

## Medical Section.

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Dr. SAMUEL GEE, President of the Section, in the Chair.

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### Observations on Endemic Cretinism in the Chitral and Gilgit Valleys.

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(Introduced by Mr. JAMES BERRY.)

THE present study of endemic cretinism is based on an analysis of 203 cases of the disease, comprising the total cretinous population of the Gilgit and Mastuj districts. These districts extend over an area of about 500 miles of Himalayan country. The cases have been collected by a house-to-house examination of almost every goitrous village in the district, so that few examples of the disease have escaped my observation.

At the outset I should, perhaps, direct attention to the fact that the observations to be detailed and the conclusions to be drawn refer only to cretinism as prevailing among the Chitrali and Gilgiti races. It will be found necessary when applying these results elsewhere to take into consideration such factors as racial differences, habits of life, climatic conditions, &c., which are of importance in determining the prevalence of the disease [4].

For convenience of discussion I propose to divide my subject into the following six sections:—

- (I) The incidence of cretinism and its relationship to the incidence of goitre.
- (II) Goitre in the individual and its relationship to cretinism.
- (III) Goitre in the mother and its relationship to cretinism.
- (IV) Debilitating factors and their influence on the mother in producing cretinism.
- (V) Types of the disease with associated symptoms; and
- (VI) Conclusions.

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### (I) THE INCIDENCE OF CRETINISM AND ITS RELATIONSHIP TO THE INCIDENCE OF GOITRE.

As is well known, endemic goitre, cretinism, and deaf-mutism are associated conditions. In this respect Gilgit and Chitral provide no exception to the rule. There are certain facts, however, with regard to the association which are deserving of comment: (a) Where goitre is commencing in epidemic form, as for example in Nagar [4] or among troops introduced into infected areas [1], the younger members of the community are the first to suffer. Such an epidemic, however, produces no cases of cretinism. (b) In Chitral, on the other hand, where a relatively high percentage of children is goitrous, cretinism does occur, but is not common. I have been unable to trace a single instance in which goitre in the child has given rise to cretinism. Cretinism does not make its appearance in a goitrous family until the second or even the third generation. (c) Now, in Gilgit, children suffer much less from goitre than do the children of Chitral, but they suffer much more from cretinism. Goitre is said to be of comparatively recent introduction into Chitral. In Gilgit it has prevailed for centuries, and, in districts where goitre is more prevalent among the adult population, cretinism is more common and of a graver type. (d) Cretinism shows a marked tendency to occur in certain families. It is common to find several children in the same family cretinous. I have met with instances where every child in the family has been a cretin. While, therefore, cretinism is found to be intimately associated with goitre, the degree of this association is determined by the age of the endemic of goitre and by the extent to which the disease prevails among the adult population.

### (II) GOITRE IN THE INDIVIDUAL AND ITS RELATIONSHIP TO CRETINISM.

Just as endemic goitre is rarely found to produce myxœdema in the adult, so this condition is rarely a cause of cretinism in the child; indeed, I have never met with such a case. This fact is opposed to the present-day view that 75 per cent. of cretinism in goitrous localities is due to goitre in the individual [6]. Facts bearing on this point have already been dealt with in the preceding section; the following further observations remain to be recorded:—

(1) There are in the present series of 203 cases eighty-eight, or 44 per cent., in which there is an accompanying goitre. With the exception of

two cases, in which the goitre was congenital, the history shows that the thyroid enlargement was subsequent and not prior to the appearance of the cretinic symptoms. It is possible that in some instances these histories may be incorrect; the accompanying chart (fig. 1), however, should establish this general truth. The unbroken line shows the number of cretins, the interrupted line the number of goitrous cretins in the district at each year of age up to and over 20 years. From the chart it will be observed that the older a cretin is the more likely he is to have a goitre. While only 17 per cent. of all cretins under the age

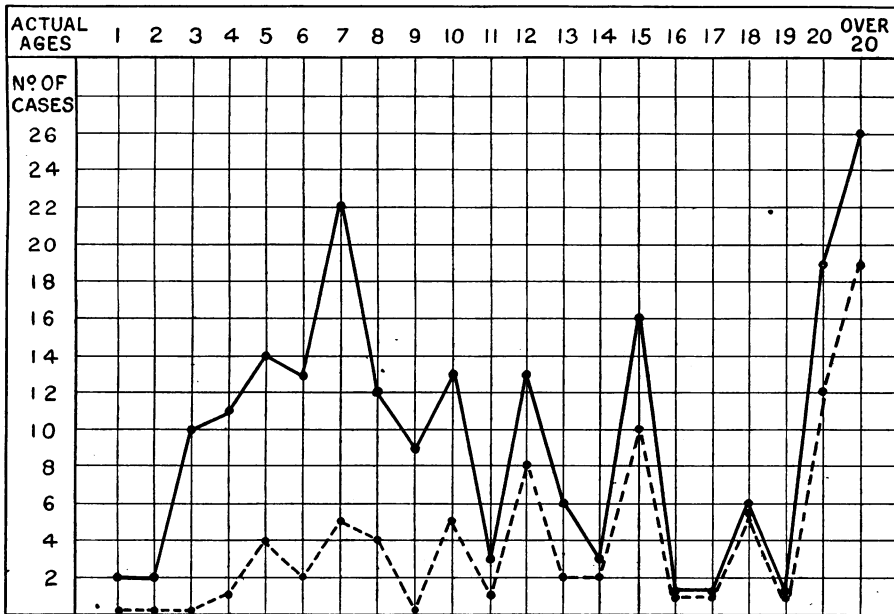


FIG. 1.

Chart showing the actual number of cretins at each year of age; also the number of goitrous cretins at these ages. The unbroken line shows the number of cretins, and the broken line that of goitrous cretins.

of 10 are goitrous, no less than 70 per cent. over that age have an accompanying goitre.

(2) I can find little support for the view that goitrous cretins are, as a rule, less swollen and their condition relatively less grave than that of those without a goitre [2]. Of the eighty-eight goitrous cretins, 20 per cent. are noted as being much swollen, while in the non-goitrous cases 25 per cent. are similarly much swollen. So far as my experience goes,

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I find that the presence or absence of a goitre is a matter of very little importance to the child's myxoedematous condition. The mental defect is, however, frequently greater, and nervous symptoms are more commonly present in these without a goitre. It is to be remembered that the so-called "goitre" is in reality made up, in the vast majority, of one or more adenomata in a functionally inactive or imperfectly active organ. The presence of such a goitre would not be beneficial to the child. There are, however, some few cases in which the development of a goitre would appear to have been beneficial. Mr. James Berry, in his work on "The Thyroid Gland" [2], has instanced a case where the general body swelling diminished as the goitre enlarged. I have met with two similar cases (Nos. 5 and 159). I have noted the presence of "fatty tumours" in 24 per cent. of my cases.

(3) Cretins are much more commonly goitrous than are healthy children.

#### (III) GOITRE IN THE MOTHER AND ITS RELATIONSHIP TO CRETINISM.

Our conception of endemic goitre has undergone some change of late years. The disease has hitherto been regarded as non-infectious. My investigations, however, have convinced me of its infectious nature. This view, although perhaps not yet sufficiently proven to demonstration, nevertheless provides the better explanation of its general phenomena and of its sequel—endemic cretinism.

There are, as is well known, certain infectious diseases of the mother, such as tuberculosis, erysipelas, acute rheumatism, malaria, and influenza, which are capable of producing pathological effects on the child's thyroid gland. It is believed that the toxins produced by the organisms of these diseases circulate in the foetus and give rise to the morbid condition. It is to these toxins that cases of sporadic cretinism, in which there is no associated goitre, are attributed [6]. Although infectious agencies have an undoubted influence in the production of endemic cretinism this action is not limited, as has been supposed, to non-goitrous cases of the disease. Of all infectious diseases which impair the unborn child's thyroid mechanism the most important is endemic goitre. It is that disease which is beyond all others most frequently associated with cretinism.

Now in almost every case of cretinism goitre is present in one or both parents. It is present in the mother in 86 per cent. of my cases, in the father in 40 per cent. The presence of a goitre was not noted in

the mother in twenty-eight cases. In twenty of these the mother herself was not seen or was dead. If these are excluded as uncertain, goitre is found to have been absent in the mother in only eight cases, or 4 per cent. While, therefore, cretinism can occur in the child of a woman free from goitre, it must be established, as a rule, that in endemic localities goitre in the mother is one of the most essential conditions for the development of cretinism in the child.

Maternal goitres are in over 80 per cent. of cases degenerated, the seat of adenomatous or of cystic change. Such an organ cannot be regarded as possessing the same potential powers of functional activity as a normal gland. The investigations of Baumann have shown that a goitre contains less thyroidin than a normal gland, thus demonstrating the functional deficiency of the goitrous organ. Despite this defect the thyroid mechanism of the majority of goitrous women is capable of meeting the additional demands which pregnancy or other accidental circumstances may make upon it. There is, however, a minority in which this is not the case, and it is this minority which constitutes the mothers of cretins.

The experiments of Halsted and Edmunds on animals have shown the effect of an impaired action of the thyroid mechanism of the mother on the offspring. They afford, I think, an explanation of the train of events which gives rise to cretinism, especially when they are considered in connexion with the infectious origin of goitre. In describing these experiments I quote from Edmunds's [3] work on the subject: "Halsted found in the puppies of a bitch from which the thyroid gland had been removed, and which had been sired by a dog that had also in part been deprived of its thyroid gland, that the thyroid lobes in the puppies were twenty times larger than those of normal puppies" (p. 35). Edmunds repeated this experiment and obtained a similar result. He found that the changes observed on microscopical examination were those of "compensatory hypertrophy," and "were presumably due to an attempt to compensate for the absence of thyroid in the mother." The function of the thyroid mechanism is to neutralize toxins produced in the ordinary course of metabolism. In the case of the partially thyroidless bitch of this experiment there were more toxins circulating in the blood than her impaired thyroid mechanism could deal with. These toxins called forth a response on the part of the puppies' glands and determined the resultant congenital goitre.

Richardson, in his work on "The Thyroid Gland," surmises that the reverse of this experiment would probably occur, and would account for

a certain percentage of the cases. He says : " Should the mother have an excess of thyroid secretion the gland in the young would not develop, and consequently the child would show cretinic symptoms after weaning. . . . The occurrence of a cretinic condition without goitre where goitre is endemic suggests that the parenchymatous increase of the maternal gland, in conjunction with the normal hypersecretion of pregnancy, prevents the development of the foetal gland." I am of opinion that it is unnecessary to assume a reverse picture to that of the experiment quoted, believing as I do that its results are applicable directly to the goitrous pregnant woman. That in such a woman there is no excess of unutilized secretion is shown by the fact that the administration of the gland extract causes a reduction in size of the hypertrophied organ in both pregnancy and goitre. It appears to me that it is not the excess of secretion, but the greater excess of demand, that is of importance. It is the failure to meet all demands which constitutes a temporary inefficiency of these glands, and places the woman in a position identical with the partially thyroidless animal of the experiment. The goitrous mothers of cretinous children very commonly exhibit in their own persons signs of thyroid insufficiency during pregnancy. Of these signs perhaps the most noticeable is that of tetany.

There is, then, a certain minority among goitrous pregnant women in which the thyroid mechanism is deficient ; these are mothers of cretins. The results of the experiment are applicable to them, but with this difference—that whereas the partially thyroidless bitch, under non-goitrous conditions, gave birth to offspring congenitally goitrous, the partially thyroidless woman, under continuous exposure to goitrous influences, gives birth to cretins.

The children of Gilgit, as I have already stated, are relatively immune to goitre. Succeeding generations have, under continuous goitrous influences, developed this degree of natural resistance to it. That children in other localities are not naturally immune to goitre, but are indeed more susceptible to it than adults, is shown by the case of the epidemic in Nagar [4]. This immunity wears itself out, and from puberty onwards the disease becomes more and more frequent, until almost half the population suffers from it during the later years of life. I regard the immunity as due to the minimal action of the toxic agent of goitre on the developing foetal organism, which gives rise in the child to considerable cumulative powers of resistance. But where, owing to insufficiency of the maternal thyroid, toxic agencies are allowed freer play, this action on the developing foetal organ is continuous and excessive, resulting in compensatory

hypertrophy, or atrophy of whole or part of the thyroid mechanism. I believe that just in so far as the mother's thyroid potentiality possesses the inherent power of response to every demand, so far may we expect her child to be born temporarily immune to goitre, with congenital goitre, or with cretinism; all of these I regard as being but stages in the same process and the evidence of the minimal, medial, or maximal action of the toxic agents on the unborn child's thyroid mechanism. The following cases may be quoted in support of the views which have been expressed; others will be found in the appendix:—



FIG. 2.

Myxœdematous mother with her cretinous child.

No. 100.—The mother is partially myxœdematous (fig. 2). She has a small goitre and suffers from tetany. These attacks are worse during pregnancy; they are more frequent during the spring months, when she may have as many as two or three during one month. There is no unconsciousness during them. She has always been myxœdematous, but believes that she is better than she used to be. She gives a very goitrous, and myxœdematous family history. She has had eight children before the present child. They were all, according to her,

“born cretins.” All were very swollen from birth, and all died before the age of 3. The child shown in the photograph is aged 2. It is remarkably swollen. This child has improved very markedly under thyroid feeding.

Nos. 190 and 191.—Family very poor. Mother has a large tumorous goitre and suffers from tetany during pregnancy; she is coarse-skinned and somewhat swollen. Her son, aged 24 (No. 190, fig. 3), is a typical nervous cretin of an extreme degree; he is a deaf-mute. Her daughter (No. 191) is a typical myxœdematous cretin, aged 18, whose hearing and speech are defective. The mother has had nine children, of whom



FIG. 3.

A “typically nervous” cretin, aged 24. The right hand is blurred in the illustration owing to tremor.

four are alive, and all show signs of cretinism, the two youngest in lesser degree than the two eldest just described. The father has a large tumorous goitre (fig. 9).

No. 82.—Mother has had three perfectly healthy children. She then developed goitre, and subsequently gave birth to the present child, who became a cretin after a convulsive fit when aged 2. This cretin is aged 20 and is very swollen.



(IV) DEBILITATING FACTORS AND THEIR INFLUENCE ON THE MOTHER  
IN PRODUCING CRETINISM, CONGENITAL OR ACQUIRED.

(1) *Mental Disease*.—The importance of mental disease in the parents of cretinous children is so slight that from an etiological point of view it may be neglected.

(2) *Alcoholism*.—Alcoholism, owing to the fact that the religion of the people prohibits its use, exerts no influence.

(3) *Syphilis and Tuberculosis*.—Syphilis and tuberculosis are rare as yet, although of late years they have become more prevalent. In only one of my cases is there a history of tuberculosis (No. 180).

(4) *Nervous Disease: Tetany*.—The only important nervous disease is tetany. In a recent study of the affection I found that of fifty-six mothers who are sufferers from tetany, thirteen, or 23 per cent., have cretinous children.

(5) *Consanguinity*.—Among the Syeds of Gilgit cretinism is much more common than among other classes of the community. The Syeds of all Mohammedan countries, as descendants of the Prophet, are permitted to marry only in their own sect. In Gilgit these Syed families are few, and it is practically impossible for one of their members to marry out of a goitrous family. As a consequence the stock is goitre-tainted and the taint is accentuated by in-breeding. There is a history of near marriage in 14 per cent. of my cases, and in some it is the only factor present in addition to goitre in the mother. In-breeding is therefore a factor of some importance.

(6) *Psychic Factors*.—Fright, worry, mental depression, and impressions received by the mother during pregnancy have great weight as determining factors. There is reliable history of one or other of these in over 40 per cent. of my cases.

The following cases are examples:—

No. 142.—A goitrous mother, haunted by spirit while pregnant with her first child. This child is a cretin and deaf-mute. Her second and third children are alive and healthy.

No. 157.—A goitrous mother lost her first two children, who were healthy, while pregnant with her third child. She (in her own words) “remained always crying and in grief for them.” Her third child was “born a cretin” and is a deaf-mute. The next three children are alive and healthy.

No. 177.—The mother is goitrous. The first two children (girls)

are alive and healthy. The third child, a son, died during the fourth pregnancy. The fourth child was "born a cretin" and is a deaf-mute. The fifth child was healthy, but was a girl. The sixth child was a deaf-mute. The cause was stated by mother to be "grief at the death of her only son."

No. 175.—The mother is goitrous. The first five children died young, the deaths of several of these occurring during the mother's seventh pregnancy. Her seventh child is a cretin and a deaf-mute. Her sixth child is alive and healthy. She attributed her evil fortune at the death of her children to a "spirit" which preyed greatly upon her mind during her seventh pregnancy. Afterwards the priests exorcized the "spirit." Her eighth child was born normal and is alive and well.

No. 22.—The mother is goitrous. After having borne two healthy sons she went to live in a house which she believed to be haunted. Her next three children are all cretins.

Nos. 85 to 90.—The mother was a goitrous woman whose husband died after she had borne to him a male child. This child fell from a roof at the age of 1 and became a typical nervous cretin (the boy to the right of the spectator, fig. 4). The woman suffers from tetany and has a small tumorous goitre. The second husband was a man of another village to whose house she took her cretinous son. She had two sons by this husband; they are both cretins and deaf-mutes, and both of an extreme grade of "nervous cretinism." There were, as is so often the case in Gilgit, living in the same house as her second husband two other married women. Of these one had already borne two daughters who are perfectly healthy. But after the arrival of the first woman and her cretinous son she gave birth to a child who is a "nervous" cretin and deaf-mute. This child is quite helpless (the boy to the left of the spectator, fig. 4). The other woman was not a mother at this time, but she afterwards had two children, a boy and a girl, both of whom are "nervous" cretins and deaf-mutes.

It will have been observed that the type of cretinism is in all cases the same. The mothers attribute the fact that they gave birth to cretinous children to "their continually seeing the first woman's cretinous boy in the house" and "to fear that their unborn child might be like him." There is no other history of difficult labour, near marriage, or illnesses during pregnancy to account for the condition of the children in the case of the last two mothers. A very exceptional fact in the case of the last mother is that she has no goitre. There is in her case no other history whatever apart from the mental impression.

A history of the baneful influence of "the powers of evil" is very common, and so much so that one is forced to acknowledge it as real. Other frequent histories are that "while in the jungle with the goats the mother was haunted by a fairy," that she "saw visions," or that she "saw the dead," forms of delusional insanity which, though regarded by the mother as being the causal or exciting factor in producing cretinism in the child, may perhaps be considered as evidence of the defective functional activity of her own thyroid gland. It is known that some cases of delusional insanity are due to this cause and that they may be



FIG. 4.

"Nervous" cretins with slight myxoedematous symptoms, swelling of face, of the wrists and ankles, and in the armpits. (Cases 85 and 86.)

relieved by thyroid feeding. On the other hand, it is possible that the psychic influences caused the functional depression.

(7) *The Influence of Illnesses in the Mother.*—As already stated, the most important factor is maternal goitre. There are, however, three other diseases which, when occurring in goitrous women, appear to favour the production of cretinism. These are malaria, rheumatism, and arthritis deformans. Others less frequently occurring are painful eye diseases and severe abscesses about the head. In 20 per cent. of

all cases there is a history of illness in the mother to which the child's cretinism may reasonably be attributed. The following will serve as illustrative cases:—

No. 169.—The mother, who is goitrous, had suffered from granular ophthalmia before her third child was born. The disease resulted in her total blindness. The first two children were healthy, the third was a cretin, and the fourth died at the age of 4, but was healthy.

No. 177.—A goitrous mother who had suffered from rheumatism while she was pregnant with her second child. This child is cretinous to a very severe degree, but is non-goitrous. The first and third children are healthy. The fourth child is dead.

No. 164.—The mother, a goitrous woman, developed severe bronchitis before her sixth child was born, from which she still suffers severely. Her first five children are normal. Her sixth is a cretin (fig. 5).

No. 161.—The mother had abscess of the jaw before her third child was born. Her first two children are healthy. Her third child is a cretin. The fourth and fifth children are dead, but they “looked cretinous” according to the mother's statement.

I believe that illnesses in the mother are of more frequent occurrence than I have noted; it was not till I had collected seventy-eight cases of the disease that a few histories of such illnesses which had been voluntarily offered drew my attention to them.

(8) *Prolonged or Difficult Labour*.—There is such a history in 14 per cent. of cases. It is very frequently given in addition to other factors, such as fright, or mental distress, or illnesses during pregnancy. Its importance is therefore difficult to estimate. It does, however, occur in certain cases where there is no other history, and in these it may be regarded as a debilitating factor acting on the child directly.

These are the main influences which operate on the unborn child to produce cretinism. They account for about 88 per cent. of the cases, and since their action is solely through the maternal environment they may be regarded as “congenital.” Cretinism, however, is not always congenital in the strictest sense of the word. It may also be “acquired.” It need not, that is to say, make its appearance at birth, but may ensue upon certain external quasi-mechanical eventualities. These may be divided into two classes: (a) nutritional, (b) accidental.

(a) The nutritional factors are: insufficient milk and ill-nourishment generally, exposure to cold, defective hygiene, and the like. Their action, however, is slow and their influence slight. They account for

2 per cent. of my cases. (b) The accidental circumstances which give rise to cretinism are three: injury, fright, or nervous shock, and disease. Many illustrations of these will be found in the appendix.

Slightly over 10 per cent. of all cases of cretinism are to be classed as "accidental." About one-half of these are goitrous, and in these also, with the exception of one case, in which the goitre is congenital, the thyroid has enlarged subsequently to the onset of the cretinous symptoms. The ages at which the disease has made its appearance in these cases vary between 6 months and 10 years. It should, however, be

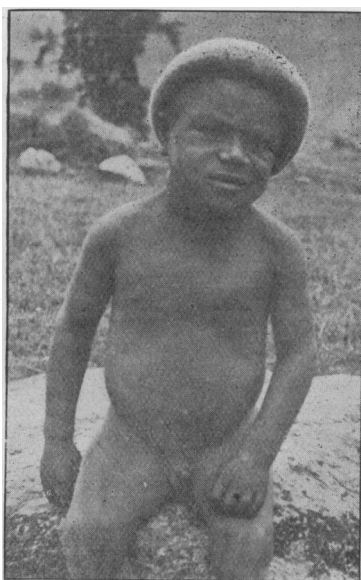


FIG. 5.

Myxœdematous cretin. Case No. 164.

pointed out that these "nutritional" and "accidental" factors are exciting rather than causal in their relation to the disease. To account for them I believe that it is necessary to presuppose a congenital instability of the thyroid mechanism together with the continued action of goitre toxins.

I recognize the possibility of a perfectly healthy child becoming a cretin after prolonged exposure to goitrous influences. I have not, however, met with such a case. These influences, of course, play a very important part in aggravating congenital cretinism, and if from any

cause whatever the child's thyroid mechanism is incapable of combating them, it is reasonable to conclude that cretinoid symptoms may manifest themselves.

*Cretinism and Sex.*—In the series of cases which came under my observation I have found a considerable preponderance of the male over the female sex. The proportion is as 5 : 2. This preponderance is still maintained among cretins who are also goitrous, but it is much less marked, the proportion being as 5 : 4. The relatively higher death-rate among female children in Gilgit is responsible in some part for the lower proportion of female cretins.

#### (V) TYPES OF THE DISEASE.

There are in this district two distinct types of the disease apart from the many divers grades of the affection which are ordinarily met with : (1) the myxœdematous type, and (2) the nervous type. Cases commonly present the clinical features of a combination of these. Deaf-mutism is an almost constant accompaniment of both types of the disease. With regard to the myxœdematous type of cretinism few remarks are necessary. It corresponds with that form of the affection met with in Europe, and it is described in any text-book of medicine. It is noticeable that in Gilgit it is found for the most part among the richer families ; such cretins are better clothed and fed, and the conditions of life under which they live correspond more closely with those of European cretins.

*Nervous Cretinism.*—One-third of all cases in the present series belong to this type of cretinism. Among these are included some of the very worst examples of the malady. Cretins of this type, in which the disability is more especially of the central nervous system, in contradistinction to those of the myxœdematous type, in whom the defect is more especially physical, are usually to be found among the poorest of the people. They are commonly quite helpless, and their bodies invariably bear the scars of burns or other injuries. Their parents frequently do not take the trouble to clothe them, and they are exposed to extremes of heat and cold greater than anything met with in England. Their diet consists only of a daily cake of unleavened bread. The general appearance of such a case is as follows (fig. 3) : The skull is elongated, the antero-posterior diameter being long in proportion to the narrow lateral diameter (fig. 10). There is, as a rule, complete deaf-mutism. There is a knock-kneed spasticity of the lower limbs, and the patient exhibits a complete or partial inability to stand upright. When supported on his feet he usually rests on his toes, and the knees may be

close together or actually crossed, or the lower extremities may remain in a position of rigid extension. There is an increased knee-jerk and there may be marked flexion of the toes on the sole. In those cases in which the cretins are capable of walking there is a peculiar stiffness of gait, and they may walk on their toes; as each foot reaches the ground there is a certain amount of "give" at the knees and ankles, which produces a sort of bobbing motion. There is sometimes flat-foot. The upper limbs assume a position of right-angled flexion; the thumb may be drawn into the palm and the fingers closed over it, whilst the wrist is flexed. Purposeless movements of the upper limbs are common. The spastic rigidity is always worse in the lower limbs. The head may be turned slowly from side to side, and in several of the worst cases I have seen, grimaces occurred. The face is characteristically cretinoid; the degree of swelling varies considerably—it may be marked or slight, and confined to the face, hands, wrists, and ankles. The abdomen is, as a rule, swollen and protuberant. There is always considerable stunting in growth, which may be extreme or relatively slight. The patient's mentality is much disordered; there appears to be a loss of sensibility in the skin; puberty is delayed and the sexual organs are ill-developed. A history of convulsive seizures has in a few instances been obtained; a coarse nystagmus and internal strabismus have been noted in some cases. All degrees of this condition are seen, from a spastic paralysis of the lower limbs to a general rigidity; in short, the condition is one of cretinous idiocy with associated cerebral diplegia. Fig. 3 affords a good illustration of this class of case. The subject is aged 24, is about  $3\frac{1}{2}$  ft. in height, is obviously myxœdematous, and presents practically every feature of the type which I have just detailed. His sister is a typical myxœdematous cretin and is very swollen.

I have sought in the course of my observations to find in the histories of these cases some etiological reason for dissociating the obvious cretinoid condition from the no less obvious spastic condition of the limbs. I have not been able to find that cretins of this type are more frequent among the class of "accidental cretins." Nor has a history of prolonged labour, of infectious diseases, of convulsions, or of any other affections of childhood afforded any grounds for the dissociation of the nervous from the cretinoid symptoms. The factors which give rise to the diplegic symptoms are ante-natal in all cases; and I believe that it is to the congenital disability of the thyroid mechanism that this condition, like the myxœdematous type, is due. Even in those cases where there is a history of possible injury at birth I believe that this

factor operates as an "accidental" circumstance acting in the way I have described in the preceding section.

In the course of this paper I have referred to the thyroid defect in cretinism as being one of the "thyroid mechanism," a defect in which the parathyroids are also included, in contradistinction to the more limited defect of the thyroid proper, which is usually considered to be the morbid anatomical factor in cretinism. There can be no doubt that such a lesion exists, but that it should extend to the parathyroids is not usually considered. These organs are, in the light of the most recent research on the subject, capable of functionally replacing the thyroid in the absence

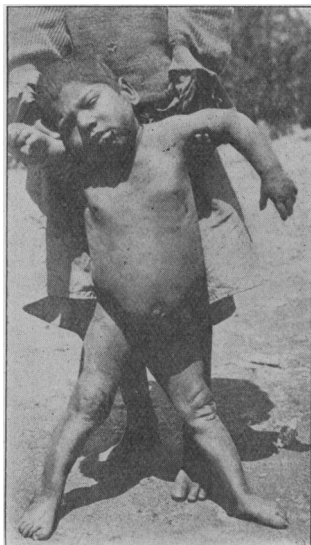


FIG. 6.

Nervous type of cretinism.

of the latter, though not completely so. [7] [8]. They are, while possessing their own functional powers, an added safeguard to the organism in the case of insufficiency of the thyroid proper, while their own insufficiency would appear, in some measure, to determine the nervous symptoms present in many cases.

The symptoms which are characteristic of "nervous" cretinism are very similar to those which occur in animals after the complete removal of the thyroid and parathyroid glands. Indeed, as the symptoms are described by Murray [5], they are practically identical—a fact which



affords some ground for the belief which I have expressed. I have, however, obtained results in three cases by means of the therapeutic test of thyroid feeding, and by detailed post-mortem examination of the glands in a fourth, which to my mind amount to actual proof that the nervous symptoms are due to a thyroid defect.

I have had an opportunity during the past year of treating three cases of nervous cretinism on the lines indicated. Without giving full details of these cases, it may be said that the administration of the fresh and dried extracts of sheep's thyroid has produced a marked improvement in the nervous symptoms. The spasm has disappeared; in one case the double interval strabismus (fig. 6), with the associated coarse nystagmus, has almost entirely disappeared. In another, a child (fig. 7) who could only rise to its feet by means of a support, and who could only take two

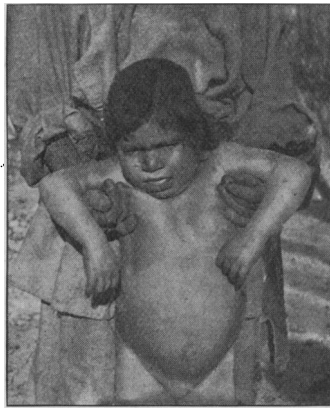


FIG. 7.

“Nervous” cretin with marked swelling.

stumbling paces before its legs gave way, after three months' treatment walked for a distance of over 30 yards without falling. This child is aged 9. It was very much swollen and, according to its mother, could not speak the simplest word. She affirms that it can now say “Ma” and “Da,” though it refused to do so before me. There is not the slightest doubt that its hearing has very much improved, and the mother has found it possible during the last month to employ it in certain little offices, such as the collecting of bits of wood. The child has grown 1 in. in height in three and a half months, while the swelling has disappeared and the skin become smooth and soft. The therapeutic test, then, has provided results in these three cases which amply justify my views as to the nature of the condition.

Since writing this paper I have succeeded in one case in overcoming the intense prejudice of the people against post-mortem examination. This case (No. 85) has been referred to in the fourth section of the present article, and is one of very great interest. The disease made its appearance at the end of the first year of life, and the factor which determined its manifestation was said to be a fall from a low roof. It will be remembered that the mother suffered from signs of thyroid insufficiency. The nervous symptoms in the case (fig. 4) were very marked and were the most striking feature of the condition. The swelling was slight and limited to the face, wrists, and ankles, with fatty pads in the axilla. There was no marked stunting of growth, and the case might readily have been considered to be one of cerebral diplegia with pronounced mental defect. The naked-eye appearances seen at the post-mortem examination of the child were a slight but uniform enlargement of the thyroid gland. It was very firm to the touch and was not nodular. Parathyroid glands could not be found in spite of the most careful search.

I have made at the Laboratories of the Royal Institute of Public Health, with Dr. H. Dold, Pathologist to the Institute, a study of the histological appearances of the thyroid gland in the case. We found that there was a great and uniform increase of the fibrous stroma of the organ (fig. 8). The glandular elements were compressed. Typical vesicles were wholly absent and such as were present were almost completely obliterated. Traces only of colloid were seen scattered here and there over the sections. The appearances were those of a struma fibrosa. We were unable to find any trace of parathyroid tissue.

Clearly, then, in this case there existed a pronounced defect not only of the thyroid but also of the parathyroid glands. The condition of the thyroid and the deficiency of colloid material furnish, when considered in relation to the results obtained by thyroid feeding in three similar cases, a very striking proof of the truth of the views which I have expressed.

I may here draw attention to the similarity between nervous cretins and cerebral diplegia, not only in symptomatology, but also in such facts as are known of their etiology. In cerebral diplegia cortical degeneration is, it is believed, due to the action of some toxic agent. In cretinism, the nervous symptoms are attributed, in my view, to toxins which, owing to a congenital insufficiency of the thyroid mechanism, are no longer restrained in their action. In these cases of cerebral diplegia, in which the etiology is obscure and in which the condition cannot reasonably be attributed to direct injury at birth, thyroid feeding may prove of benefit.

*Deaf-mutism as associated with Cretinism.*

In no less than 87 per cent. of all cases there is an associated degree of deaf-mutism. In the majority of cases it is complete; in the minority it is partial. In the nervous type it is almost always complete, less frequently so in the myxœdematous. The defect of speech may be caused in part by a swollen condition of the tongue, but it is mainly dependent on imperfect development of the higher brain centres, due, I believe, as in the case of the other nervous symptoms, to the unrestrained action of toxins. It is more frequently present in males than in females.

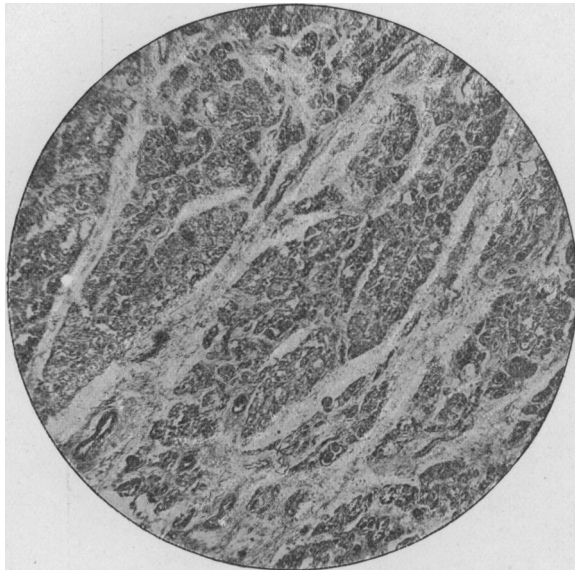


FIG. 8.

Section of thyroid gland from Case 85 (from photo. by Dr. C. E. Harris).

The following cases are of interest as showing the relationship of goitre and cretinism to deaf-mutism :—

No. 5.—The hearing and speech are said to have improved after the appearance of a goitre at the age of 12.

No. 137.—The patient could hear and speak normally before the age of 5, when he fell from a roof and became a cretin and a deaf-mute.

No. 149.—The patient could hear and speak before the age of 7, when—after a fright—he became a cretin of the nervous type and quite deaf and dumb.



FIG. 9.

Goitrous father with cretinous son.



FIG. 10.

Side view of face of Case 190.

No. 159.—The patient's hearing and speech are improving slowly since the development of a goitre at the age of 35. I have referred to the case of nervous cretinism under treatment where the hearing has undoubtedly improved and the child is said to be beginning to talk after three and a half months' thyroid feeding.

(VI) CONCLUSIONS.

(1) The degree to which cretinism is associated with goitre is determined by the age of the endemic, and varies directly with the extent to which the latter disease prevails among the adult population.

(2) Cretinism is rarely, if ever, due to the development of a goitre in the individual. The thyroid enlargement is, or may be, an effect; it is not the cause of the disease.

(3) Defective thyroid function in the mother is the essential factor in the production of cretinism.

(4) Cretinism is due to the action of toxic agents, notably that of endemic goitre, on the developing thyroid of the unborn child.

(5) The thyroid defect is congenital, but it may remain latent pending its manifestation through the impulse of some accidental circumstance.

(6) The defect in cretinism is one of the whole thyroid mechanism, of the parathyroids as well as of the thyroid gland. The diversity of symptoms is due to the extent to which the defect bears on the whole or part of that mechanism.

I should, perhaps, once more emphasize the fact that the conclusions have been drawn from data afforded solely by the Gilgit and Chitral districts.

I desire to express my indebtedness to my assistant, Sirdar Sahib Kehar Singh, whose untiring help and whose knowledge of the Chitrali and Gilgiti languages rendered possible the accumulation of material on which this paper is based.

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APPENDIX OF ILLUSTRATIVE CASES—TABLES I AND II.

Cretinism in Chitral and Gilgit.

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by the mother during pregnancy	Ordinal number of child in family	Ordinal numbers of healthy children in family	Ordinal numbers of cretinous children in family	Remarks
5	F.	15	Yes	12	3rd	Yes	Infancy	Mother	No	No	Anxiety to have son, and seeing other cretinous daughter	4th	1st, 2nd	3rd, 4th	Reported to be able to hear and speak a little since goitre developed
6	F.	20	No	—	1st	Yes	Infancy	Mother	No	No	Anxiety to have a son	3rd	1st, 2nd	3rd, 4th	Has appearance of child aged 10; "nervous cretin"; head very narrow laterally
23	M.	22	No	—	2nd	No	Infancy	Mother	Yes	No	Went to live in haunted house, which preyed greatly on her mind	3rd	1st, 2nd	3rd, 4th, 5th	First two sons healthy; then changed house; next three sons cretins; this case is very swollen and myxedematous
25	M.	18	Yes	7	3rd	No	10	Mother	Yes	No	Ditto, same mother	4th	1st, 2nd	3rd, 4th, 5th	Very swollen and myxedematous; cretinism developed after an attack of smallpox when aged 10
24	M.	15	Yes	10	1st	Yes	Infancy	Mother	Yes	No	Ditto, same mother	5th	1st, 2nd	3rd, 4th, 5th	Very swollen; fatty folds under chin; of the two healthy sons of this mother one had goitre, and his son, or the mother's grand-son, is a cretin (No. 26)
26	M.	3	No	—	1st	Yes	Infancy	Father; are Syeds; mother not seen	Yes	No	Ill with "bad eyes" for eight months before birth of child; lived with cretinous brothers-in-law	—	—	—	Very swollen; this boy's two brothers are healthy

27	F.	7	No	—	2nd	No	Infancy	Father; are Syeds; mother not seen	Yes	No	history available	No	—	—	—	“Nervous cretin”; strutting gait, falls easily, fatty pads under chin, very swollen and myxodematous; has two healthy brothers
33	M.	24	Yes	(?)	1st	Yes	Infancy	Both	No	No	No	No	—	—	—	Helpless, cannot stand, very swollen, fatty pads under chin; at birth of child mother had no milk and child was very badly fed artificially; his younger sister is a cretin
35	F.	13	No	—	2nd	Yes	Infancy	Mother	No	Yes	Constant quarreling with husband, who turned her out of house before birth of child	No	—	—	—	Slight swelling, fatty pads under chin, nervous symptoms
45	M.	3	No	—	3rd	Yes	Infancy	Both	No	Yes, 4 days pains	No	No	—	—	—	Can crawl only
47	M.	45	Yes	(?)	1st	Yes	Infancy	(?)	No	—	Just before birth husband was taken prisoner by Ghor Rhaman	No	—	—	—	Cannot stand or walk, very swollen pads in axilla; a notorious case owing to supposed connexion of case with invasion of Gilgit by Ghor Rhaman
48	F.	15	Yes	9	2nd	Yes	Infancy	Mother	Yes	No	Jealousy of another wife	No	—	—	—	Nervous type, cannot walk
50	M.	25	No	—	2nd	No	Infancy	Mother	No	Yes; 4 days pains	Believed herself haunted during pregnancy; Paradise had come to her” (lit. translation)	No	—	—	—	Very swollen and small for age
55	F.	7	Yes	6	1st	Yes	Infancy	Mother	No	No	No	No	—	—	—	Very swollen, chin pads, cannot walk, spastic condition of limbs
57	M.	8	Yes (congenital)	—	3rd	Yes	Infancy	Neither (?) ; mother not seen	No	No	No	No	—	—	—	Father married child's mother in old age; all children by previous wife healthy
63	F.	16	Yes	14	1st	Yes	Infancy	Neither (?) ; mother not seen (dead)	No	No (?)	No (?)	No (?)	—	—	—	Very swollen, pads chin and clavicle, cannot walk; nervous type (mixed)

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by the mother during pregnancy	Ordinal number of child in family	Ordinal numbers of healthy children in family	Ordinal numbers of cretinous children in family	Remarks
69	F.	30	No	—	1st	Yes	Infancy	Both	No	No	Went to live in house believed to be haunted, where this child was born	4th	1st, 2nd, 3rd	4th	Helpless, cannot walk, much swollen, pads chin and clavicle; her father was "daft"
180	F.	12	Yes	10	1st	Yes	Infancy	Father; mother dead	No	No	Phthisis, from which she died	3rd	None	1st, 2nd, 3rd; last two (dead)	Very swollen, pure myxœdematous case; mother married twice; this is family by second husband; always suffered from phthisis; had three children by first husband; reported all cretins, but dead
70	M.	18	Yes	16	2nd	Dumb; hearing defective	Infancy	Neither (?) ; mother not seen	Yes	No	Mother's first husband died, whom she loved; forced by Mohammedan law to marry his brother, whom she hated; child is son of second husband	1st by this husband	—	—	This law is a very real trouble in many cases, where the woman is not willing; in this case, also, the woman was worried about the disposal of her first husband's property; children by first husband healthy
79	F.	8	Yes	6	3rd	Defective	Infancy	Both	No	No	Possessed of a spirit	—	—	—	Suffers from epilepsy
80	M.	7	Yes	3	2nd	Yes	Infancy	Both	No	No	No	—	—	—	Is half-brother to No. 79, same father; cannot walk, pads clavicle and chin
85	M.	15	No	—	1st	Yes	1 year	Mother	No	No	No	1st	No others by this husband	—	Mother gets "fits" resembling tetany; patient nervous cretin, cannot stand; spastic condition of limbs (fig. 3); cretinism developed after fall from roof when aged 1; is first child of family referred to in text



86	M. 9 (Half-brother to 85)	No	—	2nd	Yes	Infancy	Both	No	No	“Constantly seeing her first son,” No. 85, and “fear husband that her child will be like him,”	1st by this husband	None	1st, 2nd	Nervous type, waddles, small for age, granular eyelids; mother subject to “fits.”
87	M. 5 (Brother to 86)	No	—	3rd	Yes	Infancy	Both	No	No	As above	2nd	None	1st, 2nd	Nervous type, waddles; as above
88	M. 11	Yes (small tumour)	10	1st	Yes	Infancy	Other not seen; father no	No	No	Constantly seeing No. 86; rest as above	3rd	1st, 2nd	3rd	Helpless, very bad case, so bad parents do not even clothe him; lies where placed; very extreme nervous type, granular lids (No. 2 in group, fig. 4); was born after No. 85 came to reside in house; mother had two healthy girls before this
89	F. 11	No	—	2nd	Yes	Infancy	Neither; mother small goitre now, but not during pregnancy (?)	No	No	As above	1st	None	1st, 2nd	Waddles; nervous type; father is brother to father of Nos. 86, 87, 88
90	M. 8	No	—	1st	Yes	Infancy	Neither	No	No	As above	2nd	None	1st, 2nd	Helpless, nervous type, as above; mother gives, as an added reason, insufficient milk in this case
94	F. 5	No	—	2nd	Yes	Infancy	Both	No	Yes	Mother seriously ill during pregnancy (rheumatism)	—	—	—	Waddles; mother had no milk after birth of the child, who was consequently insufficiently nourished
99	M. 5	No	—	2nd	Yes	Infancy	Mother	No	Yes	Very ill during pregnancy (fever, type unknown)	—	—	—	Nervous type, cannot walk, pads under chin
100	M. 2	No	—	1st	Deaf; too young to say if dumb	Infancy	Both	No	No	Very anxious to have a healthy child like this one,	9th (previous children like this one, all died when aged 3)	None	9th children	Enormously swollen (see fig. 2); mother myxedematous, subject to “fits,” small tumour in isthmus; father very large goitre

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by the mother during pregnancy	Ordinal number of child in family	Ordinal numbers of healthy children in family	Ordinal numbers of cretinous children in family	Remarks
108	F.	20	Yes	6	2nd	Yes	Infancy	Mother	No	No	Illness during pregnancy (nature unknown)	3rd	1st, 2nd (males)	3rd	Waddles; able to work; married, no children
124	M.	24	Yes	16	1st	Yes	Infancy	Mother	No	No	Was frightened by seeing a dead body while pregnant	—	—	—	Can waddle
<b>The following cases are from Chitral:—</b>															
136	M.	17	Yes	12	2nd	Yes	Infancy	Both	No	Yes	Death of three children and worry that unborn child would die also	6th (last child)	1st, 2nd, 3rd, 4th, 5th (died after birth)	6th	Mother was ill for a year after birth; child fed artificially; cannot walk, waddles a little
142	F.	5	No	—	2nd	Yes	Infancy	Mother	No	No	Haunted by spirit during pregnancy	1st	2nd, 3rd	1st only	—
143	M.	7	No	—	1st	Yes	Infancy	Both	No	3 days pains	Jealousy of second wife	1st and only child	—	—	Nervous type
147	M.	7	Yes	6	2nd	Yes	Infancy	Mother	No	No	Grief at loss of first two children	3rd	1st, 4th, 5th	2nd (died when aged 7), 3rd	Mother "gets possessed of a spirit" and has "fits" and becomes unconscious
148	F.	12	Yes	10	2nd	Yes	Infancy	Both	No	Yes	Grief at death of her brother and his children, to whom much attached	3rd	1st, 2nd, 4th	3rd only	Strutting gait
156	M.	25	Yes	20	2nd	Yes	Infancy	Mother	No	Yes	Husband ill-treated her	1st	2nd, 3rd, 5th	1st, 4th, 6th	Can waddle
157	F.	40	Yes	30	1st	Yes	Infancy	Mother	No	Yes	Grief at loss of two first children in infancy; had "fever" for two months during pregnancy	3rd	4th, 5th, 6th	3rd only	Mother says "she mourned greatly for the loss of her first two children, always remaining crying and in grief; she went to the mullahs (priests), who gave her some charms, after which she had three healthy girls"

161	M.	40	No	—	2nd	De- fective	Infancy	Mother	No	No	Had bad abscess of jaw, could not eat	3rd	1st, 2nd	3rd 4th (?) 5th (?)	Mother believes her fourth and fifth children were also cretins, but these died in infancy and not seen
162	M.	8	No	—	1st	Yes	Infancy	Mother	No	Yes	Her fourth child died during this pregnancy; grief; had anaemia and swelling all over body, which gradually got well after birth of the child	5th	1st, 2nd, 3rd, 4th	5th only	Helpless; typical nervous case; mother had insufficient milk for this child
164	M.	14	No	—	2nd	Yes, im- proving slowly	Infancy	Both	No	No	Had bronchitis, which became chronic during pregnancy; still very bad	6th	1st, 2nd, 3rd, 4th, 5th (3rd, 4th dead)	6th only	Very small, much swollen; mother had insufficient milk
165	M.	12	No	—	1st	Yes	Infancy	Mother only; father incom- plete myx- cedema	No	No	Rheumatism, which got well after delivery	2nd	1st (dead), 5th, 6th	2nd, 3rd	Very much swollen; pads chin, clavicle and axilla; cannot walk, helpless; nervous symptoms marked
166	M. (Brother to 165)	4	No	—	2nd	Yes	Infancy	Mother	No	No	Rheumatism re- turned during this pregnancy	3rd	1st (dead), 5th, 6th	2nd, 3rd	Nervous type; cannot walk; pads chin and axilla; the father in these two cases is slightly myx- cedematous
167	M.	4	No	—	1st	Yes	Infancy	Both	Yes	Yes	No	2nd	1st	2nd only	Nervous type, helpless
169	M.	13	Yes	10	1st	Yes	Infancy	Father; mother not seen	No	No	Ophthalmia; re- sultant total blindness	3rd	1st, 2nd (dead), 4th (dead)	3rd only	Very small, very much swollen; pads in clavicle, nervous type, flat-foot, granular lids; father partial deaf-mute and cannot walk properly
173	F.	9	No	—	1st	Yes	Infancy	Mother; father partial myx- cedema, no goitre	Yes	No	Husband ill-looking and unfaithful; grief at having to marry him	1st	None	1st, 2nd, 3rd	Slight nervous symptoms, cannot walk, flat-foot; mother hates father, who is myxcedematous; he is her first husband's brother; was forced to marry him by law, priests would not let her evade it; second and third children much swollen and myxcedematous

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by the mother during pregnancy	Ordinal number of child in family	Ordinal numbers of healthy children in family	Ordinal numbers of cretinous children in family	Remarks
201	F.	12	No	—	1st	Yes	Infancy	Mother; father partial myx- cedema	No	No	Jealous of second wife, whom husband married when pregnant with this child	2nd	1st, 3rd (dead)	2nd only	Very swollen and myxedematous
182	F.	20	No	—	2nd	Defec- tive	Infancy	Mother; father myxedema	No	No	No	2nd	1st, 3rd, 6th boys all healthy	2nd, 5th, 7th girls all cretins	Father very small, swollen, incomplete myxedema; all the boys are healthy and all the girls cretins
196	F.	13	No	—	1st	Yes	Birth	Mother; father myxedema	No	No	Jealousy; husband married second wife at time of pregnancy	2nd	1st, 3rd (dead)	2nd only	Swollen and myxedematous (very); pads chin, clavicle and axilla; father stunted and swollen
190	M.	24	No	—	1st	Yes	Birth	Father and mother	Yes	Yes	No, but suffers from "fits," probably "tetany."	1st	5 dead	2nd, 1st, 8th, 9th	Fig. 3. Much swollen, typical nervous case, very small; mother slight myxedema, says she used to be more swollen than she is now; second child very swollen, eighth and ninth less so
159	M.	45	Yes	35	3rd	Defec- tive	Birth	Mother	No	No	Bad "fever" during pregnancy	1st	2nd, 3rd	1st only	Very small, medium swelling, used to be much worse but getting less; hearing and speech also improved of late years since appearance of goitre

The degrees of cretinism noted in these appendices of cases are purely arbitrary; they have been adopted for convenience of tabulation. First degree, most grave; second, less so; and so on.

## Accidental Cretinism.

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Circumstances which determined the development of the cretinism	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by mother during pregnancy of cretinous child	Facts concerning other children in the family	Remarks
3	M.	20	Yes	17	1st	Yes	10	Not known	Mother	No	No	Mental distress; death of children	Brother also cretin and deaf-mute	The history in these two cases is very incomplete; were first cases met with at very early stage of inquiry, when points of importance were not fully appreciated
4	F.	6	No	—	2nd	Yes	2	Not known	Father; mother not seen	Yes	No	No	—	
8	F.	8	No	—	2nd	Yes	1	Fall from roof	Neither; mother not seen	No	No	No	—	
16	F.	15	Yes	12	1st	Yes	3	Fall from roof	Both	Yes	No	No	—	
25	M.	18	Yes	7	3rd	No	10	Smallpox	Mother	Yes	No	House haunted	Sister also cretin, one brother healthy	
28	M.	20	No	—	2nd	No	10	Fall from tree; injuries to head and spine; unconscious for one month	Father; mother not seen	No	No	No	Two first sons normal; then came to live in haunted house, next three sons cretins; this is fourth	Swelling marked, myxœdematous type
41	M.	20	Yes	10	2nd	Yes	10	Fall from tree	Mother	No	No	No	—	Considerable swelling and nervous symptoms; Syed family, consanguinity very marked
49	M.	22	No	—	2nd	Yes	1	Fall from girl's arms who was carrying him	Mother	No	No	No	—	Swelling marked, myxœdematous

Nervous symptoms marked, with myxœdema, hearing and speech defective since accident; symptoms might all be due to grave accident, apart from thyroid gland, but for myxœdema. Very swollen, no nervous symptoms, can walk; pads under chin

Swollen, clavicular pads, cannot walk

No.	Sex	Age	Goitre in patient	Age at which goitre developed	Degree of cretinism	Associated deaf-mutism	Age at which cretinism developed	Circumstances which determined the development of the cretinism	Goitre in parents	Consanguinity	Protracted labour	Fright, illnesses, or impressions received by mother during pregnancy of cretinous child	Facts concerning other children in the family	Remarks
64	M.	11	No	—	2nd	Yes	1	Abscess in head	Both	No	No	No	—	Child born with marked "bulging of brain" (literal translation); got gradually worse after abscess in head, swelling slight, can walk in head, swelling slight, can walk small for age, idiot; swelling slight
65	M.	15	No	—	3rd	Yes	3	"Internal trouble for three years, for which he remained constantly crying"	Mother	No	No	No	—	Cause of illness unknown; very small for age, idiot; swelling slight
75	M.	7	No	—	2nd	Yes	6 mos.	Fall; how not specified	Father; mother not seen	No	No	Possessed of spirit	—	Granular eyelids
82	M.	20	Yes	7	1st	Defective	2	Convulsions	Mother	No	No	No	Three first children healthy; this is fourth	Very swollen, pads, waddles; is uncle to three cretins; swelling said to be less after goitre appeared; hearing and speech worse; mother developed goitre when aged 30; before this she had three children, all healthy; afterwards this child was born
85	See Appendix I													
112	M.	25	No	—	Dwarf	Yes	3	Fall from roof	Both	—	—	Mother had attack of rheumatism; afterwards no milk	—	Child insufficiently nourished, typical cretinoid appearance
117	F.	9	No	—	2nd	Yes	1	Fall from roof	Mother	No	No	Fright, causing unconsciousness (nature not specified)	—	Can waddle only; swelling medium
137	M.	35	Yes	25	2nd	Yes	5	Fall from roof	Mother	No	—	—	Second child; first and third healthy, fourth a cretin	This child is believed by father and relatives to have been cretin from birth, but since fall from roof has become utterly helpless; hearing and speech also gone since then; upper part of body much swollen

146 M.	3	No	--	1st	Yes	1	Child at first looked well, but one year after birth both mother and child went to jungle with goats; "frightened by fairies"; mother brought back unconscious and remained so for three days, afterwards hysterical, after which child rapidly became a cretin	Both	No	No	First six children died in infancy	Tenth child; seventh, eighth, and ninth healthy	Very marked case; nervous; also much swollen; cannot stand
149 M.	30	Yes	20	2nd	Yes	7	Fright while playing in graveyard; was carried home unconscious and feverish; he remained in this state for over two months	Mother	No	No	No	Elder brother is healthy	Is uncle to two cretins; until aged 7 hearing and speech normal; swelling very marked, especially upper part of body, limbs paralysed, nervous type
160 M.	30	Yes	24	3rd	Defective	10	Went to jungle with mother, got frightened there, brought home unconscious	Both	No	—	—	Has one younger brother healthy	Hearing and speech normal before aged 10
163 F.	10	Yes	9	2nd	No	5	Smallpox, when she lost both eyes	Mother	No	No	Rheumatism and grief at death of child, her first-born	This is the second child; first, third and fourth died in infancy; fifth healthy; sixth, aged 27, looks normal	Was intelligent, bright child till after attack of smallpox; is now quite helpless; nervous type
198 M.	10	Yes (congenital)	—	2nd	Yes	1	Child was "haunted in jungle by spirit"; cried out; got fever afterwards and was long ill	Father only	No	Yes	Severe eye trouble, confined to house; mullabs had told her all her children would be cretins, and the charms they gave her were useless	First died, second cretin, third normal, fourth cretin, fifth cretin	Can waddle; type mixed nervous and myxoedematous

The degrees of cretinism noted in these appendices of cases are purely arbitrary; they have been adopted for convenience of tabulation.  
 First degree most grave; second, less so; and so on.

## DISCUSSION.

The PRESIDENT (Dr. Gee) remarked that the paper was a most interesting one, and although it related to India it referred to diseases which were not uncommon in England.

Sir VICTOR HORSLEY said that in response to the President's invitation he could only express his high indebtedness to the author of the paper, and would simply allude to the question of treatment. He understood from Captain McCarrison that operations were not looked on with favour in the Gilgit Valley. That was most unfortunate, because with such an enormous mass of material which he had at his disposal it ought to have been possible to have settled the question of the success or non-success of the grafting of normal thyroid in such cases. The small amount of grafting which he (Sir Victor) had done in this country had been entirely in relation to adults; he had not grafted the sporadic cretin, but treated it in the old way with dried tabloids. The rapid effects produced by grafting a piece of normal human thyroid was very striking, so much so that he thought all the sporadic cases, as soon as the disease was diagnosed, should receive a graft of normal human thyroid. The question naturally arose how such grafts could be obtained, because, although it was an extremely trifling operation to remove a portion of normal thyroid from a healthy person, still, people had a great objection to being operated upon. He suggested that the procedure he had adopted was quite good, and better than the procedure originally introduced by Bircher a long time ago, namely, grafting portions of goitres. That procedure had been carried out by Christiani to a considerable extent. He suggested that in a simple case of adenoma, when the adenoma was shelled out, a portion of the neighbouring gland could be removed, as was well known, without risk; and that could be used as a graft. He had done that with very marked success. Unfortunately, the subject of grafting, although it was long ago drawn attention to by von Eiselsberg, had never been followed out in this country, possibly because the effect of the dried gland had also been so striking. But he was sure that if anyone had a marked case of sporadic cretinism under his care he ought to get it grafted as soon as possible. Unfortunately, the question could not be answered from the experience in the Gilgit Valley, owing to the objection on the part of the natives to be operated upon. The Section was, however, under no less a debt of gratitude to the author for his paper. He did not know whether there was sufficient material in this country to compare with some of the author's conclusions, such as the relative frequency of deaf-mutism, which certainly did not accord with his own experience. He did not believe that deaf-mutism in this country bore any direct relation in degree to cretinism. The point, however, was a new one to him. With regard to the other matters, he did not know if the correlative influences of shock could have the importance which the author mentioned. But perhaps great importance was not attributed to it; the author might only have adduced the fact that any depressing agency might assist the condition.



Mr. JAMES BERRY desired to pay a tribute of respect and appreciation to the author for his valuable paper. Perhaps no one knew better than he did the amount of hard work which Captain McCarrison had been doing in connexion with the subject during the last three or four years in India. In the main, his conclusions concerning goitre in India bore out those which had been arrived at by many others, in Switzerland and other European centres notable for goitre. But the great advantage of the work was that the investigations had been carried out by one man, and for that reason he thought them in some respects more valuable than those of, for instance, the Sardinian Commission, which consisted largely of reports received from a number of people working on different lines. He thought the author had made a new point in regard to the type of cretinism which he called nervous. He was not sure whether, from the description, Captain McCarrison would include under that term most of the cretins met with in, for instance, a Swiss valley, in whom there was, as a rule, very little swelling, or whether he would include cases of what most people would call simply idiots, quite apart from cretinism. It was well known that in all goitrous districts idiots were by no means uncommon who were not supposed to be cretins, and the proportion of idiots to cretins in such places was often as high as 1 in 3. The ordinary cretin seen in European centres of goitre were by no means myxœdematous in the strict sense of the word. One rarely saw a cretin with much general subcutaneous swelling, such as was common in a myxœdema patient in a London hospital. He would like to know whether the author would include among the nervous cases those without swelling, but who had all the other ordinary features of cretinism, such as pallor, mis-shapen head, swollen ends of bones, and swollen abdomen. The author had mentioned the fatty tumours, and he supposed he meant the diffused tumours met with in cretinism, which were not lipomata. He regretted to hear the author, in speaking about parathyroids, apparently endorsed what he (Mr. Berry) regarded as a fallacy, namely, that there were two glands in the neck with different functions, the thyroid and the parathyroid. He did not believe that the functions of the parathyroid differed from those of the thyroid itself. Everyone was familiar with small masses of thyroid tissue, often undeveloped, which lay close to the main gland, and he thought that in the last few years a large amount of what he regarded as false teaching, especially with respect to exophthalmic goitre, had grown up around the idea of there being two bodies with different functions. He regretted that the author apparently lent support to that view. He had hoped that Dr. Forsyth's elaborate paper, published a few months ago, had dispelled that superstition.

Dr. GOSSAGE said there were several entirely new ideas in the paper for which members were indebted to Captain McCarrison. He (Dr. Gossage) did not propose to deal with the nervous type of cretinism, which was quite a new clinical type and of great interest, but with certain other points. The author did not agree with St. Lager's opinion that two healthy parents going into a goitrous district were liable to have a cretinous child, but said that in order to get cretinism it was necessary for two or three generations to have lived in the

district and to have suffered from goitre. Cretinism might then appear in the third or fourth generation. That was a very important point and needed fresh investigation. Anyone who had read St. Lager's book would feel inclined to be doubtful about many of the cretins which that authority accepted; he was certainly prone to exaggerate the occurrence of cretinism. It had to be remembered that cretinism and goitre were not necessarily associated, for it seemed to be proved that it was possible to find endemic goitre in a district without cretinism. Another fresh conception was that of thyroid deficiency, and the author advanced an original theory with regard to the production of cretinism on the basis of this thyroid deficiency: that thyroid deficiency in the mother allowed the circulation of toxins in her blood, and then through the placenta in the blood of the foetus, thus leading to the maldevelopment of the child's thyroid and so to cretinism. That theory of Captain McCarrison was very ingenious, but it did not seem to be quite supported by the facts. There was Edmunds's experiment in which he removed the thyroid of a bitch, and instead of that leading to a poor thyroid in her puppy, the puppy had an enormously hypertrophied thyroid. He (Dr. Gossage) thought it was possible to explain the facts brought forward by the author on another hypothesis, which had been advanced several times before, namely, that cretinism was an inherited condition, or rather that thyroid deficiency was an inherited condition. There was the old view brought forward by the brothers Wenzel that cretins could be divided into three classes: (1) what were usually called cretins, idiots incapable of reproduction; (2) semicretins, who, after reaching adult life, become capable of reproduction; (3) cretinous people who only showed certain slight signs of cretinism. He thought the author's cases of thyroid deficiency came into the third of those classes, but the class was more extensive than was usually supposed. Cretins almost invariably had a mother who showed some signs of thyroid deficiency. The author had pointed out that the condition was mainly derived from the mother, who usually had a goitre. But males were more frequently cretins than females, and in the male the condition was the more severe. The severer conditions appeared at birth and the less severe later in life; and the less severe conditions were particularly prone to be associated with goitre. Therefore one would expect that, as the woman showed it less severely than the man, a woman with thyroid deficiency would be particularly prone to have goitre. Assuming it to be an hereditary condition, it would be very much on the lines of inheritance shown by hæmophilia, in which the male was much more severely affected than the female, females often escaping; and when the female was affected it was more towards puberty or still later in life. In cretinism, as in hæmophilia, a large majority of males affected were incapable of reproduction, and so both conditions would be mainly transmitted through females. Assuming the condition was inherited, one came to the question of what were the chief features of the inheritance. First, it was mainly transmitted through the females, but, judging from the paper, it was sometimes transmitted through the male, as some of the fathers were myxœdematous. Again, the condition was not passed on to all the children, but only to some, probably to half the children. If it were assumed that thyroid deficiency was passed on by inheritance, and passed

only to half the children, it was found to show itself in a severe form only in a certain proportion of the affected. It appeared that in a number of families sixty-five children were "normal" and forty-eight were marked cretins. He would have expected a smaller proportion of cretins, but he thought the explanation was that the author had naturally chosen for illustration those families which had the larger number of cretins in them. Included amongst the normal were all the slighter cases of thyroid deficiency. Assuming these points to be correct (and more research was wanted), they suggested that the inheritance was on Mendelian lines. If so, the majority of the affected people, however slightly or severely affected, would not be what was termed "pure." The condition would be dominant to the normal condition; *i.e.*, when present it would show itself more or less. In a small community one would expect a considerable amount of intermarriage among relatives, and so intermarriage amongst persons who were both carrying the factor of thyroid deficiency. Such intermarriage would give a certain proportion of people "pure" with regard to that particular deficiency, all of whose children should be affected. In the paper there were a fair number of families in which every child was affected with cretinism. That was very suggestive, especially when one considered that the vast majority of the children in the district were normal, not cretins. The paper was extremely suggestive as to the way in which cretinism arose in a goitrous district. Cretinism would probably be first introduced from the outside by intermarriage with a stranger from a cretinous district. Whether the factor of thyroid deficiency existed concealed amongst the general population was another question, and one which it would be difficult to solve. One point was peculiar with regard to this inherited condition, if it was inherited, namely, that it required, in order to properly show itself, that the parents should be living in a goitrous district, and that the child should be born in such a district.

Dr. DAVID FORSYTH said that one of the most interesting points raised by the paper they had just heard was the influence of a goitrous mother on her children *in utero*, some of whom might be cretinous but others were healthy. The question had been referred to by Dr. Gossage, and it would be instructive to hear something further from the reader on that point. The experiments of Mr. Edmunds in this country and of Professor Halsted in America, who removed the thyroid from pregnant animals, had shown that thyroid secretion passed between the foetal and the maternal circulations. Neither mother nor child could monopolize the whole supply. If, therefore, cretinism was the result of a deficient secretion of maternal colloid we would expect that the goitrous mother would herself show signs of thyroid insufficiency during her pregnancy. Since the close connexion between goitre and cretinism had become more generally recognized, the pathology of cretinism, and therefore of myxœdema, had been brought into the domain of antenatal pathology and fresh light might be expected from an examination of the embryos and stillborn foetuses produced by goitrous mothers. He asked whether the author had had opportunities of ascertaining the number of stillborn children among goitrous women, and whether he had examined the thyroid glands in young foetuses. In the case which the author examined

microscopically no parathyroid gland was present. Had Captain McCarrison found any accessory thyroid glands, and, if so, did they show any microscopical changes? What was the condition of the brain and of the pituitary gland?

Mr. EDMUNDS said one point which had been brought out was that the cretinism came on in many of the children when they were 6 months old, which would be about the time when they were weaned. If the blood of the mother contained thyroid secretion, and the latter passed through the mammary gland, the child when weaned would lose that supply; therefore it was desirable that these children should be fed with cow's milk for a long time.

CAPTAIN MCCARRISON, in reply, said he thought shock had a very marked influence on the thyroid gland. He had known a strong, healthy young man develop a goitre purely from fright—there was no other reason. Mr. Rushton Parker had sent him a reprint of his article entitled "A Goitrous Cretin under Thyroid Extract," which appeared in the *British Medical Journal* of February 8, 1896. That illustrated certain points brought out in the present paper. The patient was born in November, 1877, the mother had goitre in 1870, and a neighbouring family presented three instances of the same complaint. The patient's mother, when three months pregnant with her, experienced a great shock from the wounding in the neck of one of her older girls by the accidental firing of a gun. There was no history of consanguinity, of disease in the mother, of prolonged labour, or of any of the other factors which had a determining influence on the production of the disease, and there were eighty cases in the present paper with a similar history. In this case also a goitre had appeared at the age of 13 years, or subsequently to the appearance of the cretinic symptoms. In answer to Mr. Berry, idiots were not included—they were always found largely in goitrous localities. But he included those who, with other symptoms of cretinism, might show practically no signs of myxœdema. Dr. Gossage had considered the subject from the point of view of heredity. In the series there were some instances of myxœdema or permanent thyroid defect in one or other of the parents, and in them hereditary transmission of the defect was possible, but the majority were cases in which the thyroid deficiency in the mother had originated during pregnancy, and in which it was only a temporary defect during that state. He did not think the question of heredity arose in those cases, but more detailed pedigrees were necessary. He had had no opportunities of ascertaining the number of stillborn children, and owing to the objection to operative interference and post-mortem examinations, he had not been able to dissect any cases; he was not allowed to open the skull in the case from which the section of the thyroid gland was shown. It had been objected that his application of Halsted's experiment was incorrect, that so far from the puppies of the thyroidless bitch being born with a congenitally defective thyroid they were born with "compensatory hypertrophy." He was of opinion that such hypertrophy was a step in the direction of incompetency, in much the same way as the compensatory hypertrophy of the heart was a forerunner of its incompetency. The hypertrophy caused by excessive functional activity was followed in time by atrophy.