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Cretinism

Herbert H. Miller
University of Nebraska Medical Center

C R E T I N I S M

by

Herbert Hamlin Miller

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Definition (1) Cretinism may be defined as dwarfism due to retarded development associated with a greater or less degree of mental defectiveness, and by fairly constant changes in the thyroid gland, bones, skin, genitals, and the special senses, occurring either endemically or sporadically. The word "cretin" is said to be a diminutive of the Rhaeto-Romanic word "Cret" which means dwarf. The term cretinism does not include all the conditions of hypothyroidism, but applies only to a pronounced clinical manifestation of severe hypothyroidism with the classical clinical syndrome of signs and symptoms, occurring in infants and children both endemic and sporadic. Being a true hypothyroidism all the degrees of severity ranging from athyroidism to a very slight decrease in thyroid function are seen.

Embryology

In embryos with five to six primitive segments there appears in the midventral wall of the pharynx, between the first and second branchial arches, a small outpocketing, the thyroid analage. Later it becomes a stalked vesicle. The stalk, the thyroglossal duct, opens at the border of the tuberculum impar of the tongue which later becomes the foramen cecum. The duct soon atrophies and the bilobed gland anlage loses its lumen

and breaks up into irregular, solid anastomosing plates of tissue as it migrates caudad. The thyroid assumes a transverse position with a lobe on each side of the trachea and larynx. In embryos of eight weeks, discontinuous lumina begin to appear in swollen portions of the plates; these represent the primitive thyroid follicles. Colloid soon forms (2).

History

Cretinism has been known for centuries, but complete clinical pictures have been lacking for the most part until the time of Paracelsus. Ideas as to the cause of cretinism have varied greatly from the times of the early Romans to the present time, but still there has been no definitely proven cause of the condition.

Pliny (3) has left indubiatable evidence of the presence of cretinism in the early days of Rome. The pagan-Romans (4) noted these young defective children and attributed their infirmities to their christian religion. These pagan-Romans called these children "Chistians", or "Chretiens" which becomes our word cretin of today. From the early Roman days down to the time of Paracelsus in the latter part of the sixteenth century and the first part of the seventeenth century, little was done towards the solution of the problem of cretinism.

Paracelsus (5,6) however gave us a fairly accurate

clinical description of cretinism. In 1603 this author first noted the coincidence of cretinism and endemic goitre. This observation was original with Paracelsus during his studies in the Salzburg region. Altho no definite statement of this observer could be found as to his idea of the cause of cretinism, apparently he ascribed the condition to the mountain air.

Wolfgang Hoefer (7), who followed Paracelsus in time of observation, was a domineering type of individual and had definite and decided views on the subject of endemic goitres and cretinism. He was not in accord with the views of Paracelsus and his followers and took means, both sarcastical and satirical, to denounce the previous views and impress his own theories on the rest of the world at that time. The following quotations will give a good idea as to the views held by Hoefer (7). The quotations are from Hoefer, *1657*

"Foolishness"

"Because foolishness is so familiar in the very many inhabitants of the Alps, and indeed is endemic, some ascribe it to the air, others to the water, and still others to food and education. But beware lest you decide upon the first. Otherwise you may be exposed to the same reply as the man, who, when he was falsely censuring the foolishness of these men and was sharply arraigning the defect of the

air, while he was using this locality in a liberal manner and enjoying the same air as guest, heard the following reply, 'Depart quickly, good sir, lest, yourself must needs, be foolish in company with us.

"Not the second, (water) because to many inhabitants of the Alps waters are very healthful to drink and yet very many of them are foolish. Therefore the third will hold (food and education) and this opinion is borne out by other considerations in my frequent examinations of their diet and mode of life. For this class of people, who delight in foods which supply much excrement but little aliment; they are displeased with the opposites; on this account they are voracious, yet never full, except to the point of bursting when the abdomen bends. Their children in this manner stuffed at least four times a day, they deposit near the oven and instruct them neither in letters, nor in morals nor in labors, frequently they pay no attention to their (children's) entreaties, so that, when their food also aids their melancholy and gloomy spirits, they are necessarily made stupid and foolish.

"They also become strumous from almost the same cause, for while the children are thus neglected and leisurely subside into themselves "They pile upon one another by the oven" like dogs devouring choice bits with full jaws; they distend and dilate the skin and the little glands about

the neck because their heads are filled with gloomy vapors by similar food, the latter being turned into liquid and flowing lower, are drunk in by the glands or form new glands and monstrous straumas."

Thus does Hoefer give his idea of the cause of the condition of cretinism and goitre. However wrong his interpretations of facts may have been, his theories were accepted at the time as being plausible.

In 1850 Curling (8) first associated the symetric swellings of the fat tissue at the sides of the neck with defective mental development.

In 1871 Fagge (9) made the following statements about cretinism. "I believe that deficiency of the thyroid body has never been observed in persons who are not cretins. An obvious inference is that its presence may be protective against cretinism;.....Thus I think that the true relation of goitre to cretinism is that they are antagonistic effects of the same unknown cause.....When this cause begins to act, but with little intensity, its sole effect is goitre. But if it acts with great intensity or upon successive generations the result is cretinism as well as goitre." Fagge gave us the first real accurate and plausible relationship between endemic goitre and endemic cretinism. It was by means of his observations and theories that progress was made along the line of etiology and treatment of goitre and cretinism.

Professor Kocher (9) of Berne observed that the removal of the thyroid for the treatment of goitre was followed by a condition that simulated adult cretinism. That was in 1873, just two years after Fagge's observations.

It was thirteen years later in 1884 that Horsley (8) removed the thyroid gland in a series of monkeys and produced myxedema. It had been known for centuries that the thyroid gland was enlarged in all cases of so called endemic goitre, but was only enlarged in a few cases of cretinism. They did not suspect that there was a secretion of the thyroid gland that was present and necessary to normal growth of the human body. So after the experiments by Horsley it became evident that there was some substance present in the thyroid whose function prohibited myxedema.

It remained for Dr. George Murray (8) in 1891 to publish the discovery showing that injections of an extract from the thyroid gland into individuals with myxedema caused a marked improvement and recovery of the condition. It was then that the thyroid treatment came into use for cretinism.

Since the time of Murray and Horsley a classification of goitre and cretinism has been possible. The greatest work being done at the present time is the work to determine the etiological factors of the condition. We know now that in cretinism there is a deficient thyroid secretion early in life, but we do not know just why and how the secretion came to be

deficient. It seems most likely that there are several factors any one of which may be responsible for the condition.

Methods of treatment of cretinism have improved greatly in the last ten years. Surgical treatment for cretinism, namely the transplanting of thyroid tissue into the cretins, has so far been of little or no practical value (10).

Etiology

1. Occurrence: Since the time of Paracelsus in 1603 it has been known that cretinism prevails in the same localities in which endemic goiter is prevalent. The greatest endemic areas occurr in mountainous districts of Europe and Asia. The Alps, Pyrenees, and the Himalayan mountainous regions are the most endemic areas. The countries involved are parts of France, Italy, Austria and Switzerland. In Asia there are scattered areas of endemic cretinism. Sporadic aretinism is scattered throughout the world. The United States and England contend with this type of cretinism. To give an idea of the prevalence of cretinism it is but necessary to quote some figures. In Switzerland for the ten year period 1875-1885 7% of the recruits in the army showed some form of cretinoid degeneration. In that same span of years 2,500 men died of the condition (3). In the Valleys of Berne and Wallace during the five year period 1899-1904 there were 336,000 school children of which 15,000 had some evidence of the disease. The fact that cretinism occurred in valleys of the mountainous regions led Bircher (11) to believe that the

disease occurred in people who live in a country formed by strata which had once been submerged under the ocean, and not in those living on strata formed under fresh water or on volcanic formations.

2. Age: (12) Usually cretinism cannot be detected at birth but appears for the most part so that it can be recognized about the sixth month of life. Cases have been known where the signs and symptoms have not appeared until the ages of eight to twelve years.

3. Sex: (12) Cretinism is more common in females. According to Murray the ratio is about 2 : 1.

4. Heredity: (12) Direct heredity from parent to child doesn't play such a great part in the production of the disease because the sexual functions are usually in abeyance and procreation is not very common. However, heredity plays some big part in the endemic cretinism for it has been found that the parents usually had been affected with endemic goitre. It is thought that if the mother was sick during pregnancy that toxins could be transferred thru the placental circulation to the fetus. Also that if the mother had an endemic goitre at the time that the same toxin which was affecting her thyroid would be transmitted thru the placental circulation and destroy the thyroid of the fetus. Herrman (13,14) believes that the condition is not due to the sickness of the mother during pregnancy or to the

transmission of toxic substances thru the placental circulation, but rather to some abnormality in the germ plasm, some chromosomal defect in the developing ovum. To prove his contention he cites three cases of cretinism in one family. These children were not born in succession but there were normal children in between. To further his contention he cites a case of twins in which one was a cretin and the other was a normal child. He states that if the condition was due to the transmission of toxins thru the placental circulation both infants would have been affected. Herrman also reports that 5 out of the 50 cases under his care were cases where the parents were blood relations. So he concludes that consanguity may be a factor if the ancestors had any thyroid condition.

5. Congenital Anomalies: Pineles (6) studies have seemed to show that there is rarely a congenital absence of the gland, but usually a very small atrophic gland is found. Kerley (15) states that in typical text-book pictures there is complete congenital absence of the gland. Kerley cites Beech who reported 16 autopsies on cretins and found that in 14 there was a complete absence of the gland. Kerley also cites Curling, Fagge and Iphophon, who preformed 100 autopsies on cretins and found that in 25 of the cases there was complete congenital absence. In the remaining 75 cases there were connective tissue and

colloidal changes. It is probable that the cases of complete absence of the gland occurred in sporadic cretins.

6. Infections: Marine (6) believes that inflammatory injuries to the thyroid, as a thyroiditis occurring independently or in association with infectious diseases such as scarlet fever, measles, typhoid fever etc., is a factor to be considered in cretinism. Marine also states that mechanical injuries to the thyroid gland may be followed by atrophy of all or parts of the gland tissue.

McCarrison (11) believes that cretinism is based on an infection, perhaps of a specific nature. It is true that bacteria have been sought and found in the drinking water but it could not be proved that the bacteria isolated had any relationship to cretinism. (11)

7. Toxins: During pregnancy there may be toxins in the maternal blood stream which would be transmitted thru the placental circulation to the fetus. Just why it should attack the thyroid gland of the fetus is not explained. These toxins may be due to bacterial endogenous material or exogenous bacterial toxins or to chemical formations of inorganic origin. McCarrison (16) made a study of the toxins and fecal contamination of drinking water and came to the following conclusion. Cretinic degeneration is caused by intestinal toxemia of bacteriologic origin in conjunction with predisposing factors. The anaerobic types

of fecal bacteria are regarded by McCarrison as especially active in the producing of the disease.

8. Water: For centuries water has been incriminated as the cause of cretinism. At first there was not even a suspicion as to what the element or elements in the water might be, but in recent years much work has been done to clarify the problem. As stated above bacteria have been sought and found in the drinking water but no definite proof could be shown that the bacteria had any relationship to the condition. It might be well to cite some experiments that have been preformed with the water from endemic areas. (11) Animals in the endemic regions that were given water from the wells and springs developed goitre. But animals fed on imported water and food but kept in the endemic area also developed goitre. Then some of the water was transferred to an area which was not endemic and given to animals in that region. These animals developed goitre. Whatever the active agent may be, it will not pass thru a dializing membrane, and therefore it is supposed that it must be colloidal in character. This agent will withstand temperatures from 75°- 85° C. so it is supposed that it is not a living organism.

Ebbell (17) incriminates the drinking water, ascribing the noxious action to radium salts and radio active substances which are frequently found in spring water. The hypothesis

is in accord with the characteristic incidence of goitre and cretinism in which the radio active substances are frequently found in the drinking water. Boiling of the drinking water is protective against the disease because these radio active substances are broken up. Ebbell (18) also uses this radio active substances theory to explain some of the pathology of cretins. He states that radio active substances injure the sex glands and in cretinism the sex glands are small, strophic and undeveloped, apparently the result of ingestion of these radio active substances. Also it is known that roentgen rays cause injury to the epiphysis in young persons and cretins show a similar injury.

9. Hygeine and Environment: Hoefer (7) in his description of cretinism in 1657 laid a great deal of stress on environment as a factor in the production of cretinism. Hygeine and environment has been an important factor to most authorities since that time. Jona and Lusso (19) have been studying the condition at Cogne, a mountain focus of endemic cretinism, and confirm the evident connection between poverty and cretinism. These two workers also believe that alcohol, syphilis and imbreeding must be of great significance. Dr. Langdon Down (9) has suggested that the cause of cretinism is alcoholic intoxication on the part of the parents at the time of procreation. Fagge (9) however could not find in his series of cases

anything which would bear out this contention. There does seem to be some relationship between poverty and cretinism, but it is not known just what the true relationship may be.

10. Iodin: It has been repeatedly shown that there is a lack of iodine in the food and water in the endemic goitre areas. It has also been shown that by giving these endemic goitre patients iodine that cures are possible. In Cretinism however the thyroid gland is of such small proportions that it could not handle the iodine even if there was an abundance of it in the water and food. So the iodine is merely a factor in endemic goitre and in that respect is related to cretinism, inasmuch as cretins are children of endemic goitrous parents.

11. Climate: Endemically the disease is found in inland and mountainous districts, for the most part in the temperate zones. Sporadically, the disease occurrs without any particular selection of climate.

12. Race: Race has very little to do with the condition. It is true that most of the cases occurr in the white races, but that can be explained by the fact that the white races inhabit the endemic regions.

Pathology and Morbidity

There seems to be a difference of opinion among the various authors as to the pathology of endemic and sporadic cretins. At present I will take up the pathology of cretins as a class and differentiate them later in differential diagnosis.

1. Thyroid Gland: Because of the wide variations in the severity of the disease it can easily be understood that the pathology of the thyroid gland will vary in the same way. As stated previously, Kerley (15) stated that in typical textbook pictures there was a complete absence of the gland. Kerley cited two series of autopsies, one in which there was complete absence of the gland, and the other in which there was complete absence in 25 out of 100 cases. The remaining cases showed connective tissue and colloidal changes.

The presence or absence of a visible goitre is of significance to some authors. Curling (9) in 1850 first pointed out that in the majority of cases of cretinism the thyroid body is not enlarged, and even is entirely absent in many of the cases. To Murray(12) this was a differential point between sporadic and endemic cretins. His conclusion was that sporadic cretins never had a visible goitre, and that only in two-thirds of the endemic cretins was there an increase in the size of the thyroid.

Judd (10) of the Mayo Clinic sums up the pathology of the thyroid gland in cretins by saying that most cretins have adenomas and cysts in the thyroid. If there is any thyroid tissue left it is usually distended with colloid. In cases of complete absence of the gland there is fibrosis in the tissue of the thyroid area.

2. Other Endocrine Glands: Disturbances of the endocrine glands are not separate and distinct but correlated, and the fact that thyroid extract improves the condition of cretinism is not proof enough that the thyroid alone is responsible (14). The thyroid gland may be the first involved and indeed show the greatest amount of pathology, but other glands of internal secretion are in turn involved. Kendall (14) believes that the thyroid secretion acts as a catalytic agent and stimulates chemical changes in all the cells of the body including other endocrine glands. Jenner (14) joins in the same view when he has noticed changes in the pituitary gland, especially the anterior lobe. He does not attribute the change as a compensatory hypertrophy, but to a lack of thyroid secretion. Schonemann (3) has reported a series of cases of autopsies preformed on cretins which bear out the same general pathology. In the series of 112 cases only 27 showed a normal pituitary. The microscopical study of the others showed an enlargement of the pituitary body. The enlargement was due to an increase in the connective tissue and chromaffin cells, increase in the stroma of blood vessels, and a hyaline degeneration and swelling of the cell strands themselves. Most of the pathology was noted in the anterior lobe.

Another of the endocrine glands often involved is the parathyroid. This gland being in such close apposition

to the thyroid often shows fibrosis along with the fibrosis of the thyroid. It is in this type of cretin that there is a tendency to tetany and diplegia (16).

The sex glands of cretins are small and atrophic. The females do not menstruate, showing a deficient activity. The males are usually not capable of procreation which also shows a deficient activity.

Witts (20) reports a case of a mother developing myxedema after the childbearing age. This mother's daughter was normal until the age of nine when she developed signs of cretinism and was treated for the condition. Then later the daughter developed diabetes (and became pregnant also). This does not show that the diabetes was the result of the cretinism, but may or may not show that there is an inter-relationship of the glands of internal secretion.

3. Heart. Assuming that cretinism ia the result of a toxin in the blood stream, some observers (21) explain the heart condition present in most of the endemic cretins due to the same toxin which is responsible for the degeneration of the thyroid gland.In endemic cretins there is usually a heart complication which is characterized by myocardial degeneration and sometimes, hypertrophy.

Whether there is any demonstrable gross or microscopical pathology in the heart itself, the electrocardiograms usually show a variation from the normal. Catherine Thatcher (22) at the Mass. Gen. Hospital made E.K.G's. of

eight cretins before treatment was instituted. The only variation from normal was in the T-wave in every instance in lead 2. In every instance the T-wave was below normal in height. One of the cases showed an inverted T-wave; one was flat; four, with a plus 1mm. T-wave, and the remaining two with a plus 1.5mm. T-wave. When it is considered that the average normal height of the T-wave is from 3mm to 5mm it can be seen that there is a definite cardiac involvement. This E.K.G. is a method of diagnosis.

4. Blood: There is usuall a simple anemia in all cases of cretinism with the exception perhaps of the child under three or four months of age (3). (see symptoms.)

Metabolic calcium is low (one-third of normal in the studies of Haugardy and Langstein(3).)

In hyperthyroidism after taking glucose by mouth there is a rapid and persistent rise in the blood sugar. In cretinism and myxedema there is delayed in the blood sugar rise. (23)

5. Skeletal System: Foster states that the pathologyof the skeletal system is due to two predominating causes. First, there is a retardation in the appearance of the centers of ossification; second, there is a failure of new cells to appear at the epiphysis. The formation of the centers of ossification being delayed, the epiphysis unites either late or in severe cases not at all. (23) The lack of growth in the long bones leads to a dwarf

stature, the lack of growth of the facial bones causes the face to be small relative to the size of the cranium, while the lack of development of the sphenoid gives a sunken appearance to the base of the nose. The fontanels do not close until late in life. In endemic cretinism the head is deformed, so that the head is comparatively larger in the biparietal diameter (9). In sporadic cretinism the head is deformed so that the largest diameter is in the antero-posterior diameter (25).

Barker (26) reported on a form of rickets occurring in association with cretinism. In his report of the X-ray findings he states, "The X-ray plates are suggestive of Legge's disease or Calve-Perthe's disease, except that in cretins we have a disturbance in ossification and in the former a necrotic condition." Kunde and Carlson (27) took young rabbits, 2-3 weeks old and removed the thyroid, using animals of the same litters as controls. They were able to produce dwarfing of growth and the other characteristic signs of cretinism. They made X-ray studies of the bones and found a widening of the epiphysis and a ricket-like condition. Later on, they took these animals and gave them cod liver oil and sunlight to see if this ricket-like condition would disappear. After again taking X-rays of the bones, they decided that there was no improvement in this ricket-like condition. From their studies it would seem that this form of ricket was independent of vitamin "D" (28).

Roentgen ray studies of the bones of cretins show failure of the epiphysis to unite with the shaft, areas of diminished calcification, and irregularities from the normal shape of the bones.

Dentition is delayed and the teeth show deviations from normal teeth. Kranz (29) found the dental condition of cretins universally poor. Abnormalities in both dental and jaw relatiohship such as, malposition of teeth, defective development, and in all cases a great incidence of caries. The teeth of cretins showed horizontal ripples similar to the hypoplasia of teeth in rickets.

6. Larynx: Josephson (30) reported a case of cretinism on which an autopsy was preformed. In this case the thyroid tissue was completely atrophied. The larynx was about the size of that of a four year old child. There was general thinkening of the walls due to a deposit of connective tissue and myxoid tissue. The vocal cords were greatly hypertrophied.

7. Skin: The skin of cretins is waxy colored in the gross, and the subcutaneous tissues are increased in amount by the myxedematous infiltration. Fagge (9) first described a fatty tissue tumor in the posterior triangle of the neck. The subcutaneous tissue shows fatty tissue infiltration throughout the body.

8. Genitals: The sex glands of cretins are small and undeveloped. The external genitalia are infantile in

appearance and size. The pubic hair is usually scanty or absent.

9. Nervous System: There are wide variations in the mental status of cretins. Some of the individuals show only weakened mental powers and are able to get about and make a living for themselves. Other cretins are mentally sluggish and beyond the mental capacity to care for themselves. In the first type, the patients may only show a slight inability to learn readily, or may show tardy reactions (3). They may be slightly negligent in their bodily care or to some duty which they are given to preform, but they usually manage to get about by themselves fairly well. In the second type, the individual is sluggish and shows very few signs of comprehending anything that goes on about him. They love to sit still and not be disturbed. The vocabulary of this type is very meagre and speech is correspondingly small. McCarrison (16) describes a type of "nervous cretinism which would fit into this group. In this type there is cretinous idiocy with associated with diplegia and tetany due to a congenital fibrosis of the thyroid and parathyroids.

Pineles' (31) studies show that in cretins there are degenerative and developmental defects of the cortical centers of the brain.

Sensory nerves of taste, smell, hearing, touch and pain are greatly dulled (3). Hearing is the special sense that suffers most frequently. This hearing defect is due to deficiencies in the chochlea and middle ear, as well as to cortical deficiencies.

10. Muscular System: From the continued disuse there may be atrophy of the muscles. There may be a complete diplegia. The musculature is usually weak.

11. Gastro Intestinal System: No gross changes have been described in the alimentary tract.

Signs and Symptoms

1. Onset: It is usually believed that evidences of cretinism first appear during the last half of the first year of life. Whether that supposition is corredt is open to doubt by some authors (32), but it is certain that the condition is not usually recognized until nearly the sixth month. Occasionally some manifestations of hypothyroidism may be observed at birth, but those instances are rare. Talbot (33) says that the reason these symptoms do not appear earlier is perhaps due to the fact that the fetus has obtained and stored up some of the thyroid secretion from the mother while still in utero. He thinks that perhaps the child obtains enough of the secretion thru the mothers milk to delay the symptoms for a time. Talbot(32) says that the usual time to recognize early manifestations is after the first eight or ten weeks of life. The signs of cretinism may be grouped into three classes, namely, early

symptoms, mild symptoms and complete cretinism.

2. Early Symptoms: As previously stated these symptoms appear between the second and sixth months of life.

A. Sparseness but not any particular coarseness of the hair may be the first sign present (32).

B. Hoarseness of the voice. This hoarseness is due to the myxedematous swelling of the vocal cords. In any case of hoarseness in an infant which cannot be explained on some other pathological basis should arouse the suspicion of cretinism.

C. Quietness, may be the only sign present that the mother of the child notices. This quietness may be due to the lessened metabolism.

D. Thickening of the subcutaneous tissues. This sign may or may not be present in the early case. If it is present, it can be differentiated from true edema by the fact that in cretinism the tissue doesn't pit on pressure.

E. Facies: Early changes are very slight altho anyone very familiar might possibly see a suggestion of thickening of the lips and tongue. There may be a slight depression at the bridge of the nose, or a suggestion of a pig-like expression of the eyes.

3. Mild Symptoms:

A. Tongue: By the end of the second or third month of life the tongue may so large as to entirely fill the mouth and interfere seriously with nursing. Accompanying this enlargement

of the tongue there is usually a dribbling of saliva. The lips are usually parted.

B. Thickening of the subcutaneous tissues becomes more marked as the disease progresses and is usually well enough marked so that there is no doubt about the swelling.

C. Hoarseness of the voice increases.

D. Eyebrows: The outter ends of the eyebrows become scanty or even absent. The hair is dry and coarse .

E. The eyes are far apart and have more of a suggestion of that pig-like appearance, which later becomes striking.

F. The sclera is a bluish white color.

G. The cheeks have a definite lemon yellow tint. This lemon yellow tint can best be seen during rest and appears especially on each side of the alae nasi.

H. The body feels cold to the touch. This is most likely due to the lessened metabolism.

I. Protruding abdomen is present but of no particular diagnostic value.

J. Anemia: Except in patients under four months old there is usually a marked simple anemia. The hemoglobin content, the red cell count, and the white cell count, may be reduced to 50% of normal. In most cases the mononuclear white cells predominate as they normally do in infancy.

4. Complete Cretinism: This is usually unmistakable after the sixth month of life if treatment has not been taken

A. Growth: There is a characteristic retardation of growth as well as an intensification of the early and mild

symptoms. The infantile bodily proportions are retained, that is, the arms and legs remain relatively short, the head large, and the trunk long. If the X-rays were taken it would be found that ossification is going on very slowly.

B. The fontanels remain open and it certain cases as stated by Talbot (32) the fontanels have remained open until the eighth year.

C. The forehead is low due to the growth of hair being low down on the face. The most striking thing about the forehead is the fact that the skin wrinkles up on it whenever the eyes are open.

D. The hair is very dry and coarse

E. The nose is broad with a wide flat bridge.

F. The mouth is large and usually widely open allowing saliva to escape.

G. Dentition is delayed, and the teeth present hypoplasia very similar to that found in rickets.

H. The lips are thick.

I. The neck appears short and thick. This is not an actual shortening, but the appearance of shortening is given by the large deposits of myxedematous tissue about the neck and clavicles.

J. The abdomen is protuberant. Accompanying this protuberance there is usually an umbilical hernia due the recti muscles being forced apart.

K. The skin is pale, dry, and coarse with myxedematous swellings and deposits of fatty tissue. Eczema is not an uncommon complication of cretinism.

L. Mental development is retarded to a striking degree. The amount of mental impairment varies considerably. In the typical case with well marked mental deficiency, the patient at first seems just abnormally quiet. This individual is docile unless teased. The speech is delayed and the vocabulary is very limited. The inability to learn the simple words that the mother tries to teach the child is sometimes the only sign that the mother complains about. Mutism is a very common and Joyce (34) states that it is commonly found in 28% - 30% of the cases. Perhaps the fact that these children are so sluggish is due to the fact that in not a few cases deafness accompanies the mutism (3).

Fagge (9), in 1886, gave a vivid description of older cretins that will be worthy of quoting.

"As I have already observed, it is their bodily con-figuration that cretins differ from ordinary idiots. Except in the very slightest forms, they are seldom more than four feet and a half in height, and often below three feet. They have large heads, especially in the direction from ear to ear. The features are broad and thick; the eyes are wide apart; the nose is very flat at the root, and spreads out enormously toward the alae; the mouth is very large, widely open, with thick lips, and allows saliva to excape. The forehead and cheeks are wrinkled and the skin coarse and rough so that they have the appearance of old age. A cretin twenty years old is exactly like a cretin of forty. The hair comes low on the forehead and is coarse and bristly. Cretins

have narrow chests, large bellies, and crooked limbs. Their hands are broad but short with short fingers....."

The one change which is constantly found in cretins is the basal metabolic rate. Magnes-Levy established the fact that the heat production of cretins is only 45% to 50% of normal. Talbot (34) has repeatedly taken basal metabolic rates of cretins and finds a constant decrease from the normal. Talbot has a special apparatus for taking the B.M.R. of children and has found a decrease in the B.M.R. even before the patients showed any particular signs of cretinism.

Diagnosis

1. The early diagnosis of cretinsim is sometimes very difficult and easily overlooked. However, there two or three signs that early in the disease should arouse suspicion of cretinism. First, the child develops a heavy expression and the eyes tend to be pig-like; second, there is a definite lemon yellow tint that appears on the mesial aspect of the cheeks that disappears when the child cries; third, changes in the voice should always arouse suspicion when no other explanation of the hoarseness can be given. In the late stages after complete cretinism is present there is usually no doubt as to the condition.

2. In all cases of suspected cretinism the B.M.R. should be taken. If this were done on all infants where there is only a slight suggestion of cretinism present, a positive diagnosis could be made and the proper treatment instituted before there had been much damage done.

3. Electrocardiographs show a decrease in the height of the T-wave (22), in Lead 2. When it is impossible to have a B.M.R. taken for lack of apparatus, then an E.K.G. should be taken, and would be of definite value in the diagnosis.

4. The glucose tolerance test (23). If a given amount of glucose is given by mouth to a hyperthyroid patient the blood sugar makes a sudden rise and remains high for some time. When the same test is applied to a cretin, there is a delayed rise in the blood sugar.

5. If there cannot be any certainty of the diagnosis then a picture of the child should be taken and thyroid gland given for a therapeutic test. The child can then be compared with the photograph for any improvement.

Differential Diagnosis

Under this heading, the differential diagnosis between endemic and sporadic cretinsim should first receive attention. Wieland (14) says, "We must admit that of the symptom complexes none is so difficult to differentiate from endemic cretinism as sporadic cretinism. The resemblance is of such a character that in endemic districts, for example in Canton, Berne, Wallis and Aargon, we do not trust ourselves to make the diagnosis of sporadic athyreosis or hypothyroidism, but in all doubtful cases rather call them cases of endemic cretinism. In districts which are free from goitre and cretinism this difficulty does not exist."

McCarrison states, (14) "Sporadic cretinism differs only from the endemic variety in that it is due to toxic agencies acting thru the maternal blood, other than the specific excitants of endemic goitre."

De Quervain (37) of Switzerland insists that there are two main types of cretinism. 1- That type in which the thyroid glands are relatively small (Athyroidism) and nervous symptoms are not marked. 2- That type in which the thyroid glands are large and nervous manifestations are prominent.

Differential diagnosis between Endemic and Sporadic

Sporadic Cretinism	Endemic Cretinism
1. Clinical picture more uniform.	1. Clinical picture varies.
2. Personality less marked.	2. Personality more marked.
3. Dwarfism more marked.	3. Dwarfism less marked.
4. Myxedema more constant.	4. Myxedema less constant.
5. Head is deformed so that it is longer in the antero-posterior diameter. (Dolichocephalic) (25)	5. Head is deformed so that it is wider in the bi-parietal diameter (9)
6. Goitre never present	6. Goitre occurs only in about two-thirds of the cases.
7. Less responsive to treatment.	7. More responsive to treat.
8. Presence of fatty tumor in the posterior triangle of the neck.	8. May or may not be a fatty tumor in the neck.
9. Nervous symptoms not marked. (37)	9. Nervous symptoms marked.

For the most part it can be said that there is very little difference between endemic and sporadic cretinism. The diagnosis usually rests with the occurrence of the case. If the case is not in an endemic region it is classed as sporadic and visa versa.

So that in the end the differential diagnosis mainly rests between cretinism and mongolism. The following chart taken from Talbot (32) explains how to differentiate the two.

Cretinism	Mongolism
1. Rarely recognizable before the second or third month of life. Always evident by the sixth month.	1. Recognizable at birth
2. Eyes horizontal and pig-like.	2. Eyes almond-shaped, tipped upward and outward. Epicanthic fold marked, and strabismus marked.
3. Complexion pale and waxy with a lemon yellow tint.	3. Skin of cheeks florid red, elsewhere marbled effect.
4. Tongue thick and square. Fills the mouth and protrudes.	4. Tongue fissured, pointed and not thick. Often it protrudes from the mouth.
5. Expression dull, stupid.	5. Expression alert. Grimaces characteristic.
6. Skin dry and coarse.	6. Skin dry and soft.
7. Hair dry and coarse.	7. Hair dry, fine and soft.
8. Hands square, spadelike.	8. Hands short, little finger much shorter than others.
9. Feet square. Great toe seldom widely separated from the others.	9. Feet short with great toe separated from the others.
10. Joints not abnormally flexible.	10. Joints lax and very flexible.

Prognosis

The average life of cretins is usually much shorter than that of a normal individual. Some cretins live to a fairly old age however. Death when it comes is usually due to some intercurrent disease.

It is known that some cretins have a complete absence of the thyroid and others have portions of the gland remaining. It would seem then that the cretin with portions of the gland

remaining would have a better prognosis that the cretin with complete absence of the gland. Kerly (15) states that he believes from his follow-up of eight cases of cretinism that have been treated with thyroid extract, that in cases where there is complete absence of the gland, the results are not as favorable as the early improvement would seem to show. He does believe in those cases where part of the gland remains that the prognosis is very good.

In untreated cases or in cases which do not receive treatment until rather late in life the prognosis is not favorable as to fitting the individual to assume an independent life.

Talbot (32) believes that complete return to normal if thyroid treatment is instituted before the child is three or four months old. During the first half year of life the child grows exceedingly fast. The body doubles its weight and the brain grows in the same proportion (32). It has been assumed that the lack of thyroid during this first six months of life causes permanent mental injury because thyroid secretion is necessary for the complete development of cerebral tissue (32). If treatment is not in progress during this critical time no amount of treatment can restore the cerebral tissue to normal.

Judd (10) of the Mayo Clinic, says that improvement under treatment progresses up to a certain point and then no matter how long the treatment is continued, no further

improvements can be made. Judd does not say whether he believes this is true when treatment is begun before the fourth year.

Improvements can usually be obtained later on in life but the extensiveness of the improvements depends a great deal on the age of the patient. (see treatment.)

So to generalize it is sufficient to say that the extent of improvement depends on the degree of athyreosis and the age at which treatment is begun.

Treatment

If the conclusions in the prognosis are correct then the diagnosis should be made as early as possible, and treatment instituted early and continued at least until after puberty. Talbot (32, 33, 35, 39) believes that early diagnosis in mild conditions can be detected in the first six months only by the B.M.R. Without the means of making a positive diagnosis when a strong suspicion is present, treatment should be begun. If time is wasted in waiting for more complete signs of cretinism, the chances of recovery are diminished proportionally.

1. Prophylaxis: (6, 38)

A. Improve the hygienic condition [redacted] so that the factors of organisms and toxins will be eliminated as a cause of the condition. Improve the drinking water, either by boiling the water or importing pure water.

B. As endemic goitre has been found to be a factor

in the production of endemic cretinism, the task of reducing cretinism should first of all be directed towards the endemic goitre. It has been found that boiling of the drinking water and the administration of iodine to people in the endemic areas reduces the incidence of goitre. Iodized salt and the administration of iodine has reduced the incidence of goitre in the school children of Vienna from 43% to 31% (6).

Pregnant women who show signs of an enlargment of the thyroid should be given iodine (10mgm. per week), and if there are any signs of hypothyroidism the women should be given thyroid in one form or another.

2. Treatment Proper: The treatment of cretinism may be divided into two classes; that of the infant, and that of the older child or adult. In either case the treatment is mainly the administration of thyroid gland preparations. These preparations may be the fresh gland, desiccated powder, aqueous extracts or glycerine extracts. These may be given by mouth or the last two may be given intradermally, intramuscularily, or even intravenously.(25)

Talbot has received the best results with the thyroid extracts, and has compiled a table of dosages for the patients at various ages(32). The matter of dosage is variable in each individual case according to the B.M.R. but the following table taken from Talbot is relatively correct (32)

Age of Child	Daily dose in grains
2 to 4 months	¼ gr.
4 to 8 months	½ gr.
8 to 12 months	¾ to 1 gr.
12 to 24 months	1 to 2 gr.
2 to 4 years	1½ to 3 gr.
4 to 12 years	3 to 6 gr.

A. Older child of adult: Cretins twenty or more years old are frequently met who have never had any or only irregular and scanty treatment with thyroid. Their mentality varies with the degree of athyreosis. Treatment may help to some extent in these individuals, but usually not very much, and sometimes no improvement can be noticed (38). Means and Aub (38) reported observations on a patient twenty years of age who underwent treatment with thyroid, without much improvement in the mental status, but the pads of fat which had been present over her back soon disappeared and her skin became warmer and moister. This patient grew 2 cm. during the fifteen months of treatment.

Murray (12) states that the general improvement as he observed it was good. In girls who had never menstruated, menstruation began. Pubic hair developed and the mental condition improved. The patients gained from a few cms. to a few inches in height.

As a rule, these older cretins tend to go into a state of hyperthyroidism while taking thyroid treatment

much more frequently than do infants, and much more readily than normal individuals (38). This fact is probably true because normal individuals can in a measure store up excess thyroxin in the thyroid gland and thus protect the blood stream from this excess. Cretins having little or no thyroid tissue cannot take care of the thyroxin which is over and above the amount that is needed at the moment. Cases have been reported (38) in which it was almost impossible to administer thyroid in an older cretin whithout the patient going into a state of hyperthyroidism. In general it may be stated that with the older cretins, thyroid may be given cautiously in small doses and it may confer some benefit. But if no benefit can be seen, and the patient tends to go into a state of hyperthyroidism, then the drug should be discontinued.

B. Infants: It is in this class of cretins that the greatest amount of improvement is noted. The early diagnosis and treatment sustained in the cases of infantile cretinism may make the difference between normal progressive development and imbecility.

Infant cretins require a relatively higher amount of thyroid to bring the metabolism to a normal level than adults with myxedema. It is also necessary to start with very small doses and work up the dosage until the exact

amount that will keep the metabolism normal is found.

Talbot (33) states that the best way to treat these cretin children is by means of the basal metabolic rate. The dosage for each individual child can be regulated by this means. Talbot in his observations also thinks that the total metabolism should be raised not only to the normal for the cretins size but should be increased to that of a normal child of the same age. In doing this the physician should be on the alert for signs of hyperthyroidism. These signs are; restlessness, sweating, insomnia, diarrhea, tachycardia, loss of weight or fatigability (26). In such event the dosage of thyroid should immediately be stopped and progressive doses again administered as soon as the signs of hyperthyroidism have subsided.

Barker (26) states that a form of rickets accompanies sporadic cretinism and that vitamin "D" in the form of cod liver oil or Viosterol should be given with the thyroid medication. There should be no doubt that all children should receive cod liver oil in the presence of cretinism or not. Kunde and Carlson (28) in their experiments on cretin rabbits with rickets would seem to show that the administration of vitamin "D" in the form of cod liver oil and sunlight had no effect. However it would seem that the administration of cod liver oil could do no harm and

possibly would do some good. The only contra indication would be in a case where the cretin was also in a state of acidosis.

General supportive treatment be given to all cases of cretinism. Efforts should be made to teach the patient to care for himself, and to learn to talk, and read as normal children. It sometimes requires patience on the part of the mother, but should be given a great deal of consideration. The child should be kept clean and comfortable. If unsatisfactory hygienic conditions are present, then every effort should be made to correct them. Correct diet is essential.

The surgical treatment of cretinism, namely the transplantation of thyroid from normal animals or humans into the cretin, has been tried on frequent occasions. The results so far are not worth offering as a cure for the condition. Judd (10) of the Mayo Clinic states that surgery has not been satisfactory. At the Mayo Clinic they have transplanted normal thyroid and also hyperplastic thyroid into cretins. The results have given some evidence of being good at the very beginning, but shortly the effects subsided and the patient was far from having a permanent cure. It would seem most evident that at present there is no need to displace the medical treatment for cretinism.

Conclusions

1. Cretinism is an athyreosis characterized by, dwarfing due to retarded development, mental defectiveness, and fairly constant changes in the thyroid gland, bones, skin, genitals, and special senses, occurring in children both endemically and sporadically.

2. Cretinism has been known since early Roman days.

3. The first explaination was that it was due to the Christian religion.

4. Paracelsus in 1603 first noted the coincidence of cretinism and endemic goitre.

5. Paracelsus ascribed the condition to the mountain air.

6. Hoefer, 1657, ascribed the condition to food and education.

7. Fagge, 1871, gave the idea that cretinism was a thyroid deficiency, absence of the gland.

8. Horsely, 1884, produced myxedema by removing the thyroid gland from monkeys.

9. Murray, 1891, first injected an extract of the thyroid gland into patients with myxedema and got cures.

10. Cretinism occurrs endemically in mountainous districts of Europe and Asia, especially in the Alps, Pyrenees, and Hymalayan chains.

11. Cretinism occurrs more often in females than males with a ratio of about two to one.

12. Direct heredity doesn't play such a big part.

13. Heredity plays a part in as much as people with cretinism (endemic) usually had parents affected with endemic goitre.

14. Typical text-book pictures of cretins show a complete absence of the gland at autopsy.

15. Infections probably play a part in cretinism.

16. Water plays a big part in the production of endemic goitre and endemic cretinism.

17. Hygeine and environment probably pay a part in cretinism.

18. The thyroid gland of cretins is either completely absent or shows adenomas and cysts with colloidal changes in the remaining tissue.

19. Other endocrine glands are involved in cretinism especially the anterior lobe of the pituitary, parathyroids, and sex glands.

20. Cretin hearts usually show a heart complication characterized by myocardial degeneration and hypertrophy.

21. The electrocardiograms of cretins shows a diminished, flat, or inverted T-wave in Lead 2.

22. Cretins over four months of age show a marked simple anemia.

23. The pathology of the skeletal system is due to a retardation in the appearance of the centers of ossification and a failure of new cells to appear at the epiphysis.

24. The dwarfing is due to a retardation in the growth of the bones.

[illegible]

25. Dentition is delayed, and the teeth show malposition, defective development and a great incidence of caries.

26. The skin shows myxedematous and fatty infiltrations in the subcutaneous tissues.

27. Genitals remain infantile.

28. Various degrees of mental defectiveness are present.

29. Senses of taste, smell, hearing touch and pain are dulled.

30. Onset of cretinism difficult to recognize until the second or third month.

31. Early signs of cretinism are, sparseness of hair, hoarseness, quietness, thickening of the subcutaneous tissue.

32. Complete signs of cretinism are not difficult to observe.

33. The diagnosis of cretinism rest on the clinical syndrome, B.M.R., E.K.G., glucose tolerance, theraputic test.

34. The differential diagnosis between endemic and sporadic cretinism is not clear-cut.

35. In endemic regions it is safer to call all cases of hypothyroidism in children endemic cretinism.

36. The main differential diagnosis is from mongolism.

37. The prognosis is good when treatment is started before the fourth month.

38. The prognosis varies proportionally to the amount of athyreosis.

39. The prognosis is poor in older children or adults.

40. Early diagnosis and persistent treatment at least until after puberty is necessary in cretinism.

41. Treatment of cretinism is essentially the administration of thyroid in one form or another.

42. Prophylaxis treatment is aimed at the water, hygienic conditions, and endemic goitre.

43. Older cretins tend to go into hyperthyroidism under treatment, and therefore should be treated cautiously.

44. Infants require a relatively larger amount of thyroid extract than do older children and adults.

45. General supportive treatment is essential.

46. The surgical treatment is at present unsuccessful.

47. The B.M.R. should be used to regulate the dosage and extent of treatment of infants with cretinism.

48. Signs of hyperthyroidism should be watched for in all cretins under treatment.

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