MacEwen or cracked-pot sign (resonant note on percussing the skull) (Nelson,1987).

DIAGNOSIS

DIAGNOSIS

All three components of clinical process; history, examination and investigation can contribute importantly to stablishing the diagnosis of mental subnormality, and paving the way for the most specific and comprehensive therapy. Frequently, despite extemsive evaluation, a specific etiologic diagnosis is not determined.

1- History:

The chief complaint of the parents will usually focus upon development in general or one aspect in particular, and it offers clues as to why the parents have sought evaluation at that time. This part is usually subject to distortions because of parental bias and anxiety. So, development in various areas; gross motor, fine motor, language and social adaptive skills should be traced (Kaplan,1983, Herskowitz and Rosman,1982).

Past history is especially important in identifying factors that might have caused or contributed to mental subnormality. History of pregnancy, labour and delivary complications such as congenital rubella syndrome, toxoplasmosis (Krogstad et al,1972), alcohol abuse and its resultant fetal alcohol syndrome (Ouellette et al,1977) determined fetal movement, lack of intrauterine growth,

prolapsed cord and alike. Birth records often provide much valuable information, gestational age, weight, hight, head circumferance and Apgar scores, neonatal infections; neonatal pneumonia, sepsis and meningitis.

Family history should be obtained in detail. Autosomal dominant and recessive pattern of inheritance may be evident; neurofibroma and phenylketonuria. Parental consinguanity should be notted; as it inhances the likelihood of such autosomal disorders.

2- Examination:

It includes physical, neurological and psychiatric examinations. In physical examination the general discription of obvious and striking abnormal physical features (Smith,1976); such as configuration of head size, hypertelorism, flat nasal bridge, prominent eye brows, epicanthal folds, corneal opacities, low-set and small or misshaped ears, protruding tongue, disturbance in dentition, colour and texture of skin, high arched palate and size of thyroid (Kaplan,1983). It also involves measuring and plotting of growth parameters on standardized charts. for example, the head size is the most important indicator of brain growth; small head at birth suggests an intrauterine or constitutional factors (Gross et al,1978), aso large head indicates hydrocephalus.

Neurological examination; helps in determining the cause and degree of mental retardation. The incidence and the severity of neorological signs generally rise in inverse proportion to the degree of retardation. Many severely retarded children have no neurological abnormalities. Conversely, about 25% of all childrem with cerebral palsy have normal intelligence (Kaplan,1983). sensory disturbance; hearing difficulties and visual disturbances such macular scarring, retinitis pigmentosa, are frequently exist with both child's delay development and mental retardation.

Disturbances in motor functions, manifests itself in muscle tone (Spasticity, hypotonia) reflexes (hyperreflexia, hyporeflexia) muscle weakness, involuntery movements (Herskowitz and Rosman,1982).

Hyperirritable infants, convulsions with assymetrical neurological signs need attention as they well produce brain damage in later life. Infants with a combination of inactivity, general hypotonia and exaggerated responses to stimuli will have the poorest prognosis. In older children, hyperactivity, short attention span, distructability and a low frustration tolerance are often hallmarkes of brain damage (Kaplan,1983).

The psychiatric examination of mentally retarded children does not differ essentially from such examination of normal intelligent children. The similarity decreases, however, in direct proportion to the severity of the mental defect. No verbal communication and the careful observation of the patient and his activity is of greater importance in psychotic mentally retarded (Kaplan,1983). It should include estimation of the child's level of intellectual development, alertness, attention, memory, orientation, behavioural adjustment and mood assessment. The result observed should be considered along with the parents' reports, putting in mind the influence of examination situation as anexiety, negativism, withdrawal or alteration of behaviour (Herskowitz and Rosman,1982). The essential part of the mental status examination is the emotional state, and the nature and maturity of child's defences particularily self-defeating, repression, denial, introjection and isolation, sublimation potential, frustration tolerance, impulse control, self-image, and self-confedance, persistance, and curiosity. All these forms of behaviour could help knowing about the cause of the retarded child's personality development impairment.

3- Investigation:

It should be guided by the history and examination. Invstigations are carried out either to confirm the diagnosis or to specify the cause. Such investigations to be considered are:-

-Thyroid function tests.

-Assessment of hearing and vision.

-Electroencephalography (EEG).

-Chromosomal analysis.

-TORCH antibody titre in blood.

-Skull X-ray.

-Cranial CT scan.

-Blood and urine for aminoacids, urine for organic acids.

-Urine for muccopolysccharides.

-Lysosomal enzyme analysis in blood.

-Serum uric acid.

-Psychologic testing.

An aggressive approach to diagnosis is usually justified in the developmentally delayed child, because early treatment may minimize or prevent some instances of permenant mental retardation as phenylketonuria, galactosemia and hypothyroidism, and occusionally can reverse the retardation at least in part.

Defferential Diagnosis:

A variety of conditions may simulate mental retardation, such as:

1- Normal variation in development and deprived homes.

2- Sensory handicaps.

3- Chronic disease, convulsive disorders, organic brain syndrome.

4- Emotional difficulties.

5- Psychiatric conditions.

1- Normal variation in development, which falls behind the mean for the population at the time, but on the long run it proves to be normal (Koch et al,1977). Also, children who come from deprived homes that provide inadequate stimulation may manifest motor or mental retardation that is reversable if an enriched stimulating environment is provided in early childhood (Kaplan,1983).

2- Sensory handicap; especially deafness and blindness. Such children typically fail to develop normally. With hearing impairment, particularily language development is delayed. Misdiagnosing a deaf child as retarded one can easily result (Kendell and Zealley,1988). While children with visual impairment will often manifest developmental lag in milestone that cause low intelligence to be suspected (Adelson and Fraiberg,1977).

3- Organic brain disease; cerebral palsy with motor function affection may be mistaken for global retardation. Seizur disorders which may be overlooked if they are subtle or subclinical that only discovered by EEG. It is if not treated will later cause actual brain damage. Over medication of anticonvulsants may even produce delayed development or a picture of behavioural regression (Herskowitz and Rosman,1982).

4- Emotional defficulties often lead to an apparent retardation. Such emotionally disturbed children do poorly in school and perform far below their actual mental level.

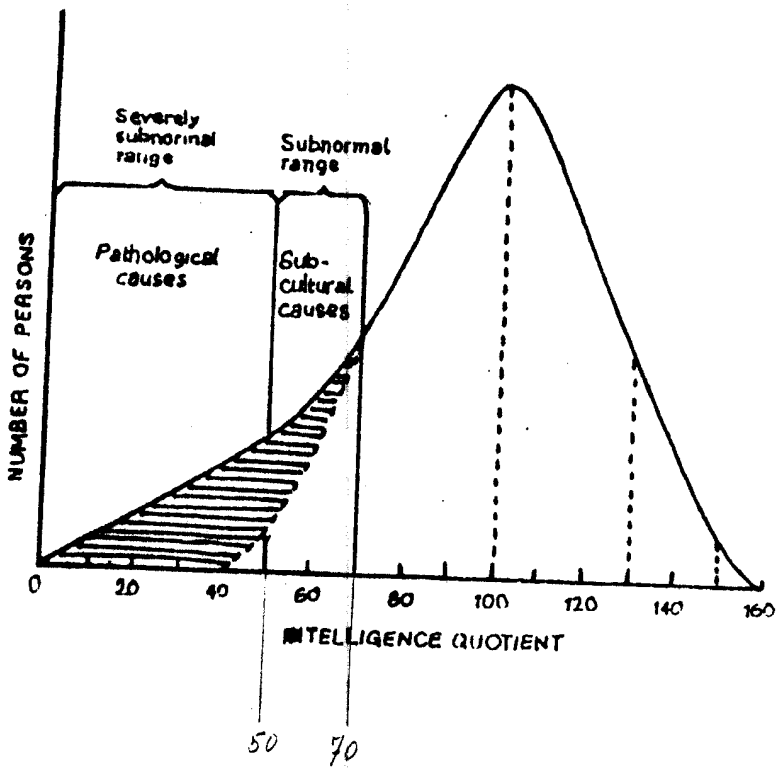
5- Psychiatric conditions; the most controversial differential diagnostic problem concerns children with severe retardation, brain damage, early infantile autism, childhood schizophrenia, and Heller's disease.

The child's early history is often unavailable and/or unreliable and by the time the evaluation is done, many children with such conditions manifest similar bizarre and stereotyped behaviour. It then, does not matter from the practical point of view whether the child's retardation is secondary to primary infantile autism or schizophrenia or whether such personality and behaviour distortion is secondary to brain damage or retardation.

Psychometry: Intelligence Quotient:

According to Eysenck (1981), the ancient Greeks introduced the concept of intelligence. They regarded it as the potential to think, reason and solve mental problems, and they differentiated it from a person's observed behaviour. Centuries later, tests of intelligence evolved, the first widely used being Binet's, which was developed in France in the early 1900s. One of the major uses of I.Q. tests in the past was to assess children in ordinary schools who had difficulties in keeping up with their classmates.

Psychological investigations have shown that one can not think of human beings as either mentally defective or normal; but must think of them as varying along a continuous scale from idiocy at one end to genius at the other. When a more or less random sample of the population, such as school children, has its intelligence measured by intelligence tests, an average is found to which most of the sample approximates. Extreme values are rare in proportion to the degree to which they vary from the average. The plotted scale of such values is a hump-backed curve; a normal curve.


Severely subnormal range
Subnormal range
Pathological causes
Sub-cultural causes
NUMBER OF PERSONS
0
20
40
60
80
100
120
140
160
INTELLIGENCE QUOTIENT
50
70

The mean gives the average value around which the majority of the population clusters and the standard deviation expresses the way in which they are scattered on either side of this point. It has often been shown that there are more people of very low intelligence that can be explained by this normal distribution alone. This excess of severely and moderately retarded individuals has termed the pathological group in contrast to the subcultural group, most of whom are only mildly mentally handicapped. The subcultural group is balanced at the other end of the distribution by a group of highly intelligent individuals, while the pathological group has no counterbalance. By this, the fact that distinction between the normal and the defective is one of degree and not necessarily of the kind.

Sperman's followers and their school found a high positive correlation coefficient between several intelligence tests and reached to a conclusion of factor analysis, which enables them to separate out a general factor; common to all tests that was called G. Thorndike's school regarded intelligence as the sum of a great number of special abilities, which explains why a person has a special ability in handling words for example, yet he is a fool in handling tools (Slater and Roth,1979). Hence, different tests measure different facets of intelligence such as verbal, non-verbal and social intelligence.

I.Q. tests measure a person's performance on a series of tasks in a particular setting, on a particular day and with a particular tester. The person's score reflects his/her underlying ability to think, reason and solve mental problems; and will depend on many factors. One of these factors is the degree to which such a score can be generalised for different days, settings and testers for the persons in question. Another important factor is the degree to which scores can be generalised for particular tasks. Thirdly is the person's motivation.

The mean I.Q. of a population is thought to rise by about 0.3 I.Q. points each year. Thus if tests with out-of-date standardisation scores are used, children's I.Q. are over-estimatd if their scores are thought to be compared to those of the current population (Glyn Murphy, 1987).

Hindly and Owen (1978) have shown that quite wide variations in I.Q. are not unusual. In their longitudinal British study, they found that between the age of 8-17 years, the scores of half of their subjects changed by 10 points or more and one quarter changed by 17 points or more.

The examining physician may avail himself of several

screening instruments such as Gesell, which studies four aspects of babies' behaviour: social behaviour, language, hand-eye coordination finally bodily coordination (Kendall and Zealley,1980, Bayley and Cattell tests that are commonly applied for infants. There is always a heated controversy over the predictive value of infant psychological tests. The correlation of abnormalities during infancy with later abnormal functioning is reported by some authors as very low and by others as very high. It is generally agreed that the correlation rises in direct proportion to the age of the child at the time of applying the test (Kaplan,1983).

Also, changes in the person's environment seem to have a major effect on I.Q.. A study done by Dennis (1976) for example, showed that normal children placed in orphanages in Lebanon before 1956 had I.Q.s of only about 50, presumably as a result of neglect. Those adopted before the age of 2 years regained a normal I.Q..

The most commonly used test for children are Stanford-Binet and Wechsler Intelligence Scale for Children, although both have been criticised for:

1- Penalising the culturally deprived child.

2- Testing mainly the potential ability for academic

achievement rather than for adequate social functioning.

3- Unreliability in children with I.Q. less than 50. (Nelson,1987).

It is wrong to place too great relaience on single score or single test; and it is only when several different assessments carried out over a period of time consistently show that a child is falling behind his peers that subnormality should be diagnosed. Yet, such phsychological tests, performed by an experienced psychologist must be considered a standard part of an evaluation for mental retardation and a principal diagnostic criterion used by health professions and agencies that deal with mental retardation.

However, such tests involve an error of measurement of approximately five points, hence an I.Q. of 70 is considered to represent a band zone of 65-75.

Social adaptive function test: It is an important area which reflecs the patient's adaptive behaviour, has been relatively neglected. The AAMD recommended that a diagnosis of mental retardation include both an individually administered intelligence test and assessment of the adaptive behaviour. The Vineland Social Maturity

Scale, based on the observation of the patient and the discription of his caretaker, the test taps the patient's comlience in meeting life contingencies and in dealing with his environment. It is especially useful in severely retarded, who are untestable by other methods (Kaplan,1983). Also, the AAMD Adaptive Behaviou Scale which includes domains that assess in dependent functioning in daily care, physical development, economic activity, language development, concepts of number and time, domestic activity, vocational activity, self-direction, responsibility and socialization. It also measures the man adaptive behaviour; violent, distructive behaviors, anti-social behaviour, withdrawal stereotyped, inappropriate interpersonal manners, unacceptable vocal and agocentric habits, self-abuse behaviour, hyperactivity, sexually aberant behaviour and use of medication. The test can be completed by parents, teachers or care takers (Jacquelin Goldman et al,1983). It was used to be carried out by social maturity scale deviced Doll in 1953 and 1965 (Anastasi,1982) also of extreme importance is information on motivational, emotional and interpersonal factors.

After the age of 3 years, mental testing is possible with standardised tests, yet difficulties are met with by

psychiatrists in diagnosing mental deficiency in those high grade defectives who show symptoms of neurotic or psychopathic reactions.

PSYCHIATRIC SEQUALAE

PSYCHIATRIC SEQUALAE

Segualae of mental retardation on the child:

When faced with the need to make a diagnosis of psychiatric illness, general practitioners and clinicians almost always relay on the way in which the patient discribes his thoughts, perceptions and feelings. Thus, if the person concerned can not speek or has a problem in communicating his thoughts, it may be difficult or even imposible to arrive at firm diagnosis. Although these problems make the dignosis of the psychiatric illness in a mentally handicapped individual difficult, it is important to be alert to the possibility of psychatric illness if such a person is displaying signs of emotional distress or unusual or disturbed behaviour.

Out of control or inapropriate behaviour of mentally retarded clients represents some diagnostic problems in determining whether the behaviour is a result of a severe emotional disturbance separate from retardation or a reflection of retardation. However, the impact of low intelligence on the development of intrapsychiatric defences, requires assessment of multiple factors to determine the nature of ego disruption (Peebles,1986).

The difficulties faced by those mentally retarded with severe learning disabilities have been succinctly described as three burdens:

1) The burden of not being sufficiently skilled to be able to adapte quickly to the world of work and the social demands of other people.

2) The burden of living in the society which fails to provide the necessary resources for those who are disabled and in which social attitudes to disability encourage rejection, segregation and isolation.

3) The burden of being aware that the one is handicapped and of the distortion in self-concept and self-doubt that this generates.

These burdens expose such individuals to psychological stress and consequently psychiatric illness (Oliver Russell,1987).

The inability of mentally retarded children to process and adapte to the environmental stimuli leads to disorganised behaviour. These which are most common are:

1- Hyperactivity: Its cause is still poorly understood, some cases are explained by sensory hypersensitivity, others by constitutional basis. Whatsoeve the cause is, the child, because of his restlessness and short attention

span finds it difficult to learn and socialise. The group members around him will reject or punish him because of his disrupting behaviour (Kaplan,1983).

2- Irritability: It is pervasive, always present or only in sporadic bursts at times of increased environmental or inner stimuli that are usually related to low-frustration tolerance.The response to the environment takes one of either extreme annoyance, anger or punitivenes or avoidence of any frustration, sabordinating the behaviour, needs and mood chages of the child (Samia Ahmad,1987).

3- Screening-out behaviour: It is avoiding the situations involving intense stimulation, anxiety or frustration or developing a capacity to turn out the environment and remain unresponsive.

The capacity to screen out excessive stimulation, although helps the child maintain emotional equilibrium, yet if it is carried out in excess autistic aloofness and withdrawal results. And this is related to the high frequency of psychotic behaviour and thinking in mentally retarded and the developmental arrest or regression that result (Samia Ahmad,1987).

4- Aggressive behaviour: it is a common behaviour met with in moderately and severely retarded children, taking

the form of pan-aggression either directed indiscriminately towards anybody approaching the child and his private world or directed towards certain people. It may be unprovoked and/or unpredictable, which is uasually due to pathological changes, mainly temporal lobe lesion with or without epilpsy. Environmental influences e.g. irritability and frustration tolerance may also induce aggressive behaviour even in normal persons. It is worthnoting that the mentally retarded child is vulnerable to both these aspects (Nelson,1987).

In the environment, the most intensive reaction to the uncontolled, distructive and aggressive behaviour is hopelessness, anger and desire to eleminate the retarded leading to institutionalisation (Mill and Bruininks,1984).

The mentally retarded child is unable to tolerate changes in the environment, even in the daily life. His reaction ranges between mild irritability to total behaviour reorganisation depending upon the severity of handicap and the magnitude of the change.

Although the physical assault is reported as highest frequent maladaptive behaviour, yet the greatest caring staff demand is reported by self-injurious action and not physical assault (Burton J.Silverstein et al, 1987).

5- Socialization in the mentally retarded child is defective as it closely correlates to the level of general intelligence. The process of self-differentiation and distinguishing from other depends upon intact sensory and perceptual mechanisms, memory and the ability to organize bits and peaces of information in a meaningful whole (Kazak et al, 1988). This results in a negativisim in his relation with his mother, the first socialization behaviour of the child.

6- A low self-steem is created into a growing mentally retarded child due to the negative evaluation of his performance by himself and other people of his environment. This explains the results of Proul Thompson (1985), which suggest that mildly retarded persons experience depression at a higher rate than do the non-retarded persons (Moen et al, 1977).

Okasha and El-Fiki (1983) attempting to classify mental disorders in mentally retarded patients, they found that the prevalence of psychiatric disorders was estimated to be 58%. Depression, schizophreenia and early child autism represented by 9.7%, neurotic disorders, behaviour diorders, hyperkinetic syndrome and hypomania were represented by about 6%. Epilepsy represented by 35.5%.

Aggression was a common sympton among epileptic retarded patients.

In a study by Gillberg et al (1986) they tried to assess the effect of the degree of mental retardation on the occureence and quality of psychiatric disorders and assessing the association between psychiatric illness and further impairment of epilepsy and Down's syndrome.

As for severely retarded individuals, psychiatric classification was impossible for about 10%, while a total of 64% showed major psychiatric disorders. The calculated frequency for the combination of severe mental retardation and psychotic behaviour in the general population was 0.15% in 13-17 years old group, 27% of severely mentally retarded suffered epilepsy.

Rating for psychiatric disorder impossible	10.0%
No psychiatric disorder	26.0%
Psychotic behaviour	50.5%
Triad of language and social impairment	27.0%
Severe social impairment	14.0%
Infantile autism	8.0%
Schizophernia	1.5%
Emotional disorders	4.5%
Conduct disorders	4.5%

Psychosomatic disorders	3.0%
Depressive syndromes	1.5%

In mildly retarded persons, there was no psychiatricaly unclassified cases ; 57% of them showed major psychiatric disorders. The frequency of the combination of mild mental retardation and psychotic behaviour in the general population was 0.05% in the 13-17 years old group; 10% of the mildly mentally retarded suffered from epilepsy and there was marked preponderance of boys.

The main finding was that more than half of the mildly retarded children had additional psychiatric handicaps.

Studying the abnormal streotyped behaviour of non-retarded infants and young mentally retarded children, Steven Schwarz et al (1986) revealed topographical difference that could be of value in early identification of this behaviour. The repetitive movements of the mentally retarded children were of greater number, smaller amplitude and longer gazing.

Abbott et al (1987) evaluated 63 persons with homocystinuria for psychiatric disturbances, intelligence, evidence of other C.N.S. problems and responsiveness to vitamin B6. The overall rate of clinically significant psychiatric disorders was 51% predominated by:

1- Episodic dpression 10%

2- Chronic disorder of behaviour 17%

3- Chronic obsessive compulsive disorders 5%

4- Personality disorders 19%

(Oliver Russell, 1987)

Aggresive behaviour and other conduct disorders were particularly common among patients with mental retardation and among vitamin B6 non-responsive patients.

Maladaptive behaviours; one critrion for suspecting mental retardation with psychiatric illness are common among mentally retarded persons (Eymann and Call,1977) and are the chieve reason for first admission (Mill and Bruininks,1984) and readmissions to public residential facilities (Intagliata and Willer,1981, Thiel,1988, Pagel and Whitling,1978, Keys,Boroskin and Ross,1973).

Sequalae of mental retardation on the family

There is a very complicated reciprocal relation between home environment and the developmental process of a mentally handicapped individual so that it can not be defined which of them affects the other. Nihira, Kazeio et al (1985) carried out a study invistigating such a reciprocal relation on a sample of 148 indiviuals of 7-14 years of age longitudinally over a 3 years period. Annual assessment of the home environment included child rearing attitudes, educationally relevant stimuli, opportunities, psycho-social climate and environmental press of the home. Meanwhile, measures of the subjects' development, including social competence, psycho-social adjustment and self-concept were done. Results revealed significant influence of the environmental stimuli on both the subjects' cognitive development and social adjustment. Harmony and quality of parenting and educational expectation as aspiration were the two most salient environmental variables associated with the subjects' development. Also, the study demonstrated the subjects' significant influences on subsequent changes in the home environment. Zettin, (1985) studying such a relation between adjusment problems of mildly mentally retarded individuals and different family environments has found that subjects from supportive families were the least

likely to experience serious behaviour disturbances. When they did, as in cases of home incouraging dependancy, it was likely to be a form of emotional disturbance. While subjects from families with conflicts, were most likely to act out and adopt anti-social forms of behaviour.

Wright et al (1985) in their study to examine how parents of a mentally handicapped child perceived themselves and how exceptional parents were perceived by their undergraduate normal children, found that:

1- Exceptional parents were 6 times as likely as parents of non-handicapped to indicate that the children caused marital problems.

2- They experienced significantly more negative emotions in relation to parenthood.

3- No significant difference between exceptional parent group and control parent group concerning self-rating or life satisfaction scores (Silbert et al,1982, Vance et al, 1980).

4- Exceptional mothers were more likely perceived by their normal undergraduate children as having had emotional problems at sometime than were mothers of non-handicapped children (Kazak, Marvin, 1984, Tavormina et al, 1981).

However, exceptional parents were rated as being no more likely than parents of non-handicapped children to be angry, depressed, alcoholic, non-supportive or divorced. The parents of retarded children are usually besetted by overwhelming feelings of guilt, anexiety, hostility and insecurity. Many of the retarded children's parents suffer from a degree of emotional disorganisation, but vary in intensity and quality of their reactions. Most of them experience considerable tension and anguish at the time of initial diagnosis, causing a weakening of the habitual defence system and a temporary breakdown of adjustment pattern. Such initial period; immediately after the diagnosis is extremely crucial and may have a deciding influence on the parents handling of the child in the future. Repeated discussions between the physician and the child's parents about the prognosis are usually necessary to help them absorb the full impact which will inevitably be followed by a slow bereavement (Nicholas, 1983).

The ultimate impact of the retarded child on the family depends on several factors:

1- Degree of retardation.

2- Personality and life adjustment of each parent preceeding the birth of retarded child.

3- The degree of parents' professional and social success, and socio-economic status.

4- The adequacy of marital adjustment.

5- Other children in the family and their intellectual progress.

Hence, some families behaving in an extremely self-destructive or resistant manner, will pose a formidable obstacle to their disabled relatives' habilitation. Such frustrating families to work with, will consequently be provided with only little professional assistance. The maladaptive family behavioural pattern may include loud, chronic complainings program sabotage, extreme overprotection, hypochondriacal obsessions overt hostility, symbiotic relationships, avoidance of the disabled person and psychosocial deprivation. (Munro, 1985).

On the other hand, if the parents are well-adjusted, with positive self-image and their marriage is based on mutual support and free communication. They will be able to absorb the retarded child with upsetting no family members. While if parents are emotionally immature, have low self-esteem and beset by neurotic conflict, the arrival of a defect child may precipitate a crisis that may lead even to family breakdown (Wright et al,1985).

The child may be cast in the role of scapegoat to drain off the family tension, rejecting him by institutionalization is followed by rising the family tension up to separation or divorce.

Social life of family frequently becomes limited and a feeling of isolation results. Low family adaptability and cohesiveness felt especially by mother were provided by Kazak Anne at al (1988) as the early closeness between the mother and child is the first stone for his development, and it is promoted by the feelings of bride and acceptance and reinforced and continued by the child's predictable responses such as smiling, cuddling and playfulness such responces are delayed in mentally handicapped children and this creates parental inner turmoil, grief, disappointment even feeling of guilt and failure (Samia Ahmed,1987). Maternal care and depreviation present to the emotional and intellectual development a great importance. The decreased amount of mothering, affection and stimulation provided to the retardod child will result in irretrievable loss of whatever inner resources the child process, as in cases of early inistitutionalisation.

Denial, infantalization, rejection by institutionalization, overprotection as a reaction formation to feelings of rejection and whatsoever predominent defences of the family may help or hinder their adjustment to presence and handling of the retarded child as well as helping him to develop and overcoming what Rodger, Sylvia (1985) addressed as arrest of the family cycle. As the parental roles remain fairly constant because they still have a socially dependent child to care for regardless of her or his position in the family, he remains the youngest. And the young normal siblings must adapt to becoming superordinate in their relationship with an older retarded siblings and decreased attention with increased responsibility, especially those concerned with parental expectation of acadmic performance.

In a comparitive study of house holding expendature pattern of families in the general population and families with intellectual handicapped members in New Zealand, there were $17/week in household items such as food, especially with diatry restriction, electricity supplies, also $27/week for handicapped child care such as especial toys, equipments health care (Alm et al,1986, Chetwynd,1985, Buckle,1984).

PREVENTION

PREVENTION

Prevention of mental subnormality is rather a complex and multifacet problem. It needs cooperation of many community services; medical and community health, nutritional, educational and public attitudes. In many countries, such as Denmark and Switzerland, the law, through a very direct way, dealt with this problem by sterilisation of defectives. It remains undoubtedly uneffective on the large scale and the problem remains. Reorientation of the public attitudes and values rather than semi-complusatory or voluntary measures directed towards a small section of the community; the defectives, is the most acceptable means of solving the problem of mental subnormality (Slater, Roth 1979).

Prevention as a strategy is composed of three steps intervention continuum. Primary prevention, is the measures taken to make the out come of high risk infants not retarded, while secondary prevention includes early detection and treatment aiming at total cure or least possible damage; total habilitation. Tertiary prevention is concerned with preventing any complication of the mental subnormality and its consequent treatment.

Primary prevention:

It is mainly the role of the whole community; although the medical services represent the major participent.

(1)Public Education: It is of great importance to sweep away many superstitions such as considering mental subnormality as a curse or visitation, but to make the public realise that it is an illness to be studied and treated and that the defectives are individuals who have needs of love and care and have feelings of love and hate, anger and compassion (Kaplan, 1983).

(2)Improvement of Socioeconomic Standards: By improving the socioeconomic standards we overcome the secondary phenomenon of malnutrition, prematurity, obstetrical hazards that precipitate mental subnormality, as well as under-stimulation or over-stimulation environment that would worsen the pre-existing subnormality. Half measures or superficial palliative solutions can not be effective in interrupting the vicious self-perpetuating cycle of poverty (Kaplan,1983).

(3)Preventive Medical Measures: This includes prenatal and perinatal care and pediatric prevention. The prenatal care is composed of restricting the number of pregnancies in adolescence and old age (after the age of 40) to reduce chromosomal aberration , to provide adequate nutrition

especially during pregnancy; vitamins, minerals and control of maternal conditions such as diabetes mellitus or pre-eclampsia, prevention of infections during pregnancy such as syphilis, German measles and toxoplasmosis (Krogstad,1972, Pasamanick and Knobloch, 1955).

Delivery techniques and drugs such as anaesthetics, and analgesics used during labour should be applied thoughtfully. Also, close observation of the mother during the process of labour is essential. Apgar scoring gives a good and significant clue about the neoborn (Nelson,1987). Pediatric preventive programs of early and adequate diagnosis and treatment of acute illnesses and convulsive disorders and its causes such as hypoglycemia and hypocalcemia.

(4)Genetic Counselling: This usually involves the question of the desirability of future off-spring by parents,siblings and sometimes more distant relatives, which can be done by private practitioners and staff physicians in clinics and hospitals. Knowledge in genetic counselling is still limited and precise data are available only in few conditions, while in many cases counselling is complex and is best left for the special centers which are equiped with cytogenetic and biochemical laboratories for specialised tests (Nelson,1987).

The first step in genetic counselling is to make certain the diagnosis is correct with whatever means possible, then the counselling proceeds as follows:

1-Review the family history of each parent and identify any unrecognised genetic risks. This can help identify carriers.

2-Review the interpretations the family has made or those offered by others.

3-Discuss the medical consequences of the defect and the variability of associated features that may develop.

4-Describe the genetic basis of the problem.

5-Explain the genetic risks using terms that the family can understand. This means that the physician's role is to present the known facts and the uncertainties.

6-Outline the options available, such as having no children or having children and accepting the risk.

7-Finally provide the parents with a summary of the issues discussed and if possible meet them again to help them decide which option they would take and be in contact with them to provide any new information that become available (Nelson, 1987).

Genetic Counselling for Prenatal Diagnosis:

Many couples seek genetic counselling to learn more about prenatal diagnosis. The most common indications for this are:

1)Advanced maternal age.

2)Previous child with Down's syndrome, anencephaly or meningiocoele.

3)Autosomal recessive inborn errors of metabolism (Kingston 1984).

Methods of Prenatal Diagnosis:

1-Ultrasonography.

2-Maternal serum alpha-feto-protein (AFP).

3-Amniocentesis

4-Fetoscopy

5-Chorion biopsy.

(1)Ultrasonography:

It is a safe, non-invasive investigation which gives, not only an accurate assessment of growth parameters, gestational age, placental localisation, but also detects some fetal abnormalities such as neural tube defects and hydrocephalus (Vardi et al 1987).

(2)Maternal Serum Alpha Feto Protein:

Raised levels of AFP in maternal serum in neural tube defect preghancies were first reported by Brock and Sutcliffe (1972) and subsequently used as a screening test

for such affected pregnancies. It was also found that it is significantly lower in pregnancies associated with Down's syndrome than in those associated with neural tube defects, during the first 14-20 weeks of gestation (Cuckle, 1984). Eighty to ninety per cent of cases of anencephaly and meningiomyelocoele are diagnosed by AFP.

N.B: Other causes of low maternal serum AFP are:

1. Low maternal weight.
2. Low birth weight.
3. Fetal sex.
4. Maternal diabetes mellitus.

Other causes of high maternal serum AFP are:

1. Underestimated gestational age.
2. Threatened or missed abortion.
3. Twin pregnancy.
4. Abdominal wall defects (exomphalos).

(3) Amniocentesis:

This comprises the aspiration of amniotic fluid sample under aseptic conditions, using local anaesthesia, at 15-17 weeks of gestation. The first 2ml of the fluid are usually contaminated by the mother's skin, then 10-30 ml of the amniotic fluid are withdrawn and the cells separated from the fluid are cultured. Fetal loss from amniocentesis is about 0.5%, 3% of mothers will suffer from transient cramps

and leakage of amniotic fluid and 5% will need a second sample. Results will be obtained within 2-3 weeks. Termination of pregnancy, if indicated, is advised to be conducted before the 20th week of gestation (Nelson, 1987).

Howard S. Cuckle et al (1984) in their study pointed to an increase in detection rate for Down's syndrome by the combination of low maternal serum AFP, young maternal age and amniocentesis, by 40%.

(4)Fetoscopy:

This enables the direct visualisation of the fetus and sampling of fetal blood or tissues during the second trimester of pregnancy. The procedure is performed under local anaesthesia with the aid of ultrasonography. Fetal mortality is less than 5% (Globus 1982). Fragile X syndrome and fetal rubella infection can be diagnosed by fetal blood sampling. Some metabolic disorders in which the enzymes are only present in the liver can be also detected.

(5)Chorionic Biopsy:

This provides the early prenatal diagnosis during the first trimester as it is performed between 8-12 weeks of gestation. The chorionic villous tissue is obtained through the cervix. It reaches up to the placenta and provides a direct chromosome analysis and enzyme assay. The risk of fetal loss after this procedure may be below 2% (Nelson, 1987).

Genetic Counselling for Detecting Carriers:

It is simpilified, more specific and more effective if the carrier state of the genetic abnormality in question can be identified by laboratory tests. Through DNA analysis techniques; such as gene mapping, identification of a restricted length polymorphism that is closely linked to a mutant gene (Daiger et al, 1986) prenatal diagnosis and carrier detection of PKU families can be done.

Persons who are heterogenous for some autosomal recessive inborn errors of metabolsim can be identified, yet, screening for such genetic diseases is limited.

As for inborn errors of metabolism, they are not strong indications for carrying out prenatal diagnosis with all its risks. For example, in PKU, many authers suggested that preconception dietary management, not only during pregnancy, should be done to reduce the fetal abnormality (Levy et al, 1982, Scott et al 1980, Smith et al 1979, Buist et al 1978).

Levy and Waisbren (1983) proved the presence of an inverse and apparently linear relation between maternal blood phenylalanine concentration at conception and the birth weight and head circumference.

Hanley et al (1987) listed these fetal abnormalities:

92% of offspring are mentally retarded.

73% have microcephaly.

40% are growth retarded at birth.

12% have congenital anomalies. Many studies prove the efficiecy of preconceptual management of maternal phenylketonuria in preventing fetal abnormalities (Drogari et al,1987, Farquhar et al,1987, Rohr et al,1987, Lenke and Levy,1980, Nelson et al,1979). In Drogari's 1987, study the group of mothers with phenylketonuria who followed restricted dietary regimin before conception which maintained the blood phenylalanine concentration below 600 mumol/l, had completely normal infants.

Secondary Prevention:

Its main concern is to early diagnose the cause of mental subnormality and treat it so as to lessen the damage to the brain as much possible as treatment could provide.

The main group of patients who would benefite most from such a preventive measure are those who represent with treatable causes of mental subnormality; phenylketonuria, congenital hypothyroidism, hypoglycemia and others.

Screening tests are of utmost importance for early suspecion of certain diseases. They, hence, invite for further invistagation and follow up and justify aggressive investigations. However, screening tests must be practically acceptable, and must combine the maximum discrimination with minimum cost and inconvienience. For instance, in congenital hypothyroidism cord blood screening offers the earliest postnatal diagnosis yet, doing additional sample is invitably complex and expensive. Also. measuring thyroxine only will not screen infants with compensated primary hypothyroidism and has 30% of cases will be missed (Barnes,1985).

Economically, the operating costs of effective mental screening program are small when compared with the costs of extented treatment and care for affected infants

(Haltzman NA et al,1981, Layde PE et al,1979).

Besides, the benefits to patients, family and society as a whole are immeasurable.

I-Congenital Hypothyroidism:

The screening policy is to measure whole blood thyroxine concentration in duplicate on all samples and follow up the lowest 20% with estimation of the whole blood thyrotropine (T.S.H.) concentration in duplicate. If thyrotropine is more than or equal to 25nU/L, the child is recalled for examination and further investigation. This procedure is usually done if the blood sample is taken early, but if the sample is delayed for few days; thyroid stimulating hormone; thyrotropine; assay will be better (ND Barnes, 1985). Despite; GA Grant et al,(1986) reported 3 missed cases and recommended a second routine screening test, done after few weeks. Also, Lazarus JH et al (1983) and Gendrel D et al(1981) have reported false positive thyroid stimulating hormone assay either spontaneously or induced by immunization of the mother with preparations containing rabbit serum respectively. So, reassessing the diagnosis before committing the child to life long replacement treatment is essential (Lazarus et al,1983, Gendrel D et al,1981).

As for replacement therapy, it should be carried out as soon as possible. Synthetic Sodium L.thyroxine is the drug of choice, as it provides both T3 and T4. An initial dose of 10 ug/Kg/day is suitable (New England Congenital Hyperthyroidism Collaboration,1984). Older children requires a dose of 100-150 ug/day rarely 200 ug/day; 4 ug/Kg/day. Adequate dosage can be judged from the patients thyroid axis; the correct dose is defined as the smallest amount which suppresses the thyroid stimulating hormone into upper half of the normal range (>8 ug/dl) (Nelson,1987).

Regular monitoring of progress, with special attention to growth, psychomotor development, symptoms and signs of thyroid dysfunction and biochemical thyroid functions test is essential. This biochemical thyroid function test gives a clue about the adequacy of dosage and compliance. Check follow up program comprises 1 month, 3 month after starting replacement therapy. Then 3 monthly check through the first year, 6 monthly check till school age. Finally, annual check up till growth and development is complete.

At the age of two; reassessment of diagnosis should be carried out, as brief interruption of the treatment will not be harmful (ND Barnes,1985).

Prognosis:

In a follow up study results showed that there is no difference between affected children treated within the first 4 weeks of life and normal control children at 2 years of age on Bayley motor development index, and at 3,4 and 5 years of age on Stanford-Binet IQ assessment, and at 16-26 years of age there was a remarkable improvement of I.Q.; a mean increament of 21 points (Money et al,1978).

II-Phenyketonuria:

In screening for phenylketonuria, Guthrie test of bacterial inhibition is more specific and widely used. Positive results of Guthrie test raise the suspecious; hence plasma phenylalanine concentration is determined as confirmatory test.

Treatment should begin at once, aiming at maintaining the blood phenylalanine level between 2-9 mg/dl so as to minimize the brain damage (Guttler,1980). Low phenylalanine diet should be closely supervised, and monitored since over treatment as well, has side effects. Phenylalanine deficiency manifests itself clinically as lethargy, anorexia, anemia, rashes, diarrhoea and even death (Nelson,1987).

So, continuous evaluation of the dietary management of

each individual treated with a low phenylalanine diet reduces the use of unnecessarily restricted diet with their attendent psychological, social and economic strains, as Alm J et al(1986) in their study showed that one third of the phenylketonuric children markedly increased their dietary tolerance during the preschool age. This also partially explains the great diversity in I.Q. scores among those children (Alm J et al,1986).

Blaskovics et al(1974) have speculated about regulatory mutations of the phenylalanine hydroxylase system induced by phenylalanine in diet, to be responsible for increased tolerance.

Prognosis

However, numerous studies have shown that even children with PKU treated early in childhood have cognitive deficits; such as deficiency in solving complex spatial problems, problem solving strategy, attention span and accuracy of mental representation despite efforts to maintain well controlled phenylalanine concentration in the blood (Brunner RL et al,1987,Dennington BP et al,1985,Brunner RL et al,1983,Melnick CR et al,1981,Koff E et al,1977).

Other studies have shown that I.Q. scores of children

with phenylketonuria may further decline, as well as reading and spelling score test when the diet discontinue which usually occurs at the age of 6 years(Fishler et al,1987,Seashore MR etal,1985,Smith,1978,Cabalska B et al 1977,Brown ES,Warner R,1976).

This was explained by Herroro E et al(1983) findings who proved that high concentration of phenylalanine interferes with dopamine and serotinine synthesis from the precursers tyrosine and tryptophan as manifested by significant decrease of homovanilliv acid(HVA) and 5-hydroxyindole acetic acid(5-HIAA).

The I.Q. scores among treated children of phenylketonuria shows a great diversity, as great as that found in the general population. The reduction in I.Q. scores noted in children who discontinued the diet may not occur in all cases and may also be seen in children who continue the diet (Cabalska B et al,1983, Waisbren SE et al,1980).

Williamson ML et al(1981) determined the factors that predict this variability among individuals with phenylketonuria as:

1-Mothers' I.Q.;the best predictor of the children's I.Q. and they are higher than children(Koch R et al

,1984, , ,Dabson JC et al,1976).

2-The age at which dietary treatment was initiated.

3-The rate of increase of blood phenylalanine levels (Kronmal RA et al,1985).

Also, Susan E et al(1987) found that children with a natural (off diet) blood phenylalanine level less than 18 mg/dl were less likely to suffer I.Q. loss after diet discontinuation than those with higher natural blood phenylalanine levels.

Lou HC et al(1987) in their study found that ristricted phenylalanine diet or addition of tyrosine in a dose of 160mg/kg/day to free diet result in increased vigilance and dopamine synthesis. And, they concluded the importance of phenylalanine restriction and its continuation or alternatively tyrosine treatment; as a second choice if satisfactory compliance becomes difficult.

III-Urea Cycle Disorder; Hyperammonemia: In acute cases of hyperammonemia, treatment should be carried out promptly and vigorously to overcome the neurologic manifestations. The treatment goal is to remove ammonia from the body and provide adequate calories and essential amino acids, minimizing the breakdown of endogenous protein. Dialysis, peritonealy or hemodialysis, normalize

the plasma level of infants within 48 hours. Sodium benzoate 250 mg/Kg/day , to form hippuric acid with endogenous glycine is the most effective way of detoxication and excretion of ammonia (Nelson,1987).

Phenylacetate 250 mg/Kg/day congugates with glutamine to form phenylacetylglutamine which is readily excreted by the kidneys

Arginine 300-700 mg/Kg/day promotes ammonia excretion by forming intermediate metabolite of urea cycle.

It will take few days till consciousness is restored again.

Protein restriction 0.5-1.5 g/Kg/day regardless of the enzymatic defect should start. Catabolic state triggering hyperammonemia should be avoided (Nelson,1987).

IV-Hypoglycemia:

Once diagnosing hypoglycemia; blood glucose is less than 40 mg/L, intravenous glucose should be administered so as to raise the blood glucose approximately by 35 mg/dl. Bolus infusion of high concentration of glucose is not necessary and should be avoided because of the rapid osmotic changes and the rebound hypoglycemia. Secured central line will help maintaining plasma glucose above 50 mg/dl and prevent sclerosis of small peripheral veins

(Stephen La Franchi,1987).

Specific treatment should be instituted once the cause of hypoglycemia is known.

1-Transient hypoglycemia is treated by supportive I.V. glucose till gluconeogenesis enzymes mature.

2-Glucose-6-phosphatase deficiency is treated by frequent day time feedings and during night time of 8-9 mg/kg/min by nasogastric (Schwenk and Maymond,1986)

3-Endocrinal replacement of hydrocortisone, growth hormone, thyroxine, protamine zinc glucagon.

4-Medical trial by frequent feeding and diazoxide; in cases of hyperinsulinemia to maintain plasma glucose level above 50 mg/dl. Otherwise 90-95% pancreatectomy is done (Campbell et al,1983).

5-Frequent high carbohydrate and protein feeding would do good with idiopathic ketotic hypoglycemia. Spontanuous resolution by 8-10 years of age always occurs.

V-Galactosemia:

Preliminary dignosis of galactosemia is made by demonstrating a reducing substance in several urine specimens collected while the infant is recieving human

milk or cows milk or any formula containing lactose.

Galactose free diet is essential to gard against liver cirrhosis and mental retardation and cataract and recurrent hypoglycemia, the prognosis is generally good (Nelson,1987).

VI-Hydrocephalus:

The ideal goal of treatment of hydrcephalus is to re-establish equilibrium between C.S.F. production and resorption. Mild and slowly progressive hydrocephalus response occasionally to Acetazolamide; 40-75 mg/Kg/day which diminishes C.S.F. production. Otherwise shunt operations; ventriculo-peritoneal, ventriculo-atrial shunts. One of the complications of shunt operation is infection which requires removal of the shunt and administration of antibiotic therapy. Obstraction of the shunt tube also occurs especially with elevated C.S.F.protein. Repeated lumbar puncture is the procedure of choice if hydrocephalus is the result of subarachnoid haemorrhage or bacterial meningitis.

Close and careful medical supervision is a must for detecting either acute or chronic failure of shunt operation (Nelson,1987).

Tertiary Prevention:

The main concern of this process is to increase the ability of adaptation and function of the mentally retarded individuals rather than the prevention of specific mental illnesses, although both are included. Through this step, narrowing of the gap between the quality of life and emotional adjustment; psychosocial prevention, is aimed at (Ludwik S, 1987).

However, there are many misconceptions about psychosocial prevention. Some of the most common misconceptions as Ludwik S,1987 mentioned are:

1-The belief that persons with mental retardation and their families develop similar problems that require similar interventions, but are different from those developed by non-retarded persons (Philips, 1966).

2-The belief that prevention and treatment should focus on single objectionable behaviour only. It is more popular among professionals with narrow training in assessment, treatment techniques and administration.

3-The belief that elimination of a specific cause of the maladaptaion will prevent or cure the maladaptive behaviuor.

4-The belief that only a specialist can deliver an intervention.

5-The belief that an earlier and more intensive intervention is always best.

6-The belief that all mental health problems are preventable.

Brimblecombe argues that the meaning of care for disabled people has become distorted because it is often considered that the type of care is decided by those who provide it and not the choice of those who need it. Unfortunately, some service providers have become so conditioned to a specific system of service that they are unaware of the possibility that their service could be more flexible and more geographically distributed, allowing a better response to the needs of young intellectually retarded adults (Brimblecombe, 1985).

Help is required in three aspects of the lives of the mentally retarded young adult :

1-Occupation.

2-Housing (Rutter, 1982).

3-Areas of extra need :health, social living and education (Reiss and Benson, 1985).

A great deal of attention should be paid to the develomental approach in preventing the emotional adjustment. Mentally retarded persons develop much as any other individual would, but at a slower rate. Successful resolution of one stage or crisis provides a good start for the next (Ludwik S,1987).

There are few studies on the association between various factors, such as relocation syndrome, and the emergence of discrete mental disorders, such as depression, in the mentally retarded population (Carsrud et al 1980, Weinstock et al 1979 and Cochran et al 1977). One might hypothesize that elimination of certain factors might prevent the emergence of these disorders. However, practical experience discouraged this concept (Ludwik S,1987).

Parents need training and advice concerning management of normal environmental crisis without creating added problems. They have to learn to foster their children's successes and to achieve gratification from them, no matter how small these successes are. This helps build positive self-esteem which is of important preventive role. This concept should be encountered also among non-family care givers.

A service, directed towards the parents themselves, providing counselling and preventing stress and exhaustion related to the care of the mentally handicapped family member is important (Ludwik, 1987).

The second aspect of tertiary prevention is early diagnosis and treatment of mental illness secondary to mental subnormality. Observation of any behaviour changes by family or care givers should be counted and not ignored as attention getting behaviour especially with non-disturbing; withdrawal in depressive disorder behaviours (Ezymansk and Beiderman 1984).

There is a lack of mental health professionals trained and motivated to work with persons who are mentally disturbed and subnormal (Cushna et al, 1980).

However, the current ternd in mental health is to focus on crisis intervention; usually by psychoactive medications alone, in order to reduce the rate of subsequent hospitalisation.

Singh and Millichamp (1985) in thier study on the effect of antipsychotics on self-injurious behaviour have found that antipsychotics and antimanics may be useful.

Other researchs conducted by Goldwater Regonal Centre for Developmental Disabilities have emphasized that administration of psychotropic drugs to mentally subnormals may depress the learning performance and interfere with the response to external reinforcement contingencies. Other studies have failed to support this. In fact they claimed that such drugs can supress maladaptive behaviour, such as stereotypies and facilitate learning at determined dosage (Aman and Singh, 1986).

Several studies have been carried out on the effect of lithium in controlling the aggressive behaviour in mentally retarded. Lithium efficiency was between 50% and 88% (Graft et al 1987, Dale 1980, Worrall et al 1975, Micev and Lynch 1974, Cooper and Fowlie 1973, Forssman and Walinder 1969). Even patients who suffered side effects had not to be withdrown from the study.

Harper and Reid (1987) found that diet with restricted protein and high energy given to a 54 years old profoundly mentally retarded female with PKU improved significantly her behaviour.

Side effects of long term administration of antipsychotics to the chronically mentally ill who are mentally subnormal might be more crippling than the mental disorder for which the drug is given. Hence, drugs should be used rationally in the lowest possible dose and with good follow up and with periodic discontinuation trials.

Finally, two major facts influencing the development of services for the mentally handicapped people should be considered:

1-The most effective way of providing help and support for such people is to create services which recognise that all people are capable of some degree of learning throughout life, even those who are suffering from the most severe learning disabilities as Clarkes',1974 included in their definition of mental subnormality.

The cognitive therapy is possible in patients with I.Q. of 80-70 and it tackles the feeling of inferiority that the mentally subnormal has.

2-Such people develop best in environments which are as near normal as possible (Oliver Russell,1987).

Total habilitation is being considered now, especially after the recent impressive study of Lovaas (1985). In this study 19 preschool children with mental retardation, ten of whom were severely retarded, participated in a 2-3 years treatment program that focused on language development. At the first grade follow up, 9 of the 19 children were functioning normally, in a regular first grade class, with an average I.Q. of 107. Only 2 of the 19 children were still functioning as severely retarded.

Perhaps in the near future with methodological development and more relaiable technology; professionals will accept the concept of total habilitation for mental retardation (Philip, Rayer and Murrin,1985). It still needs more study and harder work.

LEGAL ASPECT

LEGAL ASPECT

The Egyptian mental health act

Definitions:

1- Mental disorders: It is a mental illness, arrested or incomplete development of mind, psychopathic disorder and any other disorder or disability of mind.

2- Mental impairment: Means a state of arrested or incomplete development of the mind which includes significant impairment of intelligence and social functioning and is associated with abnormally aggressive to or seriously irresponsible conduct on the part of the person concerned.

3- Severe mental impairment: Means a state of arrested or incomplete development of the mind which includes severe impairment of intelligence and social functioning, and is associated with abnormally aggresive or seriously irresponsible conduct on the part on the persons concerned.

4- Psychopathic disorder: Means a persistant disorder or disability of mind (whether or not including significant impairment of intelligence) which results in abnormally aggressive or seriously irresponsible conduct on the part of the person concerned.

Promiscuity or immoral conduct, sexual deviancy or dependance on alcohol or drugs are not regarded as menatal

disoreder (A Okasha, 1988).

In the review of Aly AR 1989, he reported that lower intelligence or mental retardation may play a role in homocide. They may reflect poor judgement, inability to know right from wrong, or brain pathology, perhaps indicating minimal brain dysfunction or epilipsy. As in the case of diagnosis, results of I.Q. testing may reflect the nature of the institution from which the sample of killers is drawn. For example, Szymusik, 1971, studied 38 murderers in a Polish prison-hospital and found only 15% had normal I.Q.s, the rest being defective. Mc Knight et al, 1966, found that 57% of their Canadian prison hospital sample did not finish public school, while 5% had a university qualification and 20% had bright normal I.Q.s. In Lanzkron's, 1962 sample of 150 insane killers, 60% had average I.Q.s but the rest were lower with 11% of moron level. however, in the case of severely disturbed psychiatric patients, the validity of the I.Q. assessment may be questionable. Pegan and Smith,1979, found that 97% of 30 murderers had achademic or behavioral difficulties in school and that 79% were in dull/normal range of intelligence. Hays et al, 1978, found juvenile murderers had significantly lower I.Q.s than other offenders on the

WISC but Deiker, 1973, found that WAIS I.Q. was generally average in 190 prisoners convicted for murder. Also as Aly AR, 1989 reported in his review study that Kahn, 1959, in one of the very few controlled studies of homocide, found that 15 killers in contrast to 24 burglars at Bellevue Hospital were older (mean age 41 years, vs 27 years), had fewer previous criminal records and were more often legally insane, but there were no significant differences in I.Q.. Once again, the more frequent use of a non-homocidal control group would elucidate greatly the over all role of I.Q. in understanding homocide. Langevin et al 1982b, compaired 109 killers with 38 non-violent offenders and 54 community controls in psychiatric diagnosis, I.Q. and clinical results. There was no difference in the incidence of mental retardation in killer from non-violent patient. It was diagnosed in 4% of killers and 3% of non-violent offenders. In over all I.Q. scores killers scored lowest. They did not differe significantly from non-violent offenders on V.I.Q. but they scored significantly lowered on the Raven (performance) I.Q.. However the great majority of killers scored in the normal or suprior range on both tests. They did show trend to scoring lower than non-violent offenders in both I.Q. mesures and this

finding warrants further investigation. Neurological evidences suggested in some cases that the brain patology may play a role in the I.Q. scores and perhaps in the homocide. Surprisingly, fewer killers than non-violent control were given the E.E.G. examination but of those who recieved it, there were no significant difference between the 2 groups. Only a small portion of each group recieved other neurological examination and, of those there were significantly more killers with abnormalities. This was reflected in history of seizures or brain pathology. In general the results were equivocal and only involved a small portion of homocide cases.

القانون المصرى والمتخلفين العقليين

تنص المادة ٦٢ من قانون العقوبات على الآتى:

" لاعقاب على من يكون فاقد الشعور أو الأختيار فى عمله وقت ارتكاب الفعل اما لجنون أو عاهة فى العقل واما لغيبوبه ناشئة عن عقاقير مخدرة ايا كان نوعها اذا أخذها قهرا عنه او على غير علم منه بها"

(حسن صادق المرصفاوى ١٩٨٥)

كما تنص المادة ٦٥ كما جاءت فى موسوعة الأحوال الشخصية (معوض عبد التواب ١٩٨٦) مايلى:ـ

" يحكم بالحجز على البالغ للجنون او للعته أو للسفه أو للغفله .ولايرفع الحجز الا بحكم.وتقيم المحكمة على من يحجز عليه قيما لادارة امواله وفقا للأحكام المقرره فى هذا القانون" .

وقد قال الامام ابو حنيفة رحمه الله ان للحجز ثلاثة أسباب مالها رابع .

واستدلالا بقول الله تعالى" يا ايها الذين آمنوا اذا تداينتم بدين الى أجل مسمى فاكتبوه وليكتب بينكم كاتب بالعدل ولا يأب كاتب ان يكتب كما علمه الله فليكتب وليحل الذى عليه الحق وليتق الله ربه ولا يبخس منه شيئا. فان كان الذى عليه حق سفيها او ضعيف او لايستطيع ان يمل هو، فليملل وليه بالعدل.."

ومن الآية الكريمة نستدل على أن الله سبحانه وتعالى سوى بين السفيه وبين الضعيف وهو مخلول العقل ، ناقص الفطنة وبين العاجز عن الاملاء اما لعته أو لخرسه أو لجهله بأداء الكلام . وجعل الله لكل واحد من المذكورين فى الآية وليا.

وقد عرف البله كعاهه فى العقل توقف نمو الملكات الذهنية ومن بلوغ مرحلة النضج الطبيعى . اما العته فقد عرفه الفقهاء بانه من كان قليل الفهم، مختلط الكلام، فاسد التدبير سواء اكان ذلك من أصل الخلقه ام لمرض طارىء. واكثر الفقهاء على أن المعتوه حاله كحال الصبى المميز. وقد قال الكردى ان العته آفة تنقص العقل حتى صار كلامه بين كلام الجنون والعقل ، مستقيم البعض مختلط البعض الآخر. وكذا سائر افعاله.

وجاء فى المذكرة الايضاحية تعليقا على هذا النص(محمد كامل مرسى ١٩٥٤) الجنون والعته يشتركان فى أثرهما بالنسبة الى العقل ، فكلاهما افة تصيب العقل وتنقص من كماله. والمرجع فى ذلك هو خبره المتخصص فى الافات العقلية. فاذا أثبت الطبيب المنتدب من قبل المجلس الحسبى لفحص المطلوب الحجز عليه انه ضعيف العقل فانه يتيقن توقيع الحجز عليه ولو لم يصل ضعف العقل الى درجة العته التام.

DISCUSSION & CONCLUSION

DISCUSSION

Doll's definition, 1941, the standard definition for mental subnormality for many years, insisted on six criteria, as listed before: (1) social incompetence, (2) due to mental subnormality, (3) which is developmentally arrested, (4) and appears at/before maturity, (5) and is constsiutional in origin, (6) finally, essentially incurable.

This definition proposed a causal link between the social incompetence and menatl subnormality which is denied by Grossman (1973). Considering Jane Mercer (1973) view, who posits the social expectations of the individual to determine his being mental subnormal or not. Hence, Grossman's AAMD definition (1973) stated "mental subnormality refers to significantly subaverage general intellectual functioning existing concurrently with deficits in adaptive behaviour and manifested during the developmental period". Clarke and Clarke's definition (1974) also considered the impaired social adjustment, learning and maturation as association and not causally linked to mental subnormality.

Bijou Sidney, 1966, who is learning theory oriented scientist, considered the subnormal individual as one who

is only has a limited learning ability, yet can learn.

Grossman's and Clarke's definitions have a similar view on mental subnormality, but only differ in that Clarke's definition explained the retarded aspects; maturation, learning and social adjustment, while Grossman's definition included all aspects under one term; adaptive behaviour. It broads the scale of mental subnormality, making it more flexible but requires more work to label the individual subnormal.

As a result of accepting the new concept of intelligence in retardation to the society it became no more absolute but with comparison to the requirements of a particular social system. In other words, a person could be considered retarded at school aspect but normal at family life. Also, The number of people labelled retarded in an area is determened by the social structure of that area; as what is expected of them (Kaplan,1985).

This explains why people of rural areas; with low I.Q. and who are considered retarded is brought to live in a city society, yet they are not so in their own society, since they can fulfill their society's expectation.

The course of mental retardation is a function of both biological factors; such as an underlying etiologic

physical disorder, and environmental factors; such as education and other opportunities. Hence, the course of mental retardation is variable; as with good environmental influences, functioning may improve and vice versa.

It is worth noting that prevalence of mental retardation due to known biological factors is similar among children of upper and lower socioeconomic classes, but in cases in which no specific biological causation can be identified, the lower socioeconomic classes are over represented(DSM III R,1987).

It is very clear that, the environmental influences, playing certainly a not inconsiderable role, have attracted attention. Whatever their effect on the result of intelligence test is, society should aim at providing conditions of home and schooling for that part of the population, which is intellectually less well indowed.

The mental subnormality has two aspects; the degree of severity and the cause. Hence, subnormal individuals are to be classified through these two ways. In the classification by severity; the old type depends and is linked with the mental age and the I.Q.. It is only used for administrative purpose. And it devides the subnormals into:

Idiot	below 20
Imbecile	between 20 and 50
Feeble minded	between 50 and 70

And the educational system also classifies the subnormals; according to I.Q. to educable and trainable and custodial (Kirk and Johonson,1951 and Kirk, 1964) regardless the individual's ability.

In the recent way of classification by severity used by AAMD system, which considered mental subnormality as a point along a continuum and used other terms; mild, moderate, severe and profound which overcomes the old negative streotyped description of mental subnormality and gives a chance to consider the child's abilities inspite of its I.Q. scores that might classify it in lower category.

The Egyptian diagnostic manual of psychiatric

disorders 1979 and the DSM III R 1987 both employ the AAMD system of classification with few differences the DSM III R considered the mental subnormal the one whose I.Q. is below 70, and is classified as mild.

317.00	mild mental retardation	50-55 to 70
318.00	moderate mental retardation	35-40 to 50-55
318.10	severe mental retardation	20-25 to 35-40
318.20	profound mental retardation	below 20-25

While the Egyptian diagnostic manual of psychiatric disorders considered the mental subnormal the one whose I.Q. is below 83 and classified him as borderline.

01.0	borderline mental retardation	68-83
01.1	mild mental retardation	52-67
01.2	moderate mental retardation	36-51
01.3	Severe mental retardation	20-35
01.4	profound mental retardation	below 20

The second difference is that the categories of mental subnormality in the Egyptian diagnostic manual of psychiatric disorders are precise while in DSM III R are overlaping. Finally, the 2 systems add another category; the unspecifid mental retardation (01.5 and 319.00 in the egyptian diagnostic manual and DSM III R respectively) which is used for the clinically subnormal but the

intellectual functions could not be evaluated.

The ICD 10 is similar to the Egyptian diagnostic manual of psychiatric disorders in having a sharp levels for its categories, and it differes from it in having no borderline mental retardation category.

Errors in the distribution of genetic material underlie Down syndrome and other chromosomal disorders. Two mechanisms are employed: mitosis and miosis. The first involves the orderly separation of replicated chromosomes to produce 2 daughter nuclei identical to the parent nucleus in number of chromosomes, and occurs in all human tissues. Miosis occurs only with the formation of gametes. Unlike mitosis, it reduces the numer of chromosome per cell, so that each daughter nucleus contains an unpaired complement of chromosomes. Union of 2 gamets, ovum and sperm, the process of fertilization restores the paired condition.

The mitotic distribution system breaks down in producing trisomy 21, the most frequent form of down syndtrome at any age, in which the pair of number 21 chromosome fails to separate during gamete formatiom. This failure is termed non-disjunction. This error in distribution occurs with increased frequency with advancing maternal age. Aging of oocytes and exposure to toxins have been suggested, since oocytes are produced only before birth to be a cause of such error. Whereas spermatozoa are made continually throughout a male's reproductive life. Mothers should be assumed to bear the sole responsibility

for producing a child with down syndrome as male gamete has been implicated in carrying the extra 21 chromosome in nearly 1/4 of cases of down syndrome.

Non-disjunction also occurs in trisomy 18, trisomy 13, Klinefelter syndrome (XXY), Turner syndrome (OX) and the XYY syndrome.

Although many mentally retarded persons have normal appearing brains, central nervous system malformations are recognized in many of the mental retardation syndromes. The brain in down syndrome for example is slightly smaller than normal and has a globular rather than elongated shape. There is underdevelopment of cerebellum, brain stem, frontal lobes and superior temporal gyri. The trisomy 13 syndrome is typically associated with a much more stricking malformation than either down syndrome or trisomy 13. The most severe form is haloprosencephaly in which the olfactory tracts and bulbs are absent andthe frontal lobes are fused, containing a single ventricle in lieu of paired lateral ventricles.

Phenyketonuria provides a prototype of genetic metabolic disease that produce metal retardation. The underlying biochemical defect is deficiency of the enzyme phenylalanine hydroxylase. Phenylalanine, thus can not be

hydroxylised to form tyrosine. It accumulates in large amounts in blood where it is converted to phenylpyruvic acid which is excereted in urine. The phenylpyruvic acid is responsible for the production of green colour when the ferric chloride is added to the urine of a person with PKU. It is thought that phenylalanine in excess, phenylpyruvic acid and their metabolites exert a toxic effect on the devloping central nervous system. In addition, the child is deprived of tyrosine, a semi-essential amino acid important in the synthesis of melanine, norepinephrine, thyroxine and many proteins.

The out of control or inappropriate behaviour of mentally subnormal should be considered a sign of psychiatric problems. Due to the lack of understanding the developmental psychology of the mentally retarded by their parents, maladaptive behaviour results (Oliver Russell,1987 and Samia Ahmed,1987). Hypersensitivity, irritability, screening out and aggressive behaviour, socialization and low self-steem all are developmental pattern that the retarded exhibits to overcome the environmental demands and stresses. Unfortunatelly, the maladaptive behaviour leads the child to psychiatric illness especially the mildly retarded among whom? more than 50% suffer from psychotic symptoms (Nelson, 1987, Gillberg,1986, Eymann and Call,1977 and Moen et al,1977), and also permenant institutionalization (Mill and Bruinink,1984, Intagliate and Willer,1981, Thiel,1981, Pagel and Whitling,1978, Keys et al,1973). The study of Okasha and El-Fiki,1983 estimated the psychiatric morbidity among Egyptian mentally retarded. They did not assess the effect of mental retardation on the occurrance of psychiatric morbidity among the Egyptian mentally retarded.

The estimated prevalence was 58% which is similar to the results of Gillberg et al,1986, who assessed the effect of degree of mental retardation on psychiatric disorders. They found it to be 57% in mild and 64% in severe mentally retarded. The incidence of epilepsy among the Egyptian mentally retarded is 35.5% which is much higher than that in severely and mildlly mentally retarded in Gillberg's study (27% - 10% respectively).

Looking at Gillberg's results; one can conclude that the degree of mental retardation has an effect on psychiatric disorders in that their prevalence is higher in severe mental retardation than in mild mental retardation and the association between both among the population of 13-17 years old is 0.15% and 0.05% respectively also points to the same conclusion. In severely retarded individual, 11% show psychotic symptoms that could not be classified while all psychotic symptoms of mild retarded individuals are classified. This reflects as well the difficulty in diagnosing them, the severely mentaly retarded.

Still the question of; whether the psychotic symptoms is the reflection of mental retardation or is it separate from it?.

In Nihira Kazuo's study,1985 a domenstration of the reciprocal relation between the home environment and the subjects' development resulted in the fact of harmony and quality of parenting beside the educational expectations are the most salient environmental variable on the cognitive development and social adjustment. Zettin,1985, found that the more stable, supporting and understanding families will experience the least behavioural disturbance and vice versa (Munro,1985, Zettin,1985).

Kazak Anne et al, 1988 and Samia Ahmed,1987 explained The result of Kazak Marvin,1984, Tavoramina et al,1981 about the increased emotional problems experienced by mothers of retarded children. They are frustration, disappointment due to the delay development of their retardd babies, feeling of grief, guilt and turmoil especially at the time of diagnosing the child as mentally retarded are of great importance. As they determind the way the child will be handled by parents. Counselling during this period and even psychiatric consultation will help the parents understanding the condition of their child and educating them methods of suitable rearing.

CONCLUSSION

The following is an outline of the proposed procedures for the prevention of cases of mental subnormality, suggested by the study. It is a four stages program, on an individual level:-

1- Preconceptual stage.

2- Prenatal stage.

3- Perinatal and neonatal stage.

4- Postnatal stage.

The community development,improving socio-economic standard is the basis of prevention of such a disease. As for normal unaffected person, reorientation of their attitudes towards mental subnormality; sweeping any superstition, and the educational program of young adults, and school students; males and females, should include at least simple information about genetically transmitted disorders, and the nature of transmission and methods of prevention, are the main subareas for a broad scale prevention of mental subnormality.

Health education is very important, as it helps changing some wrong feeding habits; rice water given as main and only nourishment for infants suffering from gastroeteritis, which is endemic in Egypt. Education of simple hygiene procedures and proper nutrition, explaining

the dangers of marrying girls at young age which exposes them for premature labour and all its hazards as well as all kind of complications of pregnancy and labour. Also, explaining the dangers of consainguanity that increases the incidence of recessive genetic disorders.

Good housing and proper schooling are essential for normal and retarded persons to function better.

special schools for retarded persons provided with trained educators, traineers, caring staff. Their program should include cognitive stimulus aiding program, behavioural therapy and rehabilitation program. These progrms would decrease the degree of dependancy of the retarded, teaching him the basis of self-care, simple profession, and social skills.

Social help and medical services, community support to increase the family stability and hence dealing with their retarded child, minimizing the sequalae of retardation.

Finally, the better organization of efforts done by different medical associations to coordinate and cooperate in scientific researches and field application.

I-PRECONCEPTUAL STAGE:

People asking help at this stage are female before conception and/or couples before marriage. Past history

and family history should be taken thouroughly, especially previously poorly explained neonatal deaths or mentally retarded individuals. Negative family history does not exclude the possibility of inborn metabolic errors. Positive history should be reffered for more specialized centers of genetic studies.

Genetic counselling; should be done for all positive past and family history individuals including education of the nature of the disease, methods of transmission, methods of prevention, and the possibility of having affected children. Detection of the carriers is also of utmost importance among family members of affected persons. Such service is complicated and need a well trained highly qualified persons available in large cities in a scientific societies that are in medical faculties.

Health promotion measures: includes vaccination against viral infections; especially rubella, medical and dietary care for diabetes and phenylketonuria and other complicating pregnancy. Advice about proper dietary especially in rural area and slums where malnutrition preveales. Also advice about smoking and alcohol in urban areas where they preveal.

II- Frenatal Stage:

Pregnant females; who come seeking medical care, a good history should be taken including tracing family and past histories of mental retardation, and identifying the risk group; old age mothers, and young age mothers, parents with previously affected pregnancy or child. The old mother will suffer more from anomalies and chromosomal disorders, while the young will be predisposed to complications of pregnancy.

Individuals with positive family and past histories should be reffered to genetic centers to be investigated. The early prenatal diagnosis is done for selective abortion. Such methods are ultrasound which detect growth retardation, microcephaly, hydrocephaly, neural tube defect; alpha fetoprotein level; especially if combined with maternal age and amniocentesis; for genetic, chromosoml abnormalities, chrionic villus biopsy. Screening for rhesus incompitability. Such service should be available in almost all general hospitals all over Egypt.

As for negative history a good antenatal care should be given. It includes, good nutrition, routine urine and blood analysis, complete physical examination, control of any medical condition such as diabetes, pre-eclampsia,

eclampsia(Toxemia of pregnancy). Early detection of infection; especially viral ones and providing adequate proper treatment. Control of drug administration, and phenylalanine level in blood. Such services of antenatal care, yet, are of significant preventive value should be available at the level of primary health care in urban and rural areas; outpatients, local clinics, community health centers and maternal and child care units.

III- Perinatal and natal stage:

At this stage hypoxia, hypoglycemia, and trauma are the events that predispose greatly for mental subnormality. Improved obstetric care; aiming at reducing the previous events includs skillful obstetricians and advanced technical preparations.

Neonatal care with close cooperation of pediatricians and neonatologist, significant data about the neoborn will help in the follow up, will be gathered. They are:

1) Apgar scoring system.

2) Convulsive disorders; such as in hypoglycemia and hypocalcemia .

3) Abnormal signs e.g. musty odour of urine; is found with phenylketonuria and hereditary tyrosinemia, or maple syrup odour of urine is found

in maple syrup urine disease, and pathological neonatal jaundice.

4) Screening tests for:

a- Congenital hypothyroidism (T3,T4,TSH)

b- Phenylketonuria; ferric chloride test which is also positive in hereditory tyrosenemia, maple syrup urine disease, and histidinemia. Guthie blood test is more specific for phenylketonuria and positive at the first week of life.

c- Galactosemia; non-glucose reducing substance.

5) Providing proper treatment; phenylalanine free formula, galactose free formula, thyroxin replacement, surgical treatment for hydrocephalus, anti-D immuno globulin in mothers at risk of rhesus incompetability.

IV- Postnatal Stage:

Its main concern is the wellfare of the child. It includs vaccination against viral infections particularly females. Close observation of physical and mental development including measuring head circumferance, premature closure of sutures hinders brain development and indicates surgical interferance, hight and weight, milestones. All should be drawn on a chart. Any abnormalities then can be easily detected. This services

should be available at the level of primary health care in urban and rural areas; outpatients, local clinics, community health centers and in all maternal and child care units all over Egypt.

Since the majority of mentally retarded are of mild degree, they will be able to learn to read at a third to fifth grade level. This academic potential should be recognized. Comprehinsive educational planning; not only educational but also occupational should be prepared to enhnce and maximize the child's role within his family consequently in his society. Naturally this require special shools with trained and problem-oriented persons.

SUMMARY

SUMMARY

The problem of mental subnormality is frequently encountered by pediatrician, neurologist, psychiatrist and social worker. Because of its widening area of involvement, and its accumulative nature and seqalae, the subject is important to be studied. It is expected to find about 1,350,000 retarded individual in Egypt, according to Nelson, 1989, and about 554,494 retarded child in primary school.

Also the increase in householding expendature of families with subnormal child, (Alm et al, 1986, Chetwynd, 1985 and Buckle, 1984) in a developing society such ours, calls for deep study for mental subnormality.

The definition of mental subnormailty requires more than the demonstration of an intellectual inferiority of defect. It involves both the degree and character of the effect that results in a wholy or partly inadequat independant social adjustment. Doll's definition was the most widely used one, and is modefied by Grossman's definition by the AMMD, which has broaden the definition and allow new concepts; such as social system definition and behavioral definitin, to be viewed help managing the

problem of mental subnormality. However, such inadequacy must be demonstrated in the environment in which the individual is expected to live. The incidence of mental subnormality differes according to age group, while the prevalence depends on prevention. It is found that the prevalence in any population is not less than 3%.

There are 2 ways in which the subnormal is classified; by the degree of severity and by the cause. In the classification according to the degree of severity; the old one (idiot, imbicil, feeble minded) is only used for administrtive purposes, while the recent one (mild, moderate, severe, profoun) is clinically used as it puts the mentally retarded on a point along a contiuum and allows the society to deal with some of them through various social services which enables the subnormal; especially the mild to live independently.

The etiological classification does not change either the characteristics of mental subnormality or the educational program. The causes are either exogenous or brain damage and endogenous or cultural-familial.

The review includes a study of the etiology of mental subnormailty. These causes are grouped under 3 major categories:

I- Metabolic disorders:

1- Defects in amino acids metabolism.

2- Defects in charbohydrate metabolism.

3- Defects in lipid metabolism.

4- Miscellineous metabolic disorders.

II- Chromosomal abnormalities:

1- Abnormalities of autosomes.

2- Abnormalities of sex chromosomes.

3- Autosomal dominant disorders.

4- Recessive and unknown genetic disorders.

III- Prenatal factors:

1- Maternal and fetal infections.

2- Fetal irradiation.

3- Prematurity.

4- Seasonal and geographical variations.

5- Prenatal nutrition.

6- Fetal alcohol syndrome.

7- Socio-economic factors.

8- Prenatal emotional stress.

A stress on the treatable causes ,such as phenylketonuria,maple syrup urine disease, galactosemia, hypoglycemia, hypothyroidism and hydrocephalus is done.

The diagnosis of mental subnormality has two aspects, one is to evaluate the mental abilities and that is done through psychological testing and the second, aspect is to know the cause, through clinical examination; proper history, physical examination and investigation. Finding out the cause of mental subnormality,the availability of treatment hence prevention increases and can be carried out immediately.

Investigations to be considered

1-Thyroid funtioning tests.

2-Assessment of hearing and vision.

3-E.E.G.

4-Chromosomal analysis.

5-TORCH antibody titres in blood.

6-Skull X-ray.

7-Cranial CT scan.

8-Blood and urine for amino acid

and urine for organic acid.

9-Urine for mucopolysaccharides.

10-Lysosomal enzyme analysis in blood.

11-Serum uric acid.

12-Psychologic testing.

Defferential Diagnosis

1-Normal variation in development.

2-Cerebral palsy affecting motor and speech functions.

3-Seizure disorder or excessive anticonvulsant medication depressing development.

4-Hearing deficit and visual impairment.

5-Degenerative diseases

6-Dull facial appearance.

7-Depression.

8-Specific learning disability.

The mentally retarded is deprived from the ability of verbal expression, that is a broblem met with by psychiatrists dealing with them, so the abnormal behaviors displayed by the subnormals are the main clue for psychiatists. Such behaviors are; hypersensitivity, irritability, aggression, screening out, socialization and low self-esteem.

There is a very strong reciprocal relation between the environment and the developmental process of the mentally subnormal, which appears on the parents' self-evaluation,

emotional distress, and pattern of psychological reactions also on house holding expendature.

Prevention of mental subnormality is composed of 3 steps. Primary prevention aiming at protecting the high risk infants, so as not to be retarded. It includes public education, improving socio-economic standards, preventive measurs and genetic counseling. Secondary prevention, which includes early detection and treatment. Tertiary prevention is concerned with preventing further complication resulting from mental subnormality.

Selected aspects of treatment of mental subnormality

Medical:

Thyroid hormone replacement for hypothyroidism.

Dietary therapy for PKU, Maple syrup urine disease and galactosemia.

Treatment for intercurrent medical problems.

Neurologic:

Anti-convulsants medication for associated seizures.

Surgical

Shunt for hydrocephalus.

Psychological

Family planning.

Counseling regarding behavioral problems.

Individual therapy.

Group therapy.

Behavior modification.

Socio-environmental:

Group homes in community.

Chronic institutionalization.

Respite care.

Day-hospital programs.

Educational:

Special education.

Physical:

Remedial(to maintain and improve skills).

Fitness.

Socialization and emotional outlet.

It is now known that not only some mental retardation syndromes specifically treatable but early treatment sometimes will prevent the development of mental retardation. Hypothyroidism and PKU are examples of such disorders. In other disorders the problem may not be so specifically treatable, but certain features may be amenable to therapy. The child with hydrocephalus due to

congenital toxoplasmosis or bacterial meningitis for example might undergo ventriculoperitoneal shunting. Seizures occuring in mental retarded persons are generally treated in conventional fashion.

Most mentally retarded persons are in the mildly retarded category and will be able to care for themselves and to contribute to the society, though often in a less than fully independant manner. The outlook for the mentally retarded child in latter life may be brighter than parents may anticipate during early period of gloom. Such an outcome may not fit the streotype of the mentally retarded person held by many parents and professionals and is useful to consider in the erly, difficult phases of decision making when a child is recognized as being defective.

Finally, a suggested 4 stages preventive program to be applied on individual level in Egyptian culture which aims importantly at early detection of high risk group individual. The first stage; preconceptual stage whose goal is deting genetic carriers through proper family and past history taking, genetic cuncelling and health promotion measures. secondly; prenatal stage whose goal is prevention of any complications of pregnancy such as

diabetus mellitus, toxemia of pregnancy, or malnutrition. Also early prenatal diagnosis for selective abortion. Thirdly, perinatal and natal stage that provides the most relaiable discription of the neoborn state through apgar scoring system, observing the convulsive disorders, abnormal signs, screening tests and treatment. Finally, postnatal stage that aims at the welfare of the child. Vaccination and follow up are included.

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الملخـــص العربـــى

ان تعريف التخلف العقلى لايتطلب توضيح النقص فى القدرات العقلية فحســـب بل انه يشمل ايضا درجة ونوع هذا النقص الذىينتج عنه عدم التوافق مع البيئة ســـواء جزئيا أو كليا. وقد أعتبر تعريف "دول" ا كثر التعريفات استخداما حتى اخيرا حيـــن أعتبر المتخلف عقليا حسب تعريف الجمعية الامريكية للقصور العقلى هو شخص وظائفـــه العقلية دون المتوسط، وسلوكه التكيفى معيب خلال فترة النمو.

وبظهور تعريف النظام الاجتماعى والتعريف السلوكى، يعتبر الفرد متخلفا قياسيـا على مدى تأقلمه فى البيئة التى يعيش فيها ومسايرته للنظام الاجتماعى وا لسلوكى لها.

ويختلف معدل انتشار التخلف العقلى بين الأفراد تبعا للمجموعة السنيـــة أما معدل انتشاره فى أى مجتمع حسب الدراسات المسحية ـ فهو ٣٪.وهذا المعدل مرتبط بمعدل الحدوث وطرق الوقاية والعلاج منه .

و توجد طريقتان شائعتان لتصنيف التخلف العقلى: الأولى تعتمد على تصنيـــف المتخلفين عقليا تبعا لدرجة التخلف الى درجات منفصلة تماما، **الآبله ، الآفـــن ، الأحمق** ، وهذا التقسيم قديم اما التقسيم الحديث من التصنيف، فيضع المتخلف عقليا فـــى أربع درجات متتابعة ومستمرة، الطفيف، المتوسط ، الشديد والعويص .

أما الطريقة الثانية للتصنيف، فتعتمد على اسباب حدوثها، سواء اسباب عضويـــة او اجتماعية بيئية.

وقد قسمت الأسباب الى:

اولا : اسباب متعلقة بالتمثيل الغذائى وتشملعلى:

١ـ اسباب متعلقة بالتمثيل الغذائى للاحماض الامينية.

٢ـ اسباب متعلقة بالتمثيل الغذائى للمواد الكربوهيدراتية.

٣ـ أسباب متعلقة بالتمثيل الغذائى للمواد الدهنية.

٤ـ أسباب أخرى متنوعة.

ثانيا : الأسباب المتعلقة بالكروموسومات وتشتمل على:

١ـ تشوهات الاتوزومات

٢ــ تشوهات كروموسومات الجنس.

٣ــ اضطرابات الاتوزومات السائده.

٤ــ اضطرابات الاتوزومات المنتحية.

ثالثا : العوامل المتعلقة بفترة ماقبل الولادة.

وقد درست هذه الاسباب من جاب الصور الاكلينيكية والاسباب ا لباثولوجية لها عامة ، مع التنقيق بالاسباب التى يمكن علاجها كمثال "الفنيل‌كيتونوريا ، فحص الجلوكتوز بالدم، نقص وظائف الغدة الدرقية، نقص سكر الدم.

تشخيص التخلف العقلى يعتمد اساسا على التاريخ العائلى والاسرى ودقة ملاحظة الاسرة للتطور النموى للطفل بالاضافة الى الفحص الاكلينيكى والفحوصات المعملية الأخرى ، يلى هذا تحديد درجة التخلف العقلى باستخدام القياس النفسية واسبابه باستخدام فحوصات معملية اكثر دقة.

والتشخيص المبكر لحالات التخلف العقلى من الاهمية بمكان ، حيث انه يمكن من معرفة السبب واتخاذ كل الاجراءات الممكنة لتجنب تضاعفه او منع حدوثه كمثال حالات الفنيل كيثوثوريا ، قصور الغدة الدرقية.

ويعانىَ المتخلف عقليا من أمراض نفسية عديدة لايقدر أن يعبر عنها بغير اضطرابات السلوك والتى يعتبرها الأطباء النفسيون الموءشر الوحيد لهم لتشخيص هذه الامراض النفسية. و ا هم هذه الأضطرابات السلوكية هى فرط الاحساس، الانفعالية ، العدوانية، الانعزالية وغيرها.

ونظرا لوجود علاقة قوية متبادلة بين المتخلف عقليا وسلوكه وبين الأسرة المحيطة به فان هذه العلاقة قد ظهرت موءثرة على انماط الحياة بالاسرة واتجاهات افرادها الأسوياء نحو المتخلف وكذا على اقتصاديات الاسرة.

وللوقاية من مشكلة التخلف العقلى، يجب دراسة المشكلة من خلال ثلاثة اوجه. الاول يرمى الى توعية المجتمع ورفع مستواه الاقتصادى والاجتماعى وتوفير الخدمات الطبية العامة والخاصة والتثقيف والاستشارة الوراثية، والثانى يهدف الى الكشف المبكر عن

التخلف العقلى ومعرفة سببه حتى يتسنى البدء المبكر للعلاج ان وجد او منع هـــذا الحمل • اما الوجه الثالث فيهتم بالمتخلفين العقليين انفسهم من حيث منع اىمضاعفات عضوية او نفسية ناتجة من امراض، هذا ومحاولة تحويله الى مرض يمكنه الاعتمـــــــاد ـ ولو جزئيا ـ على نـفسه•

واخيرا ومن خلال هذه الدراسة وضع اطار عام ومبسط لعمل برنامج وقائى للتخلف العقلى منأربع مراحل على المستوى الفردى ، وهى مرحلة ماقبل ا لحمل ، مرحلة ماقبـل الولادة، مرحلة الولادة وأخيرا مرحلة مابعد الولادة•

والله ولى الـتوفيق

مراجع عربيـــــــة

٢٩١ـ حسن صادق المرصفاوى، المرصفاوى فى قانـون العقوبات ، تطوراته التشريعية ومذكراته الايضاحية، والاحكام فى مائة عام ، منشأة المعارف بالاسكندريـــــة، ١٩٨٥ (ص ٢١٧ـ ٢١٨)

٢٩٢ـ محـمد كامل مرسى ، الالتزامات (شرح القانون المدنى الجديد) الجـــزء الاول المطبعة العالميه، القاهرة، ١٩٥٤ (ص ١٩٢ـ٢٠٥).

٢٩٣ـ معوض عبد التـواب ، موسوعة الأحوال الشخصيـه، الطبعة الثالثة، منشـأة المعارف بالاسكندرية، ١٩٨٦ (ص ٢٢٣ ـ ٢٢٨).

جامعة عين شمس

معهد الدراسات العليا للطفولة

القسم الطبى

بحث نظرى

" بعض أسباب التخلف العقلى التى يمكن علاجها "

تمهيدا للحصول على درجة الماجستير فى دراسات الطفولة

قسم الدراسات الطبية معهد الدراسات العليا للطفولة

اعداد

طبيب / ايهاب روءوف ناشد

بكالوريوس الطب والجراحة

* * **

تحت اشراف :-

الدكتوره / عفاف حامد خليل

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المدرس لعلم النفس - كلية الآداب

جامعة عين شمس

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