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BIOMEDICAL TYPES OF MENTAL DEFICIENCY

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BIOMEDICAL TYPES OF MENTAL DEFICIENCY

The first attempts to isolate specific types of mental retardation in the large population of defectives dates from the last century when cretinism, mongolism, and tuberosclerosis were identified. These attempts have continued with increased success and at present a few hundred biomedical types are on record.

The purpose of this chapter is to describe briefly some of these types. They can be classified into two large categories according to the etiology, i.e., the genetically determined and the environmentally determined. A third category may be added to include types of mental defect of unknown etiology.

The genetically determined types are usually classified into three groups: due to (1) mental defect associated with chromosomal abnormalities; (2) recessive genes, and (3) dominant genes.

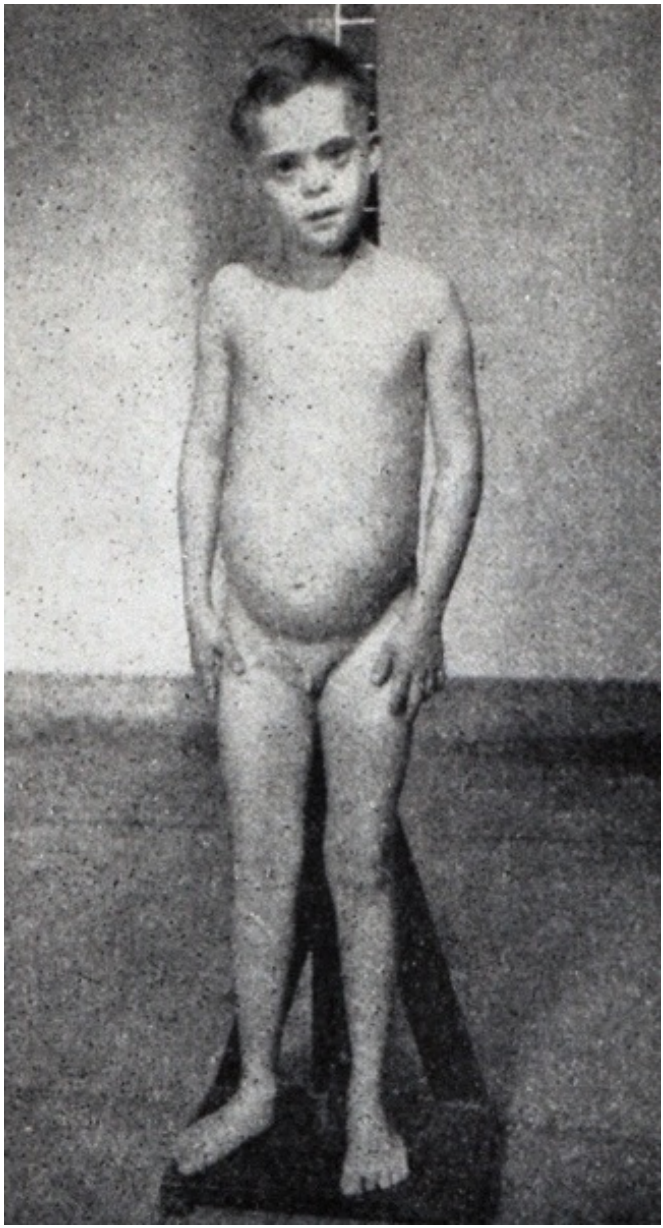
Chromosomal Abnormalities

Downs Syndrome, Mongolism

Frequency is estimated at about 1 in 600 births and increases some ten-fold in children born of women over forty years of age. The symptomatology consists of a conglomeration of abnormal physical traits: stunted growth,

brachycephalic small skull, round flat face, almond-shaped palpebral fissures which slant inward and downward, epicanthus folds, large tongue, and small chin. The extremities are small, the fifth finger is usually curved and the palm of the hands shows a marked transverse line. There is general muscular hypotonicity. Congenital defects of heart or other organs are common. Mental retardation varies from severe to mild but the majority show a moderate degree of it. See Figure 20-1.

Figure 20-1.



Down's syndrome.

In about 90 percent of the cases, the abnormality of chromosomes consists in an extra chromosome in the twenty-one chromosomes of group G. There are, therefore, forty-seven chromosomes instead of the normal complement of forty-six. In a small percentage of patients there is a different chromosomal arrangement, the extra chromosome is not free but is attached (translocated) to a large chromosome, usually of D group. The total complement is therefore apparently the normal forty-six chromosomes. In a situation of this type the mother may have also a similar translocation, the total amount of her chromosomes being forty-five. The mother, then, has a theoretical chance of one out of three of having other affected children.

Edwards Syndrome, Trisomy E

Frequency is about 1 in 3500 births. Clinical manifestations consist of hypertelorism, palpebral ptosis, small chin, low-set malformed ears, macrognathia, shield chest, flexion deformity of finger, short neck, and congenital heart disease. Mental retardation is severe. Early death is common. The diagnosis rests on the demonstration of extra chromosome eighteen in the E group.

Patau Syndrome, Trisomy D

This is rarer than Trisomy E, the incidence being about 1 in 6000. Clinically, there is microcephaly, microthalmia, cleft lip, cleft palate, malformed ears, polydactily or syndactily, and other malformations. Mental retardation is profound and life expectancy short, from a few months to a few years. The extra chromosome in the D group is number thirteen.

Cat-Cry Syndrome

This syndrome—deletion of short arm of chromosome 5—is characterized by microcephaly, round face, hypertelorism, micrognathia and severe mental retardation. The voice in infancy has a characteristic catlike quality. Numerous other abnormalities in number or structure of autosomal chromosomes resulting in mental deficiency are documented. They are, however, rarer than the ones mentioned.

Several aberration of sex chromosomes in mentally defective individuals are known. The major categories are the following:

Klinefelter disease is clinically manifested by tall stature, underdeveloped secondary sexual characteristics, small and firm testes, clinodactily, cubitus valgus, and often obesity. Mental retardation when present is mild. The karyotype is XXY. The number of chromosome thirty-seven.

In the same group of excessive number of sex chromosomes are cases with *karyotype of XXXY and XXYY,* clinically similar to *XXY* male. Patients with the karyotype XXXXY (thirty-nine chromosome) show, in addition, more severe mental retardation. The hypogenitalism is more evident and several skeletal abnormalities are present.

In the female, the major categories of aberrations of sex chromosomes associated with mental retardation are the *multiple X types.* In patients with three X (instead of two) there is no distinct phenotype and mental retardation is not always observed and, when present, is mild. Cases with four or five X have been occasionally reported. These women are usually mentally defective. The syndrome of multiple X may be promptly diagnosed by examining a buccal smear. The epithelial cells of the mouth mucosa have one less Barr bodies than the number of X's.

Mental Deficiency Due to Recessive Genes

Numerous uncommon types of mental defect may be grouped under this heading. In each condition the family data of the patients are consistent with the hypothesis of a recessive gene being associated with the disease. Therefore, in a group of affected families, when the sibships are examined with proper statistical methods, the ratio of affected to normal sibs is 1 to 3 and the rate of consanguinity among parents of affected children is

significantly higher than in the general population. A number of recessive types, in addition, are characterized by the defect of a specific enzyme. However, the causal relationship between the biochemical abnormality and mental defect is not always clear.

Among this group, the following may be briefly described.

Phenylketonuria

The incidence is of the order of x in 15,000 children, the highest in these metabolic types. The degree of mental retardation varies but it is usually severe. Physical development is little impaired and life expectancy is not much shorter than normal. Seizures are often present and minor neurological abnormalities can be demonstrated in most patients. The diagnosis is based on the finding of phenylpyruvic acid in the urine. In addition, phenylalanine (an essential amino acid) is present in abnormal quantity in the blood. The demonstration of excess phenylalanine in the blood is diagnostic in the newborn infant when phenylpyruvic acid is not yet present. Early diagnosis is crucial for a successful treatment of the disease. The metabolic abnormality consists in the absence of a specific liver enzyme which metabolizes phenylalanine. The unmetabolized phenylalanine or some of its derivatives are apparently toxic, interfering with normal postnatal development of the brain. Treatment consists of special diets poor in phenylalanine.

Homocystinuria

The main clinical manifestations are arachnodactyly, stiff joints, high stature, long limbs, and dislocation of the lenses. The presence of peculiar malar flush may be of help in the diagnosis. Glaucoma and cataracts may be present. Arterial and venous thromboses are frequent. Mental retardation, when present, varies from very mild to moderate. The metabolic abnormality consists of the absence of cystothionine synthetase, the enzyme of sulfur amino acid metabolism catalyzing the conversion of homocystine to cystothionine. The unmetabolized excess of homocystine is excreted in the urine and is easily recognized by a simple test. Low methionine diet may help in the treatment and in a certain number of cases the administration of Vitamin B_6 is useful.

Maple Sugar Urine Disease

The first clinical manifestations occur in early infancy. There are feeding difficulties, vomiting, spasticity, generalized seizures and unresponsiveness. Hair is coarse, sparse, and kinky (hence the term of kinky hair disease). The urine has a strong odor similar to maple sugar. The metabolic abnormality is in the branched amino acid metabolism. Leucine, valine, isoleucine, and their corresponding keto acids accumulate in blood and urine because of a lack of their proper enzymes. Keto-aciduria results which is diagnostic of the disease. Unless controlled with very difficult dietary measures, the disease is fatal.

Histidinemia

There are no distinct clinical manifestations aside from mild mental deficiency which is present only in about 50 percent of the cases. Speech defect is noted in some 60 percent.

The metabolic abnormality consists of a missing enzyme (histidase) in the catabolism of histidine. The absence of histidase results in the presence of an abnormal amount of histidine and of its ketoacid (imidazole pyruvic acid) in the blood and urine of patients. A few other rare amino aciduriae with mental defect have been reported.

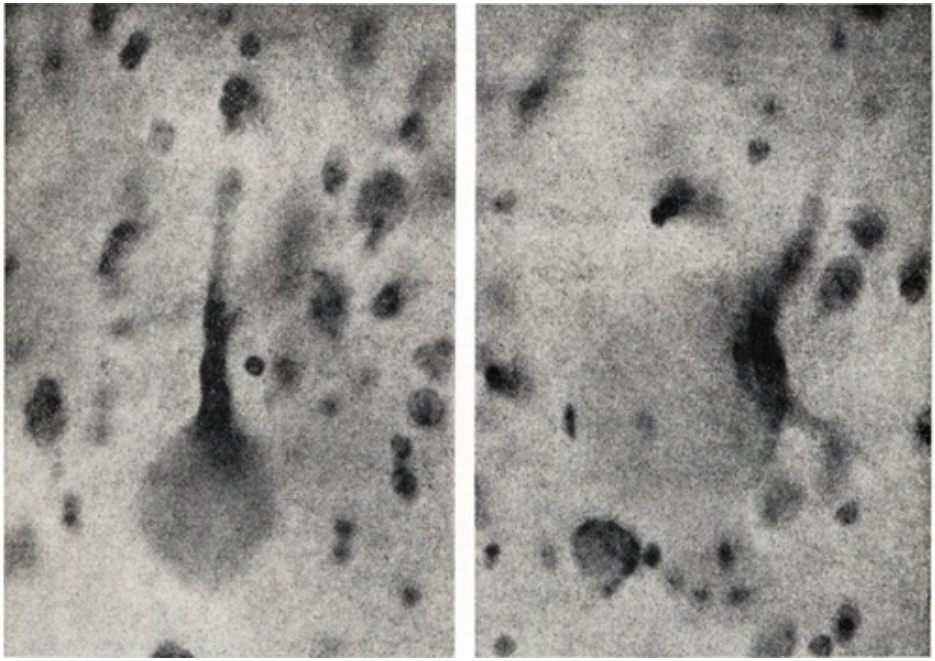
Neurolipidoses

The term is used to denote a group of diseases of the central nervous system characterized by the storage of lipid in the brain and other organs. Mental retardation is always present and the conditions are fatal.

Tay-Sachs Disease, the onset of this disease (infantile amaurotic idiocy) is during the first years of life and leads to death in a few years. Neurological deterioration, blindness, and convulsions are major symptoms. Pathologically, the nerve cells are ubiquitously distended and repleted with gangliosides, a complex lipid, small amounts of which are normally present in the brain (see Figure 20-2). The disease is prevalent among Ashkenazi Jews.

Prenatal diagnosis may be made by demonstrating the defect of a specific enzyme, hexoseaminidase A, in the cells of the amniotic fluid.

Figure 20-2.



Swollen "balloon like" nerve cells characteristic of amaurotic idiocy .

Batten Disease, this disease, neuronal ceroidlipofuscinosis, is a widely investigated lipidosis causing progressive mental retardation and blindness. There are several varieties which are classified according to age of onset and duration. Their common trait is the storage of a complex lipid (lipofuscin) in the brain cells. The nature of the defective enzyme (if any) is not known.

Nieman-Piek disease, in its infantile form, is characterized by a severe progressive mental retardation, blindness, and hepatospenomegaly. The substance accumulating in brain, liver, and spleen is sphingomylin, a lipid normally present in the brain but in smaller quantity. The missing enzyme is sphingomyelinase which normally breaks down sphingomyelin.

Gaucher disease, in the acute infantile cerebral types, with severe mental deterioration is usually fatal. Spleen and liver are enlarged because of the accumulation of a glycolipid (glucocerebroside) which cannot be metabolized because of the congenital lack of its specific enzyme.

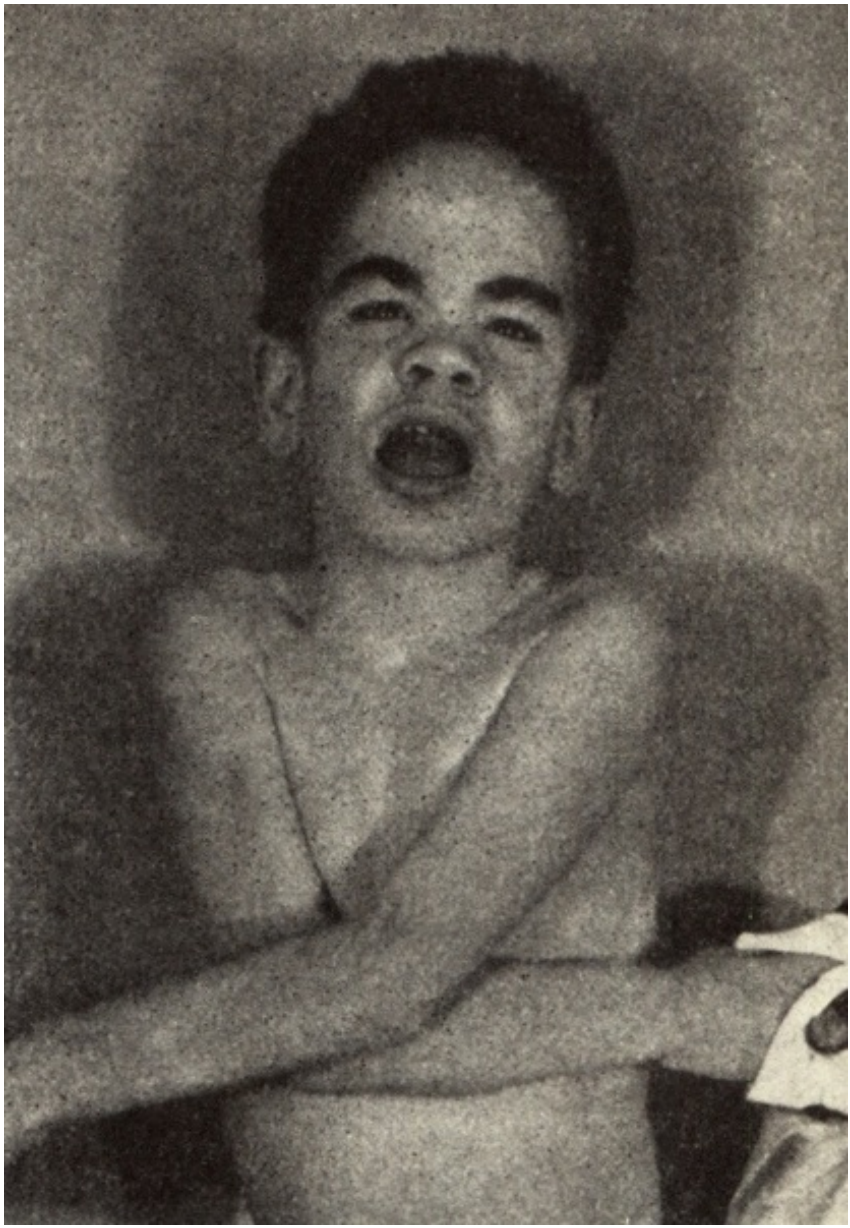
Mucopolysaccharidoses

This is a group of diseases characterized by accumulation of mucopolysaccharides in the cells of various organs, including the brain. With few exceptions the children are mentally defective. Several varieties have been recognized showing minor clinical differences but distinct enzymatic characteristics. The most common are:

Type I, *Hurler Syndrome,* characterized by stunted growth, large head, distorted coarse facial features, clouding of the corneas, large nose, thick tongue, abnormalities of osseous system, short neck, gibbus, and hirsutism (see Figure 20-3). Mental retardation is usually severe and slowly progressive. Mucopolysaccharides in the form of dermatan sulfate and

heparan sulfate are present in the urine and the tissues of the body. The enzyme which is missing is alpha-L-Iduzonidase.

Figure 20-3.



Hurler syndrome.

Type II, *Hunter Syndrome,* has clinical features similar to Type I but cornea clouding is lacking, mental retardation is less severe, and life expectancy longer. The disease is recessive but sex-linked, so that the patients are only boys. The biochemical characteristics are also similar to Type I, but the missing enzyme is different (sulfoiduromate sulfatase).

Type III, *Sanfilippo syndrome,* has physical features similar to Type II and I in the other varieties of the disease but mental retardation is usually much more marked. In the urine, blood, and tissues mostly heparan sulfate is present. The specific missing enzyme is heparan sulfate sulfatase.

Galactosemia

The main symptoms of this disease are mental deficiency, hepatosplenomegaly, and cataracts. In newborn, jaundice is usually present. Biochemically, large amounts of galactose and its phosphate are found in the urine and body fluids. The enzymatic defect is in the metabolic pathway from galactose to glucose where a block exists after the galactose phosphate step, due to the missing enzyme which converts galactose phosphate to uridine-galactose. This disease is rare, about 1 in 60,000-70,000 births and can be treated by eliminating milk and milk products from the diet of the infant.

Wilson Disease

This disease, hepato lenticular degeneration, is a recessive condition, characterized clinically by progressive extrapyramidal syndrome with intellectual deterioration, and pathologically by cirrhosis of the liver and degeneration of the basal ganglia of the brain. Biochemical alterations consist of very low blood copper, increased excretion of copper in the urine and deposit of copper in the brain, liver, and other organs. Normally, blood copper is closely bound to ceruloplasmin, a blood protein. In Wilson disease, ceruloplasmin cannot bind copper because of a genetically determined structural alteration (for further review see Chapter 16). Free copper, then, is deposited in the brain, liver, and other organs causing degenerative change. Treatment by chelating agents such as penicillamine is of benefit.

Hyperucemia

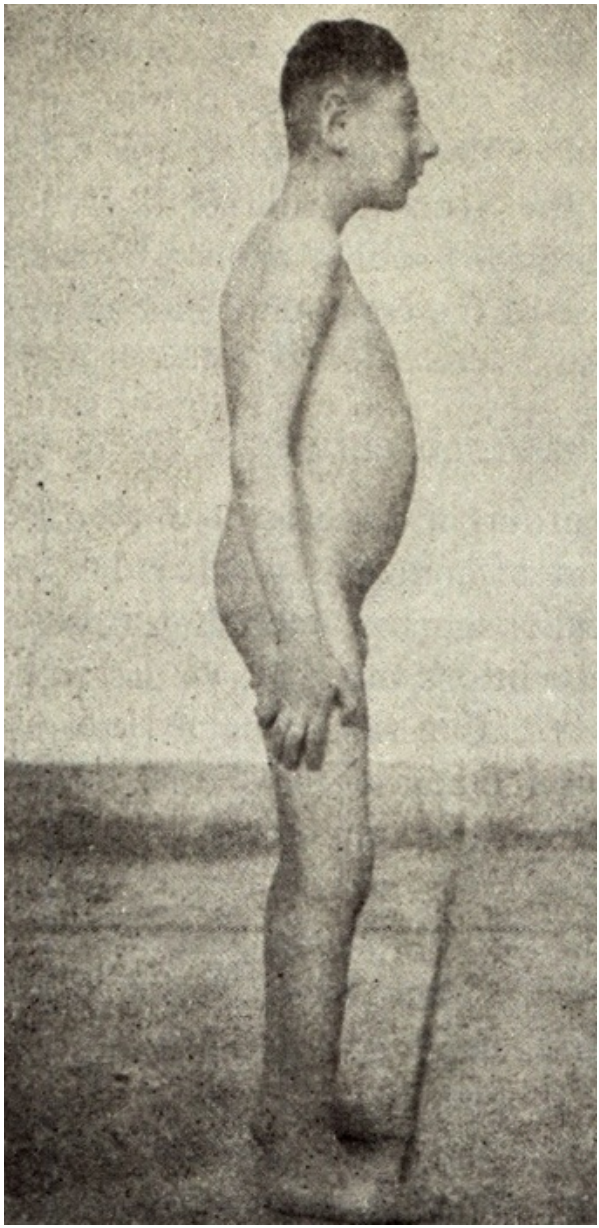
In this disease, Lesch-Nyhan, mental and motor retardation are accompanied by athetoid movements and spasms. Peculiar self mutilating behavior, such as lip-biting and finger-chewing are characteristic. Biochemically, there is an increased production of uric acid, due to a defect of inhibitory enzyme in the uric acid metabolism.

In a second group of recessive conditions associated with mental deficiency, no biochemical abnormalities have been detected thus far.

Primary Microcephaly

Patients are of small stature and the head is particularly small (see Figure 20-4). There are no neurological manifestations but mental deficiency is usually serious. The condition should be differentiated from secondary microcephaly which is more common and is caused by various environmental factors.

Figure 20-4.



Microcephaly. Chronological age fifteen, mental age three.

Ataxia Telangiectasia

In this disease, Louis-Barr syndrome, mental defect is accompanied by progressive cerebellar dysfunction and by characteristic telangiectasiae of the bulbar conjunctiva. There is in addition immune incompetence due to the deficiency of immune globluline A.

Laurence-Moon Syndrome

This disease is easily recognized by a cluster of abnormalities, such as pigmentary degeneration of the retina, mental retardation, polydactyly, obesity, and hypogenitalism.

Sjögren-Larson Syndrome

This disease consists of congenital generalized ichtyosis, pigmentary degeneration of the retina, slowly progressive spastic extensor plantar response, and mental defect. Epileptic seizures are not uncommon.

Cockayne Syndrome

Mental defect is usually severe and associated with dwarfism,

microcephaly, pigmentary degeneration of the retina, hypogenitalism, and malnutrition. The condition is often progressive.

Lowe Syndrome

Cataract is present early, often at birth, and is frequently accompanied by glaucoma. Metabolic acidosis, rickets, and organic aciduria of renal origin are usually present. Life expectancy is reduced. Mental deficiency is usually severe. The condition is X-linked recessive affecting only boys.

Smith-Lemli-Opitz Syndrome

The features consist of microcephaly, epicanthus with ptosis, strabismus, small upturned nose with broad bridge, micrognathia, lowset upturned ears, syndactyly or polydactyly, and various deformities of the lower extremities. Mental defect is usually severe and patients fail to thrive.

Mental Deficiency Associated with Dominant Genes

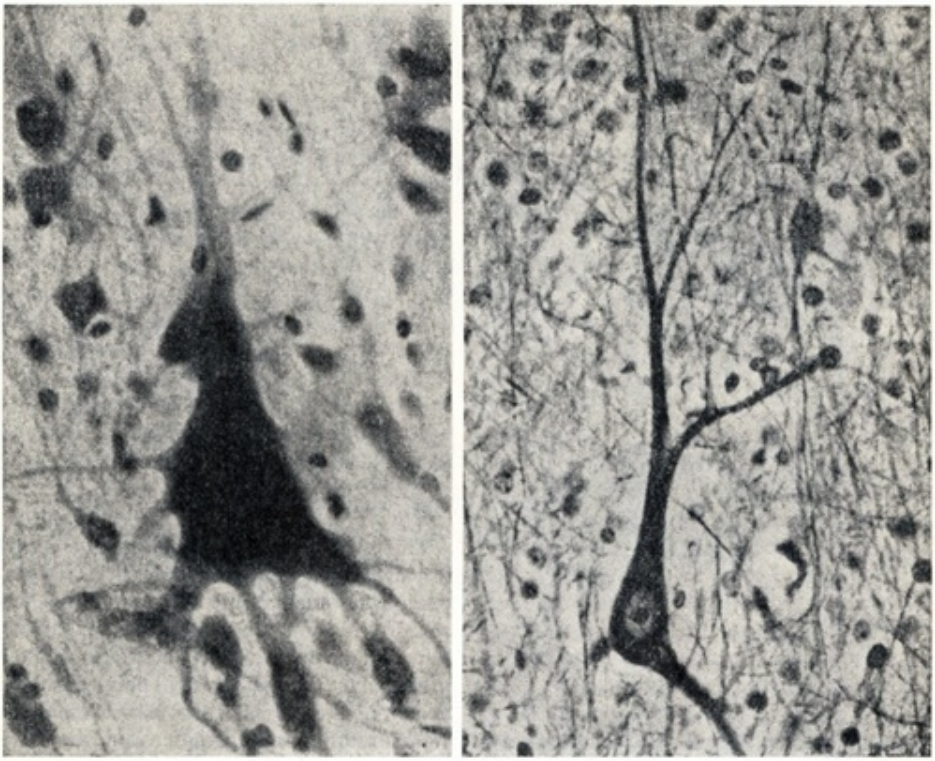
In this group are a few types of genetically determined instances of mental deficiency which are transmitted directly from affected parent to half of the offspring. The occurrence of sporadic forms is explained by assuming that the isolated instance is caused by a mutation in the parental gene. The mutated gene is then transmitted to the offspring. If there are no offspring the

instance remains unique. Incomplete symptomatology is often noted in dominant conditions thus adding difficulties to the recognition of the disease.

Tuberosclerosis

This disease is characterized by the triad mental deficiency, adenoma sebaceous, and epilepsy. Other skin lesions are common, such as areas of discoloration, cutaneous fibroma, and shagreen patches. Retinal nodules and intracranial calcifications are often present (see Figure 20-5). Mental retardation varies from profound to mild. Occasionally, patients with normal intelligence have been on record. Incomplete forms ("formes' frustes") are not rare.

Figure 20-5.



Tuberosclerosis .

Achondroplasia

Shortening of the limbs, particularly of the proximal segments, large head with prominent forehead, and short broad hands are the main physical features of this disease. Mental retardation, usually mild, is present in no more than a third of the patients.

Craniofacial Dysostosis

In this disease (Crouzon), distorted shape of head, exopthalmos strabismus, and hypertelorism are characteristic. The orbits are poorly developed. Mental deficiency is mild or moderate, increased intracranial pressure may develop.

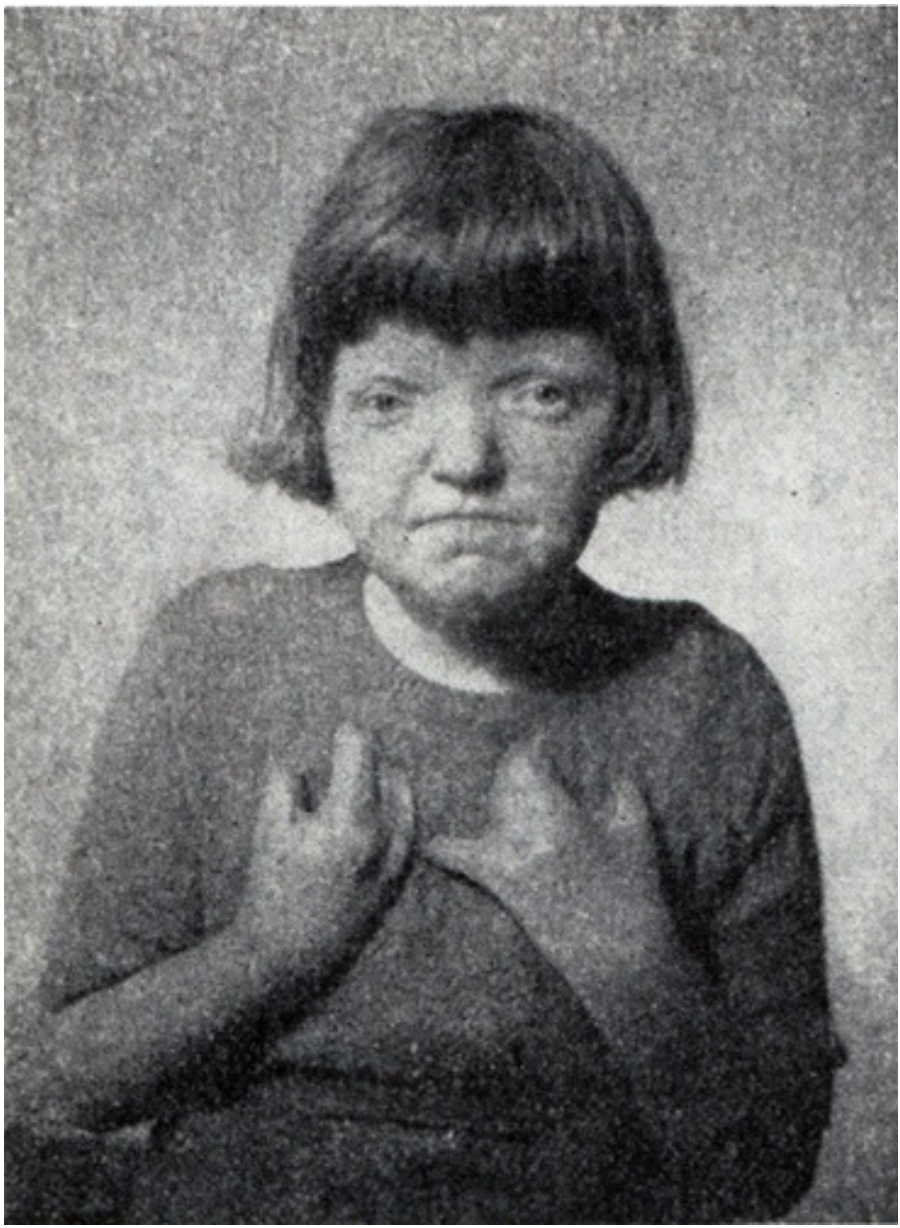
Acrocephalosyndactylia

In this disease (Apert), the head is misshaped, resembling that of Crouzon disease. There is, in addition, fusion of fingers and toes (see Figure 20-6). Several varieties have been described. Mental defect is usually less mild than in Crouzon disease.

Arachnodactyly

In this disease (Marfan), long limbs, spidery fingers and toes, dislocation of lenses, and cardiac defects are the main physical features. Mental deficiency, when present, is mild.

Figure 20-6.



Acrocephalosyndactilia.

Mental Deficiency Caused by Environmental Factors

Known types of mental deficiency caused by exogenous factors are not as many as those genetically determined, but include a higher incidence in each category.

Mental Defect Due to Infection

Infection may damage the nervous system during intrauterine life, or during infancy and childhood. Damage varies according to the type of infectious agent, the age of subject, and the severity of the acute infection. Among prenatal infections causing mental retardation are rubella, cytomegalovirus, toxoplasmosis, and syphilis.

Rubella

Infection of the mother during the first trimester of pregnancy may be transmitted transplacentally to the developing fetus, and damage various organs and systems, including the developing central nervous system. Clinical manifestations in the child are microcephaly, cataract, retinopathy, hepatitis thrombocytopenia, heart defect, and other malformation. Anamnestic data

and the clinical picture make possible a prompt diagnosis. Rubella virus can be isolated at birth or shortly after. The widespread vaccination of girls against rubella has considerably reduced the incidence of this condition.

Cytomegalovirus Infection

This is increasingly recognized as a significant cause of mental retardation. Usually the disease develops during intrauterine life. Apparently nonimmune women who acquire the infection during pregnancy are the most likely to transmit the disease to the fetus. Mild microcephaly is the major clinical manifestation. Chorioretinitis, intracranial calcification, and hepatosplenomegaly may be present. Mental deficiency varies from mild to severe. Excretion of the virus may persist for months after birth. Treatment is of little avail but preventive vaccination has been attempted.

Toxoplasmosis

Transplacental intrauterine transmission of toxoplasmosis is well known although its frequency has not been established. Clinical manifestations in the child consist of microcephaly or, at times, hydrocephaly, with intracranial calcifications. Chorioretinitis is common, cataract, glaucoma, or micropthalmia may be present. Mental retardation is often severe. There is no satisfactory treatment of the disease although the toxoplasm responds to certain sulfa drugs.

Syphilis

Congenital syphilis is the classical example of prenatal infection causing mental deficiency—but its symptoms and signs—saddle nose, notched teeth, interstitial keratosis, deafness, bone lesions and others—are rarely seen among mentally retarded. On the other hand, positive serology in a mentally defective is no evidence that the intellectual impairment is due to syphilis. A peculiar, but today rare, type of congenital syphilis is "juvenile paralysis." This serious deteriorating disease, due to multiplication of the syphilic agent in the brain, shows progressive mental defect, motor paralyses, and often epilepsy.

Encephalitis in Infancy or Childhood

Encephalitis is not rare in children and the accompanying brain damage may result in various degrees of mental retardation. The clinical history of the acute phase is usually characteristic and dramatic. Upon recovery from the acute episode, mental retardation becomes apparent. It is rarely progressive and, in fact, is often regressive. A first group of encephalitides is caused by neurotropic viruses of which many are known.

A particularly severe form is the herpes encephalitis in newborn, probably acquired during delivery from the infected genitalia of the mother.

A second group of encephalitis is due to bacteria and is usually

associated with meningitis. The increasing use of antibiotic treatment during the acute phase of bacterial meningo-encephalitis has resulted in a dramatic decrease of the death rate but in a noticeable increase of the number of partially recovered, and often defective, children.

A third group of encephalitides follows common diseases of childhood such as measles, scarlet fever, or chickenpox. Brain involvement usually develops after the original disease has subsided. An allergic mechanism is apparently responsible for this encephalitic reaction.

The clinical picture of the postencephalitic retardate shows a few distinct features indicative of the type of the original disease. Evidence of brain damage often present includes paresis, spasticity, speech defect, disturbance in eye movements, and behavior alterations. The degree of mental retardation varies considerably from case to case and usually cannot be correlated with the type of encephalitis.

Mental Retardation Clinical Syndromes

In numerous clinically characteristic types of mental deficiency, the data are not sufficient to establish the genetic or environmental nature of the condition.

De Lange Syndrome

Moderate microcephaly and small stature are usually present. Facies is characterized by bushy eyebrows with synophrys, small upturned nose, wide philtrum, low set ears, small mouth, and small chin. There is inability to extend the elbow completely. Syndactily, micromelia oligodactily, actodactily, and clinodactily are often present. Characteristic is a shortening and proximal placement of the thumb. Hirsuitism is common. Mental deficiency is usually severe.

Rubinstein-Taybi Syndrome

Mild microcephaly, hypertelorism, strabismus, antimongoloid slant of the eyes, beak nose, and high palate are common features. The most characteristic trait consists of broad terminal phalanx of the thumb or first toe. At times duplication of the first toe is noted. Laxity of joint ligament, hyperactive reflexes, stiff gait, and unfrequent seizures are other signs. Mental retardation is always present.

Sturge-Weber Syndrome

This is easily recognized because of the presence of angioma covering unilaterally a usually large area of the face. This is accompanied by a calcified angioma of the meninges in the occipital region on the same side as the facial angioma. Associated angioma of the choroid with glaucoma is not rare.

Epilepsy is common and hemiplegia often develops. The disease is slowly progressive. Mental retardation is generally present but its severity varies considerably.

Praders Syndrome

This consists of small stature, striking obesity, particularly in the lower parts of the body where characteristic cuffs around the ankles usually develop. Feet and hands are very small. Secondary sex characteristics are underdeveloped. There is characteristic muscular hypotonia, particularly in infancy. Mental retardation is usually moderate. Diabetes has often been observed in adult patients.

Sotos Syndrome

This is characterized in infancy by the very large proportions of height and weight which are above the 90 percentile. Therefore the term “cerebral gigantism.” The head is also large and often dolicocephalic in shape. There are, in addition, hypertelorism, antimongoloid slant of the eyes, drooping eyelids, large ears, and prognathism. Various degrees of mental retardation are noted. The adult patient may have normal height and weight.

Beckwith-Wiederman Syndrome

Large tongue, omphalocele, large kidneys, and a large liver in a large body are distinct features. Hypoglycemia at birth and polycythamia are often seen. A common finding is hyperplasia of endocrine glands. Mental retardation is not always observed and when present is not severe.

Angelmcin Syndrome

This curious condition (happy puppet syndrome) is recognized by peculiar paroxysms of unjustified laughter and severe mental retardation. Other signs are microcephaly with flat occiput, hypertelorism, prognathism, muscular hypotonia with hyperreflexia, and incoordinated, jerky movements. Epileptic seizures are usually present. A curious trait is the tendency of the child to protrude the tongue for long periods of time.

Williams-Beuren Syndrome

A so-called “elfin face” is characteristic of the syndrome with hypertelorism, epicanthus, upturned small nose, wide mouth, full cheeks, low-set ears, and small chin. Hypercalcemia and supravalvular aortic stenosis are features of the syndrome. Mental retardation, which is not always present, is usually moderate.

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