GARGOYLISM (HURLER'S DISEASE).

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HURLER'S disease is a condition characterized essentially by mental defect, chondro-osteodystrophy, hepatosplenomegaly and corneal opacities. The complex was first noted in 1900, by John Thomson of Edinburgh who, recognizing that he was dealing with a new disease, named it after his first patient "Johnny McL—'s Disease." Subsequent descriptions were those of Hunter (1917) and Gertrud Hurler (1919).

The variety of synonyms makes difficult an estimation of the number of cases recorded, and although the disease is uncommon, by 1936 Ellis *et al.* were able to collect ten cases in the literature and add seven more personally observed.

In 1933 the era of eponymous names ended when Binswanger and Ullrich (1933) introduced the term " dysostosis multiplex " into the German literature. In this country Ellis, Sheldon and Capon (1936), because of the grotesque facies and enlarged head, suggested the colloquial description " Gargoylism," while in the United States Washington (1940) favoured " Lipochondystrophy."

Numerous other descriptions followed, so that twelve years later Strauss (1948) was able to estimate the number of recorded cases at 150, a figure with which Lindsay *et al.* (1948) agree. Since that time about a further fifty cases have been added, but the diagnosis in some of these is doubtful. It is likely that as the condition is not well recognized such patients are not infrequently misdiagnosed, while others, though diagnosed, are not recorded.

Recent reviews of the literature are those of Ellis *et al.* (1936), Henderson (1940), Lindsay *et al.* (1948), Strauss (1948), and excellent text-book pictures are those of Washington (1942), Van Creveld (1951) and Ellis (1951).

Gargoyles have been described in most European countries, in the United States and in South Africa and Australia in those of white descent. Only two instances have been found in negroes, Hubeny and Delano (1941) and Lahey *et al.* (1947). Engel (1939) has recorded the disease in Chinese patients. The condition is rather more frequent in the male and may have a familial incidence and an example of this will be described. The genetics were crystallized by Halperin and Curtis (1942), who, after factorial analysis of the reported cases, showed that a single autosomal recessive gene was responsible. In view of current theories of pathogenesis which incriminate faulty glycogen metabolism, it may be significant that a similar inheritance has been suggested by Abramson and Kuntz (1946) in von Gierke's glycogen storage disease, which likewise shows a somewhat similar histological picture.

Parental consanguinity has previously been described on only four occasions, Binswanger and Ullrich (1933), Harvey (1942), Halperin and Curtis (1942), and a fifth instance will be recorded below.

It is generally agreed that in gargoylism all the tissues of the body are the site of an abnormal storage process, and upon the nature of the substance stored depended much of the early nomenclature. The abnormal substance was at first thought to be a lipoid, and accordingly, gargoylism was included with the other lipoidoses—Gaucher's disease, Niemann-Pick's disease, Hand-Schuller-Christian's disease, and Tay-Sachs' disease—and with these eponymous names Hurler's disease fitted well as the " fifth lipoidosis." This concept that a lipoid was responsible originated with Tuthill (1934), who carried out an examination of the brain in one of Hurler's original cases. Ashby, Stewart and Watkin (1937) found changes in the ganglion cells similar to Tay-Sachs' disease, and a lipoid substance which had the staining reactions of a cerebroside ; Kressler and Aegerter (1938) likewise found considerable lipoid

deposits in the tissue, and de Lange (1942) reported cells similar to those described by Ashby *et al.*, but with slightly different staining reactions. In addition, Strauss, Merliss and Reiser (1947) found in their fatal case masses of foamy cells and increased lipoid in the lymph nodes and emphasized that the main weight of the disease falls upon collagen—the fascia and ligaments—and that contraction of these is responsible for much of the deformity.

Despite the evidence, the idea of a lipochondystrophy has neither been universally accepted nor confirmed histologically. Reilly (1935) could find no lipoid in the liver and spleen of his patient at autopsy, and chemical analysis of the organs of another patient by Lahey *et al.* (1947) failed to show any increased concentration of lipoid. Indeed, the work of Lindsay *et al.* (1948) indicates that the abnormal substance is in fact a carbohydrate in combination with a protein, though unlike the majority of storage diseases this macromolecular substance is found principally not in the reticulo-endothelial system, but in the parenchyme cells themselves. About half the patients show a peculiar granulation in 60 to 90 per cent. of the neutrophil leucocytes ; these granules are large and stain dark violet with the Giemsa-Wright Technique, and are also said to consist of glycogen (Reilly, 1941). Similarly, liver biopsy may show glycogen in excess in the liver cells (Jackson, 1951).

Experimentally, Hueper (1942) has shown that macromolecular substances, notably methyl cellulose, acacia, polyvinyl alcohol and glycogen, after repeated intravenous injections are deposited in the parenchyme cells of many organs, with histological changes, which resemble those of gargoylism. Lindsay (1948) confirmed this by repeated injections of methyl cellulose into rabbits over several months, and in 3 out of 22 animals corneal opacities developed.

The cause is generally ascribed to a fault in a gene, Liebenaur (1937), Besdziek (1938) and Halperin and Curtis (1942) have demonstrated a recessive transmission. Engel (1940) attempted to explain the deformities by the theory that in early embryonic life blebs of cerebrospinal fluid escaped into the praemodial tissues. The age of onset varies, and in the majority of cases the disease is diagnosed in the first year of life ; Strauss *et al.* (1947) reported a boy who was apparently normal till his ninth year, but other patients have been diagnosed at birth (Ashby *et al.*, 1937). It has been suggested that the abnormal storage substance accumulates in the tissues, and when its quantity is sufficient it alters structure and interferes with growth. The majority of patients affected die about the tenth or twelfth year, sometimes from a respiratory infection to which the deformed thorax predisposes, or more often from cardiac failure resulting from a congenital cardiac lesion. In the 19 autopsies reviewed by Lindsay (1950) 14 patients died from the latter cause. An occasional patient lives precariously into the twenties.

There are post-mortem changes in almost all the tissues of the body, with storage of an abnormal substance. There is subcutaneous fibrosis, which produces flexion deformities of the limbs. In the long bones the zone of proliferating cartilage is narrowed, the cells vary in size and the calcified matrix is present only in traces. These changes indicate failure of cartilage growth (Washington, 1940). The anterior pituitary, liver and spleen may be enlarged. The characteristic microscopic lesions are swelling of the cells, and in some of these the perinuclear portion shows a clear vacuolated space ; other cells are coarsely or finely granular, but some nerve cells show this change in only part of the cytoplasm.

While epithelial cells and the reticulo-endothelial system are involved, mesodermal cells also show marked changes, being enlarged and vacuolated, and in the central nervous system there is an increased amount of altered collagenous intercellular substances (Lindsay, 1950). The granules in the cells have been variously claimed to be of lipoidal nature (Tuthill, 1934 ; Ashby *et al.*, 1937 ; Strauss *et al.*, 1947) or of glycogen in protein combination (Lindsay *et al.*, 1948).

On physical examination the patient is usually of short stature and may be a dwarf. The head is large and may show acrocephaly, scaphocephaly or dolicho-cephaly. The hair is fine and silky. Deafness is not uncommon and the ears are set low. The supraorbital ridges are prominent and the nasal bridge depressed, with a persistent purulent nasal discarge. The cheeks are ruddy, the tongue large, fissured and protruding, and the teeth widely spaced, peg-shaped and often carious. In about 75 per cent. of patients the corneae are cloudy, and slit-lamp examination shows the substantia propria to be speckled with yellow-grey refractile points of varying size. The eyes themselves are large and widely spaced, the eyelids puffy and the eyebrows and lashes are coarse.

Strabismus, ptosis, nystagmus and anisocoria may occur. Primary optic atrophy has been described and the response to mydriatics is poor. The neck is short and the head appears to sit directly on the shoulders. The thorax may show a rachitic rosary, or *trichterbrust*, and is held in the position of full inspiration. A congenital heart lesion is common. The abdomen is protuberant, often with an umbilical hernia, and the liver and spleen are enlarged. The joints of the extremities tend to take up a position of flexion and cannot be passively extended ; deformities such as genu valgum, talipes and pes cavus are often found and a kyphosis in the upper lumbar region is usual. Occasionally there is evidence of a pyramidal lesion.

Hirsuties may occur on the face and back and the skin is dry, waxy and thickened. W.R. is negative.

The blood may show a hypochromic microcytic anaemia and a relative lymphocytosis and characteristic granules in the neutrophils have been described (Reilly, 1941). Similar cells have been found in the spleen and bone-marrow. The blood cholesterol is occasionally raised and liver function tests have sometimes shown impairment. Reducing substances have never been found in the urine. X-ray examination in a typical case shows a large, shallow sella turcica without clinoid erosion, an upper lumbar kyphosis with deformity of the anterior part of the vertebral bodies producing a hook-like process, an increased transverse diameter of long bones and demineralization in the ossific centres for the femoral and humeral heads, poorly formed acetabular and glenoid fossae, and epiphyses which are irregular and appear late.

The mental changes have attracted attention since the earliest descriptions of the condition, and the majority of patients have followed Hurler's (1919) original two cases and shown some degree of mental defect. On a number of occasions however the patient has appeared to be of normal intelligence (Hunter, 1917 ; Nonne, 1924 ; Cockayne, 1935, 1936 ; Liebenaur, 1937 ; Orr-Ewing cited by Ashby *et al.*, 1937 ; Henderson and Ellis, 1940 ; Reilly and Lindsay, 1948 ; Channarond, 1950 ; Jackson, 1951). A smaller group have intelligence which has been described as being above average. In the majority of these no formal testing was performed and the assessment of mental capacity was mainly descriptive ; thus, Nonne (1924) recorded three sisters " who were among the best in school "; Helmholtz and Harrington (1931) described a patient as being " mentally alert," and there are others : Liebenaur (1937), Ashby *et al.* (1937), Engel (1939), Meyer and Okner (1939), Hubeney and Delano (1941), Harvey (1942). One of the most interesting is the case of Strauss *et al.* (1947), who was "an outstanding student at high school, an intelligent and voracious reader, an intense lover of music ; he played chess and gained recognition locally as an outstanding player."

As might reasonably be expected, histological changes at autopsy have been found to vary with the presence or absence of mental defect. Reilly and Lindsay (1948) showed in a gargoyle of normal intelligence that storage of the macromolecular substance occurred in only the connective cells of the brain, while in patients with retarded mental growth there were deposits in all the cells of the central and peripheral nervous system.

Cockayne (1936) postulated that when the physical deformities were less severe, mental defect was similarly less marked, but a review of the reported cases does little to confirm this. A much more important feature is the marked mental deterioration which was noted by Ellis (1936) in his early cases, but which has received scanty prominence and which will be emphasized further in the illustrative cases about to be described.

Differential diagnosis is usually easy, and gargoyles—like mongols—resemble each other far more closely than other members of their own family. However, congenital syphilis may give rise to difficulty, but here the W.R. is positive, the corneal changes are different and there is a good response to antisyphilitic treatment. In cretinism the corneae are normal, hepatosplenomegaly is rare and thyroid administration gives good results. Hypertelorism has no changes in the long bones, and neither corneal opacities nor splenomegaly. Rickets is unlikely to cause confusion. In Morquio's disease the spine is heavily involved and the skull usually escapes, though the nasal bridge may be depressed. Corneal opacities, mental defect and evidence of abnormal storage are absent and the radiological appearances are helpful, being chiefly metaphyseal in Morquio's disease and epiphyseal in gargoylism. Intermediate forms have been described, and splenic or hepatic puncture may be useful in diagnosis.

The incomplete forms of gargoylism have been considered in detail by Jervis (1950), but the clinical criteria of even the gross case are doubtful. Strauss *et al.* (1947) divide the signs into two groups, the first being constant and the second significant, but not constant. The former group includes dwarfism, large head, flexion deformities and a protuberant abdomen, and the latter mental retardation, corneal clouding, hepatosplenomegaly, umbilical hernia and bony changes. However, there is little general agreement among the different authorities. Corneal opacities were regarded as an essential feature by the early writers (Helmholtz and Harrington, 1931), yet generally the features emphasised by Ellis and his co-workers in 1936 remain adequate, i.e., mental deficiency, corneal opacities, hepatosplenomegaly, chondro-osteodystrophy and grotesque facies, but with the provision that one or rarely more than one of these may be absent. The diagnosis of " gargoylism " has been made in patients who have shown neither mental defect nor physical deformity, being based purely upon the X-ray evidence (Channarond, 1950)—a practice which is contrary to the original concepts of the condition and which brings the term into disrepute.

Five illustrative cases will now be described :

Case 1.

Margaret C—. Female born 17.ix.45. An only child whose parents were married for five years before conception. The mother's age at birth of the child was thirty years. Pregnancy was uneventful, but labour was difficult, and forceps were required. The patient weighed 6¾ lb. at birth and was breast-fed until 5½ months. The parents are unrelated, and there is no family history of mental disease apart from a maternal uncle who has been a voluntary patient in a mental hospital since 1939 suffering from a depressive illness. The father is a picture-framer by trade, and considered that the child was unduly ugly from the age of two months.

In 1950 she was referred to a Child Guidance Clinic because of mental retardation ; a diagnosis of gargoylism was made and she was admitted to a mental deficiency hospital. She was unable to dress or undress herself ; she was incontinent and could not speak ; she was able to walk a few steps and made climbing movements in her cot. Physically she weighed 2 st. 3 lb. and had a height of 2 ft. 9 in. She evidenced most of the stigmata of gargoylism : thus, the head was large, the biparietal diameter was 14 cm. and the occipitofrontal 20 cm. but the hair was unusually coarse. The nasal bridge was depressed and the supra-orbital ridges prominent. The teeth were carious and the tongue large, fissured and protruding. The corneae shows marked opacities. The neck was short, she was slightly breathless and there was a soft mitral systolic murmur. The abdomen was protuberant, with a small umbilical hernia ; the liver was three finger-breadths enlarged and the lower pole of the spleen just palpable. There was a persistent thick purulent nasal discharge and slight deafness. The fingers were stubby and flexed and there was a considerable lumbar kyphosis. An X-ray of the skull showed the typical long, shallow pituitary fossa. There was no abnormality in her nervous system. W.R. was negative and the urine normal.

In 1951 she developed lobar pneumonia and this recurred early in 1952. Her physical state has deteriorated steadily, deafness becoming more pronounced and the corneal opacities increasing in size. Biochemical investigations are normal, apart from an increased sugar tolerance with a flat blood-sugar curve. The blood shows a mild hypochromic anaemia and numbers of the neutrophils contain purple-black granules—some basophil and some acidophil. An E.E.G. gives a grossly abnormal but unspecific record. The eyes are more like adult eyes in size. The conjunctival vessels are injected, with a corneal haze. The corneal microscope shows numerous dot-like opacities in the substantia propria which resemble snowflakes and are evenly distributed throughout the tissues. The pupils are moderately dilated and react sluggishly to light.

The level of her intelligence is too low for the application of a standard test, but some estimate can be obtained from Gesell's norms and the Vineland scale. In the former she passes the majority of the requirements of the 6-month level—following a moving light with her eyes, lifting a paper placed over her face and sitting up alone, etc. At the 9-month level she showed some response to the mirror image of herself and sits satisfactorily. Her speech is *nil*. She passed none of the criteria of the 12 and 18-month levels. She passes approximately 80 per cent. of the criteria on the Vineland Social Maturity scale at the 0 to 2-year level. She has never imitated sounds, but she used to draw herself upright and walked alone about the age of 2½ years. At the 1- to 2-year level she fulfils none of the requirements, apart from eating with a spoon, and this not without making a mess. Formerly, she walked unattended, marked with a pencil and drank with a cup almost by herself. She would therefore seem to have had about 15 to 20 per cent. of the requirements of this level. Her mental development at present seems to be about the 9- to 10-month level, but it is difficult to make an accurate estimate while she is chronically sick and confined to bed, especially with regard to walking.

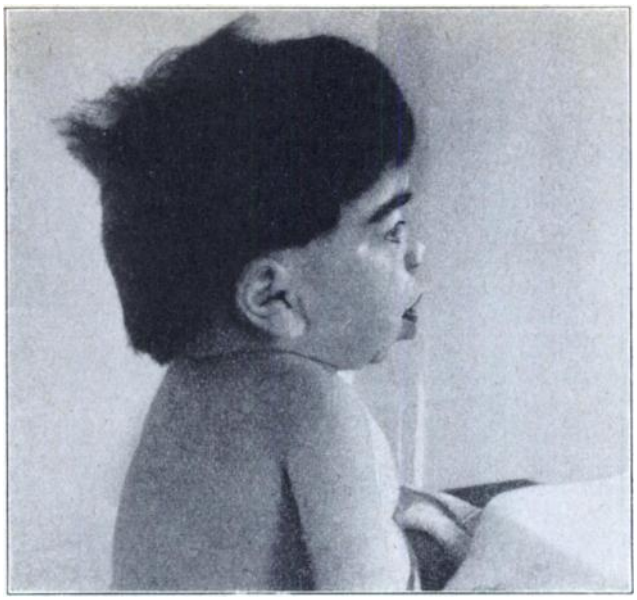

FIG. 1.

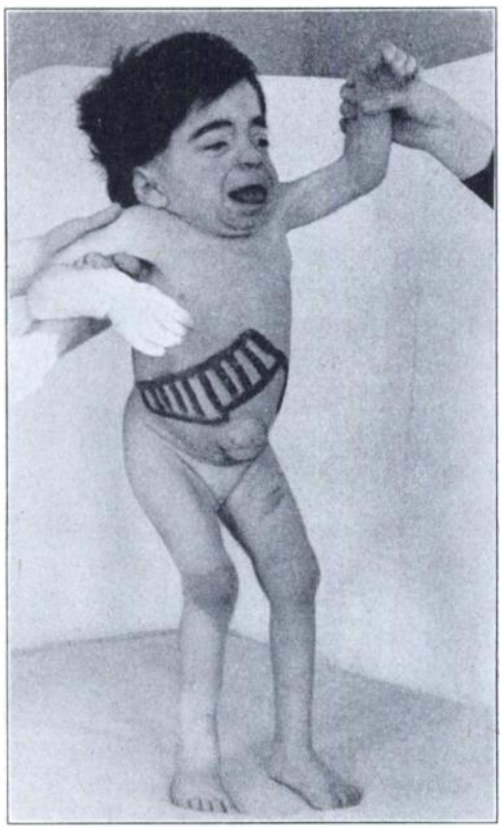

FIG. 2.

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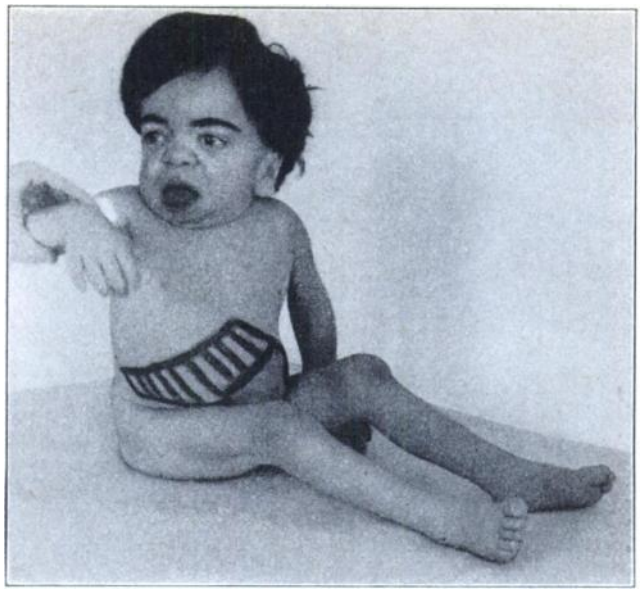

FIG. 3.

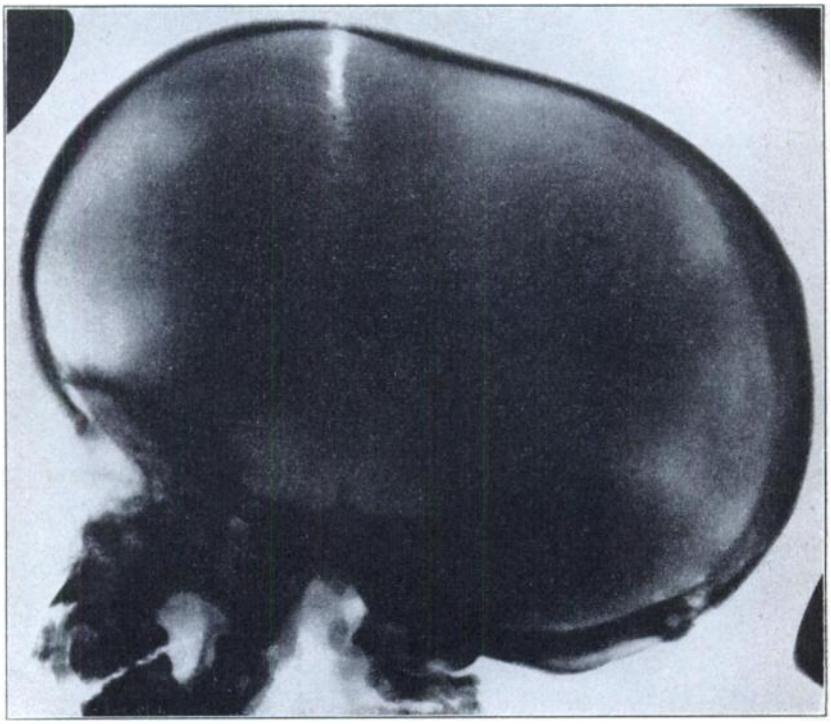

FIG. 4.

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Reports do not suggest that much deterioration has so far taken place. Her speech is absent as formerly. Her walking is not evident at present but it is premature to say that the skill is lost. Her milestones were late—she walked at 2½ years and only started climbing at 5 years. Her development never appears to have been much beyond the 12-months level. However, her fine muscular control is not now so good as formerly. She could previously mark with a pencil, turn a door-knob and pull off her boots, but how far lack of opportunity for practice during the past year accounts for this deterioration is a matter for conjecture. It may well be inaccurate to measure her development in comparison with a normal child because her deafness has been a handicap to general social progress as well as to the acquisition of speech, yet in the circumstances it is difficult to do otherwise.

Case 2.

Maurice D—. Male born 28.v.43. An only child whose parents were ten years married before the child was born. There is a history of gargoylism on the mother's side, and one of the first features noted on entering the home was an early photograph of the mother nursing a younger gargoyle brother. The maternal grandmother is said to have had two brothers of grotesque appearance who died at an early age, and the mother herself had two younger brothers whose photographs were typical of gargoylism. One of these died at the age of 3½ years and the other died aged 6 years. A maternal aunt gave birth to a similar male child who died at the age of 10 years. It was in fact a family tradition that the eldest daughter produced such male children, this being the case in the patient's grandmother, mother and mother's aunt. A maternal uncle and aunt have normal children, and on the father's side there is no family history of mental or nervous disease with the exception of one paternal uncle who is described as " dull." The parents are not related.

Pregnancy was uneventful, but labour was difficult, the child being two weeks post-mature, forceps were necessary and the child was said to have been jaundiced and the vernix golden. He was breast-fed, but never hungry, and cried day and night. Maurice passed the usual milestones early, having bladder control at one year and taking a few steps at that time. His mother had, however, noticed that he had a lumbar kyphosis at the age of 9 months, and photographs show increasing facial stigmata from the age of 6 months. In 1946 he had an operation for umbilical hernia, and in 1947 a diagnosis of cretinism was made and he received treatment with thyroid extract. At the age of 5 years he spoke in simple sentences, obeyed simple commands and did small messages for his father, who is a gardener. He was fond of music.

At 6 years a Terman Merrill Form L, however, gave him a mental age of 2_{12}^{8} and an I.Q. of 42. By 1950 the patient had lost all interest in his surroundings and was restless, noisy, destructive and incontinent of urine and faeces, and in 1951 he had a transient episode of flaccid paraplegia. Now (1952) his head is large with an occipito-frontal diameter of 16 cm. and a biparietal diameter of 14 cm. His nose is depressed. The optic discs are on the pale side of normal.

He has a marked kyphosis; the arms are held in a position of flexion and cannot be extended; he has knock-knees, pes cavus and brittle nails with small ulcers on the fingers. There is a harsh systolic murmur over the praecordium, and attacks of dyspnoea at night are frequent. The abdomen is protuberant and the liver two finger-breadths enlarged. Blood-films failed to show any of the characteristic abnormal cells.

As regards his mental state; attention and comprehension were insufficient to pass any of the Revised Stanford-Binet Intelligence Scale tests at the 2-year level. He understands only a few very simple commands such as " Come here." His speech is very indistinct and now rare. His habits fulfil all the requirements of the Vineland Social Maturity scale at the 0–1-year level, and about 25 per cent. of the 1–2 stage. Maurice walks about the room unattended, drinks from a cup with assistance, scribbles with a pencil, etc. According to Gesell's norms, he is about the 12–18-months level. He opens a door, walks alone, and puts a cube in a cup after much persuasion. He cannot indicate any part of his body. From these criteria the level of his development would seem to be about 15–18 months and his I.Q. therefore below 30. Considerable deterioration would appear to have taken place, because at one stage he could eat from a spoon, draw a circle or cross, say nursery rhymes, count up to ten, drink unassisted, build blocks instead of flinging them to the floor as he now does, and walk upstairs alone. It is difficult to estimate his previous mental level without accurate knowledge of the time when the various skills were accomplished, but to be able to draw a circle and say nursery rhymes, etc., he would seem to have had a mental age of 3–4 years at one point; certainly in 1949 it was 2_{12}^{8} as contrasted with that of 15–18 months which he now shows.

Case 3.

Beryl G—. Female born on 20.xii.41. A paternal uncle was epileptic, and a paternal aunt died in a mental deficiency hospital in 1940 from cerebral diplegia. The parents were cousins and the father's surname is the same as that of the mother in Case 1, but no relationship can be traced. The mother's age at birth of the child was 20 years, and the patient has two brothers older and one younger than herself, all of whom are normal. Pregnancy was uneventful and the labour was normal. The patient weighed 7½ lb. at

birth and was breast fed. She was seldom hungry and was breathless and snuffly. She had control of her bowels at one year. By the age of two years it was apparent that she was definitely abnormal and she was taken by her mother to a general hospital. At that time she made no attempt to walk, the abdomen was protuberant, and a diagnosis of cretinism being made she received treatment with thyroid extract. She had bladder control at three years and commenced to walk about the same time. By 1947 her head was enlarged, there was a pigeon chest and an umbilical hernia. A Terman Merrill Form L gave a mental age of $3\frac{1}{12}$ and an I.Q. of 66. A year later her height was 2 ft. 9 in., she shuffled along with her knees bent and on her toes. She could feed herself and undress, but not dress. She could count up to ten in a husky voice, carry out simple commands and could write the alphabet. A Terman Merrill Form L test now gave a mental age of $4\frac{8}{12}$ and an I.Q. of 70.

Her physical state (1952) shows a large head with an occipito-frontal diameter of 18 cm. and a biparietal of 14 cm. The supra-orbital ridges are prominent, the tongue protrudes and the voice is whispered. She is left-handed. The limbs are held in a position of flexion and the short neck in extension. The liver is five finger-breadths enlarged. There are marked hirsuties on the back and brown pigmentation of the trunk and limbs. Blood films show numbers of the neutrophils to contain purple-black granules. The pupils react to light, and there are no corneal opactities. Her eyesight is, however, failing rapidly and the retinal vessels are described as tortuous. Her physical disabilities—inadequate sight, poor muscular flexibility in drawing and husky voice—are now so pronounced that no full-scale standard intelligence test can be applied. On the Terman Merrill Scale Form L her performance indicates roughly a mental age of 5 to 6 years with an I.Q. of 50–60. The Goodenough rating of a drawing of a man suggests a mental age of 5 years. Her general knowledge appears to be superior to her present functional level. She knows her birthday, age, the number of pennies in a shilling and can name the days of the week. Although her arithmetic book contains subtraction sums, she fails to give the change of 5*d*. from 1*s*. or of 10*d*. from 2*s*. She repeats five digits forwards but only two reversed. Her vocabulary and comprehension would seem to be the brightest aspects of her intelligence and least handicapped by her physical deterioration, but even those would seem more impaired now than three years ago when she was last tested. Neither of these abilities could be rated at the 7-year level, and it would appear that an I.Q. of 70 as previously obtained is now beyond her power.

Her general social maturity has also grossly deteriorated with her physical disabilities. The degree of her physical and sensory deterioration makes the field very limited for testing the extent of her intellectual deterioration, which would, however, also seem to have taken place. She died in March, 1952, from bronchopneumonia. Autopsy was refused.

Case 4.

Diane H—. This girl was born on 22.vii.42 during an air raid. A paternal uncle and a maternal aunt were epileptic. The father was aged 28 and the mother 26 years, and were not related. She was an only child; labour was normal and she was bottle-fed. At the age of 9 months she was seriously ill with pneumonia and about that age began to say "Dada." She is said to have appeared normal apart from a severe kyphosis of the lumbar spine which was first observed at this age. By 2 years the head was large, the eyelids puffy and the nose flat. A diagnosis of mongolism was made. She could, however, walk alone. Her weight was 2 st. 4 lb. and her height 2 ft. 6 in. The W.R. was negative, and although an X-ray of the lumbar spine showed notching of the anterior parts of the vertebral bodies of L2.3.4, the diagnosis was now changed to cretinism and she was treated with thyroid extract.

By the age of 4 years she could control her bowels but not her bladder. The liver and spleen were enlarged; there was hirsuties on the face; the corneae were cloudy and polydipsia marked. She could speak a few words such as "all done" or "quack quack." She was walking well and still on thyroid gr. 3 daily.

At 5 years of age she developed an umbilical abscess and at 6 years otitis media. She had repeated attacks of bronchitis. She now walked stiffly and extension of the limb-joints was limited.

The Terman Merrill gave a mental age of less than 3 years and an I.Q. of under 40. By 1949 she was unable to walk, speech had disappeared and she was doubly incontinent. She was completely blind and could do nothing for herself. She died in 1950 from lobar pneumonia at the age of 8 years.

Case 5.

John W—. An only child born on 4.iv.42. His father suffered from diabetes mellitus and failing eyesight. Labour was uneventful, but the infant was abnormal at birth. The head was large and the corneae were cloudy with internal strabismus. The abdomen was protuberant and a large umbilical hernia was prominent. The nasal bridge was depressed, breathlessness was pronounced and there was a harsh systolic murmur all over the praecordium. He was described as "a typical achondroplasic dwarf." Bladder control was established at 18 months; he could walk a few steps at 2 years and speak

a few words at 2½ years. In 1948 he commenced attending an occupation centre, but his mental condition deteriorated and he became incontinent, unco-operative and difficult to handle. By 1950 he had become very deaf and could only say words and short sentences. He knew the primary colours and where his home was situated. He fed himself clumsily with a spoon and played with a tricycle. In May of that year, on the Terman Merrill Scale Form L his mental age was 3 years and his I.Q. 37. He suffered from repeated attacks of bronchitis, and died early in 1951 from broncho-pneumonia at the age of 9 years.

Summary.

A brief review of the literature on gargoylism is given and five further cases are reported. The characteristic granulation of the neutrophils described by Reilly (1941) was confirmed in two out of three patients investigated from this aspect. Waarenburg's (1940) assertion that complete blindness never occurs cannot be sustained, as Case 4 went on to this state. Although Helmholtz and Harrington (1931) claim that thyroid extract improved one of their cases, no similar benefit resulted from prolonged thyroid medication in these five patients, but its value as a therapeutic test in the differential diagnosis of cretinism has been mentioned above. No other treatment is known apart from palliative orthopaedic measures for the deformities.

It is suggested that gargoylism is more common than is indicated by the number of reported cases, and that the condition is not infrequently misdiagnosed—of the five patients described two were considered to be cretins, one a mongolian imbecile and one an achondroplasic dwarf.

As well as describing the progressive physical impairment, an attempt has been made to emphasize the mental deterioration which may also occur. This was definite in four patients and may yet appear in the fifth and youngest, where its existence is at present doubtful. That mental deterioration exists is not widely appreciated, and as no mention of the intellectual progress of the patient is made in many of the reported cases, it is impossible to assess the percentage of patients in the literature where such deterioration has in fact taken place. Ellis (1951) speaks of " a rapid regression during later infancy in some cases " and while valid conclusions cannot be drawn from so small a series, the incidence of mental deterioration was striking and is of obvious importance in prognosis.

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