THE MENTAL CAPACITY IN ACHONDROPLASIA.

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ACHONDROPLASIA (micromelia, chondrodystrophia foetalis) has been defined as " an absence, arrest or perversion of the normal process of endochondral ossification of the most definite and universal character in every element of the skeleton, in which the process normally takes place during intrauterine life " (Symington and Thomson, 1892).

The condition has been recognized since about 2,500 B.C., and is seen in statuettes of the Egyptian gods Bes and Ka. Many of those so afflicted, such as the poet and grammarian Philetas of Cos, have been famed for their wit and wisdom. In the Middle Ages this vivacity, charm and intelligence led to their employment as court jesters, while more recently they have achieved popularity in the circus ring.

The first scientific description is generally attributed to Glisson, Bate and Regemorter (1651), but more than two centuries were to elapse before the condition was observed in living persons and the term achondroplasia introduced by Parrot (1878).

The earliest case material comprised stillborn children, and the first aetiological theory ascribed the condition to foetal rickets (Romberg, 1817). Virchow (1856) considered the disease to be related to cretinism, and claimed that the premature synostosis of occiput to sphenoids was " typical of cretinism." De Paul (1857) incriminated congenital syphilis, Scharlau (1867) intrauterine inflammation of cartilage, Kaufmann (1892) primary malformation of epiphyseal cartilages and early cessation of endochondral bone formation, and Durante (1902) sclerosis of the zone of endochondral ossification. Poncet and Leriche (1903) postulated atavism, that these patients are remnants of a past pigmy race, while Jansen (1912) concluded that achondroplasia was due to retarded foetal growth resulting from either hydramnios or amniotic constriction. Keith (1913) suggested glandular dysfunction, and Crewe (1924) believed disturbance of the anterior pituitary in the early months of foetal life to be responsible.

The genetics rest on a somewhat firmer basis, and achondroplasia seems to be due to a single dominant gene (Stevens, 1943 ; Penrose, 1951). The influence of heredity was first emphasized by Porak (1889). The condition occurs in animals, and may be local or generalized. The former variety was found in the niata ox by Darwin and in Yorkshire swine. Similarly, Crew (1926) described a bulldog lamb with the signs confined to the head. A short-legged

race of cattle is seen in the English Dexter and dwarf horses and zebus have been observed by Henseler (1925). Stockard (1928), experimenting at his dog farm, showed short-leggedness to be dominant, and while the inheritance of chondrodystrophy varied in different parts of the skeleton, micromelia was always dominant. Brown and Pearce (1945), working with rabbits, demonstrated that the gene concerned was invariably lethal at birth or a few hours later and that it also produced visceral effects.

In man, numerous reports have been made of chondrodystrophy in two generations (Cockayne, 1928; Kemp, 1937; Günther, 1938), in three generations (Hunter, 1928), and in six (Phemister, 1924). Achondroplasic parents have produced a living achondroplasic child (Potter and Coverstone, 1948) and the disease has been present in one of twins (Benjamin and Brookner, 1934). It was previously assumed that the disease was due to a dominant gene with high mutation rate giving a considerable proportion of sporadic cases. Mörch (1941), in his series, found a mutation rate of 1 in 10,000 in terms of individuals, and of the 108 dwarfs studied, 90 were sporadic, and 18 belonged to 8 sibships where the gene had been received from a similarly affected parent; Mörch could not find a single affected individual among the more distant relatives of any sporadic case.

Penrose (1951) has pointed out that the genetic background has a certain superficial resemblance to mongolism. Thus, in Mörch's series, the mothers were frequently elderly; the affected children were often the last arrivals among the siblings, and the fathers were generally older than in the average population.

The pathology was divided by Kaufmann (1892) into three main forms, the hyperplastic, the hypoplastic and the malacic, but these often coexist. The child may be born dead, and 80 per cent. die in the first year of life (Mörch, 1941). The sex incidence is equal.

The characteristic lesion is failure of bone formation in cartilage; intramembranous ossification proceeds normally and these features are evident at birth. The limbs are short, and as there is comparatively more growth of soft tissue than of bone, the skin may hang in folds. There is frequently an excess of subcutaneous fat, and sometimes oedema. The long bones, although short, are relatively thick, with prominent muscular ridges. The tibia and fibula are of almost equal length, leading to a marked outward curvature. The clavicle is not decreased in length. The cartilaginous epiphyses are considerably enlarged, and with the small shaft, present a mushroom appearance; areas of softening in cartilage may be evident. The scapula is short, the glenoid fossa shallow, and expansion of the ends of the long bones is responsible for marked beading of the ribs. The epiphyses commonly unite late, and in children the joint spaces are increased. There is a lumbar lordosis, the pelvis is contracted and the sacrum projects into it. The vertebrae show the same changes to a lesser extent, and Donath and Vogel (1925) state that the adult spine in achondroplasia is never normal.

The fontanelles are widely open at birth. There is indrawing of the root of the nose from early ossification, frequently accompanied by premature union of the sphenoidal and basi-sphenoidal sutures. The head itself is large,

and sometimes interferes with labour. The moderate degree of hydrocephalus is due to disturbance of the normal relationship between the brain stem and the floor of the skull (Meyer, 1924; Welter, 1936). Meyer's case showed shortening of the tribasilar and deformity of the posterior fossa, including narrowing of the foramen magnum. In Welter's case the jugular foramina were narrow, and he attributed the hydrocephalus to constriction of the sigmoid sinuses. These findings were evident in autopsies in children. However, Dandy (1921), in a nineteen-year-old adult achondroplasic, demonstrated a conspicuous degree of general ventricular dilatation by ventriculography. He considered the hydrocephalus to be due to obstruction in the posterior fossa producing an internal hydrocephalus which is not progressive, as the yielding skull in infancy leads to a readjustment of brain to bone.

In this connection it is interesting to note that Grüneberg (1943) has shown that inherited hydrocephalus in mice is due to a recessive gene. There is retardation of cartilage growth at the base of the skull with compression of the hind brain and obstruction to the cerebrospinal fluid, the condition being reminiscent of achondroplasia (Russell, 1949).

The histology was first described by Müller (1860), and later by Parrot (1878). The latter showed the changes to be present early in foetal life and localized to the epiphyses of cartilage bones. The cartilage cells are arranged irregularly and there is little or no ossification. The most characteristic change is the "histological streak" first demonstrated by Urtel (1873). This consists of fibrous connective tissue in the proliferative zone of the epiphyseal line containing blood-vessels and islets of cartilage cells. Sometimes the streak is coarse and sometimes delicate and found only in a single bone. The periosteum and periosteal bone formation are normal; the medullary canal may be obliterated by spongy bone.

Early workers described changes in the endocrine glands. Kaufmann (1892) noted in two cases that the thyroid was enlarged and vascular, resembling the condition of the gland in toxic goitre. Increased numbers of basophils have been demonstrated in the anterior pituitary, and a hypoplastic pituitary has been noted by Landauer (1929) in experimental chick embryos. The reported alterations in the cell pictures of the pituitary, thyroid, parathyroids, pineal and gonads have never been generally confirmed, and the endocrine glands are essentially normal. The structure of the brain has received little attention, but is said to show no gross abnormality.

The most conspicuous clinical feature is dwarfism, adults seldom attaining a height of more than 4 to 4½ ft. Many are under 3 ft., and this shortness of stature is evident at birth. There is commonly a depression at the root of the nose, and the head is brachycephalic with prominent frontal bossing. Atypically shaped skulls have been described by Müller (1860) and Hecker (1862), but exceptionally the head and face are normal. More often the nostrils are large, the lips thick and the lower jaw prognathous. The palate is usually high and arched and in infants the tongue may protrude from the mouth. Hearing is impaired in about a quarter of the patients.

The trunk is of normal size, broad and well developed; lumbar lordosis is increased to a variable degree; occasionally there is a scoliosis. The chest

is flattened antero-posteriorly and the ribs may show beading. The extremities exhibit micromelia, most pronounced in their proximal parts. Thus the arms are short, reaching the trochanters or even only as far as the iliac crests. Defective extension of the elbows is common and increases with age, varying from 10°–60° and averaging 30°. The hands are broad and plump, the fingers of equal length and the third and fourth may deviate to the ulnar side, producing the " main en trident " of Marie. The legs are short, the femora being particularly involved, and there is a varying degree of bowleggedness. The feet are broad and the gait waddling.

The genitals are normal. Neurological changes have recently been emphasized by Spillane (1952), and occasionally other malformations, such as congenital heart disease, spina bifida or polycystic kidneys are associated. Rarely the disease may be localized to a single bone.

There are no alterations in blood chemistry and the W.R. is negative. The haemoglobin, red and white cell counts are normal. Eosinophilia is sometimes evident (Mörch, 1941), similar to that found in chondrodystrophic chick embryos (Landauer, 1928) and in Dexter cattle (Landauer and Thigpen, 1929). Estimation of urinary sex hormones gives normal results.

Radiological examination in the adult shows short thick bones. In children there is delayed epiphyseal union, increased joint spaces and narrowing of the intervals between epiphyses and metaphyses. According to Mörch (1941) the pathognomonic clinical features are four in number, i.e., micromelia, lumbar lordosis, defective elbow extension and dwarfism.

The mental state of achondroplasia has attracted scant attention in British literature. Thus Rankin and Mackay (1906) state that intelligence is average, as do Beaumont (1948), Price (1950), Neale (1951) and Conybeare and Mann (1952). Tidy (1949) refers to mental development as being " normal or quaint," and Parsons (1950) writes, " the mental condition is normal, although since they are rather fascinating little creatures, they may develop into spoilt children. They are perhaps rather fond of the applause of the multitude which not a few obtain on the variety stage." Tredgold (1952) refers to the achondroplasic as " usually of average intelligence," but includes in his textbook an illustration of the condition with oligophrenia. Spillane (1952) in his neurological studies recorded one of his patients as being " below average intelligence."

A contrary view is held by some Continental workers. Marie (1900) described his two original patients as being mentally infantile ; Lauze (1910) referred to the personality as being vain, boastful and with " a tendency to mania " ; Parhon and Schunda (1913) claimed intelligence to be subnormal in more than half their cases, and more recently Nielsen (1941) found intelligence to be " partially lowered, so that they can hardly grasp the elements of arithmetic, are barely able to read, and cannot write." However, Mörch (1941), in his cognate study of 108 achondroplasics, found only one patient who showed " a low degree of knowledge and orientation," while the majority were " well balanced, pleasant and of normal emotional nature." In all of these, however, no formal psychometric examinations were performed.

Diagnosis of a classic case is relatively simple, but where the disturbance

is confined to the base of the skull the resulting hydrocephalus may obscure the general condition (Jansen, 1912). In infancy achondroplasia may be confused with cretinism, but signs of the latter develop some months after birth, while the former are present in the newborn. The blood chemistry and radiological findings in rickets are characteristic, and dwarfing is due to deformity of the limbs, not to congenital shortening. Dwarfism in osteogenesis imperfecta results from multiple fractures readily confirmed by X-ray examination. Morquio's disease exhibits dwarfism and occasionally a depression of the root of the nose, but the short trunk, the long extremities, the hypermobile joints, the vertebrae and metaphyses are diagnostic. Grotesque facies, corneal clouding, hepatosplenomegaly, dwarfism and epiphyseal changes are found in gargoylism. Ollier's disease can only be diagnosed radiologically, the patient seeking advice because of pain, shortening, thickening or deformity of an extremity. Ateleiotic, mongolian, renal and cardiac dwarfs are obvious, while osteomalacia and progeria should not give rise to difficulty. In all cases of chondrodystrophy the diagnosis can be confirmed by radiography.

The County of Norfolk, with the City of Norwich and the County Borough of Great Yarmouth, have a combined population of 546,500. A search was made for cases of achondroplasia born in this area and a total of sixteen cases were found, of whom five were mentally defective and are described below.

CASE 1.—Female, born 9.vi.1926.

Her father, a farm worker of over 6 ft. in stature, was born in 1899. Her mother, born in 1901, died at the age of 47 from cancer. There was no history of mental disease or defect in the ascendants. There were two other children—a son aged 27 who served in the Navy and is 6 ft. 4 in. tall, and a married sister of 25 who has one normal child. There is no history of miscarriages, and the father's family have a record of excessive height dating back three generations. She was admitted to a certified institution in 1937.

She is an idiot, and fails all sub-tests of the Terman Merrill Scale Form L at the two-year level; her I.Q. is below 30. The Vineland Social Maturity Rating is 18 months and Gesell's Norms of Adaptive Behaviour are equal to the 12 months level. Speech is confined to monosyllables; she can feed herself but not discriminate food substances. She continually picks her hair, and if playing with a toy desired by another patient exhibits severe temper tantrums when it is taken away. She is doubly incontinent by day and night. Physically she is 3 ft. 9½ in. in height and weighs 4 st. 10½ lb. Her head and face are typical of the condition, the occipito-frontal diameter being 18 cm.; the biparietal is 15·2 cm. The jaw is prognathous, the palate notably arched. Her arms are short with limited extension, the trunk of normal length, lumbar lordosis is slight. The legs are bowed laterally and grossly shortened. The central nervous system is normal, the blood picture and urine are normal. The W.R. is negative.

CASE 2.—Male, born 14.viii.1911.

The father, a retired builder's labourer, born in 1884, and the mother in 1886 are alive and well. There were two younger brothers of normal appearance, one of whom died as a prisoner-of-war. There is no family history of mental disease or deficiency. His milestones were delayed, and he has for many years attended an Occupation Centre.

He is an imbecile, with a mental age of $5\frac{7}{12}$ years and an I.Q. of 34 on the Terman Merrill Scale Form L; he was unable to attempt the Seguin Form Board.

He can run messages, do simple rug work and helps with younger patients at the Centre. He is extremely facile and childish and has poor attention, habitually wandering aimlessly away and needs very careful supervision. He is 4 ft. 2 in. in height and weighs 5 st. His head is large, with a prominent forehead, depressed

nasal bones, the occipito-frontal diameter being 17 cm., the biparietal diameter 14·5 cm. The arms are short, the fingers thick and of almost equal length. His trunk is of normal size and there is marked lumbar lordosis. He has a scrotal hernia. The femora are short, and there is slight external bowing of the tibia and fibula. X-rays of the long bones confirm the diagnosis. Haematological examination and E.E.G. were refused.

CASE 3.—Female, born 9.viii.1920.

The father was born in 1853 and died in a county home in 1931. The mother, who was born in 1880, was admitted to a county home in 1928, dying therein in 1940. The home was poor, and the parents tried ineffectually to sell her to a travel-

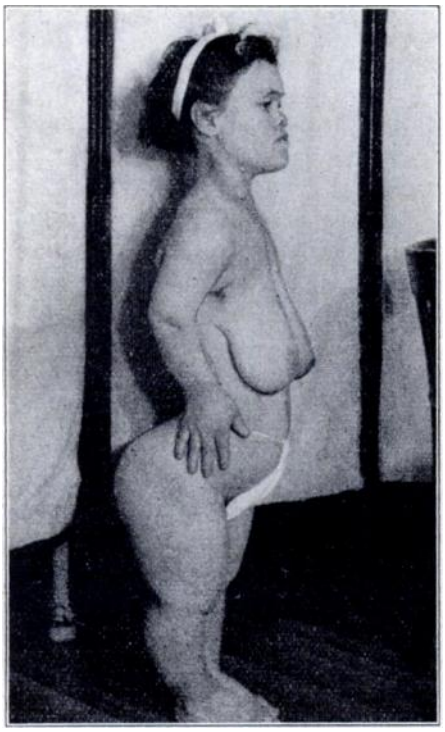

FIG. 1.—Showing typical head, flexed elbows and increased lumbar lordosis.

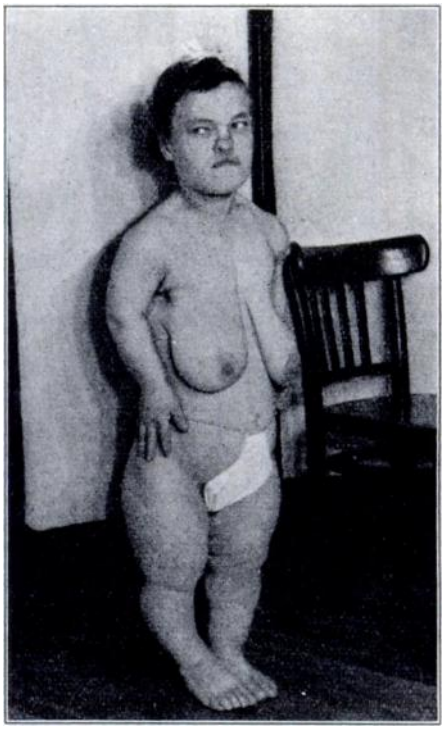

FIG. 2.—Showing micromelia with trunk of normal length.

ling showman. There is one other sibling, a male, born in 1918, who was admitted to a certified institution in 1935 with a diagnosis of moral defect, and a mental age of 11 years on the Stanford Revision of the Binet scale. He was discharged from the Mental Deficiency Acts in 1942 and is now married with two normal children, a boy and a girl.

She is an imbecile, with an I.Q. of 34 and a mental age of $5\frac{2}{12}$ years on the Terman Merrill Scales L and M, there being an interval of two years between the tests. The Seguin Form Board test gives a performance at the $6\frac{1}{2}$–7 year level. Generally her non-verbal ability is slightly better than her general intelligence, but she is unable to copy a simple bead chain from memory. Physically she is 3 ft. 9 in. in height and weighs 5 st. 3 lb. The head is typical, with frontal bossing; the occipito-frontal diameter is 18·5 cm., the biparietal 15 cm. There is a marked depression at the root of the nose and the jaw is prognathous. Her palate is high and arched. The arms are short, with restricted extension of the elbow-joints. Her trunk is normal, and lordosis is very marked. The legs are grossly shortened and externally bowed.

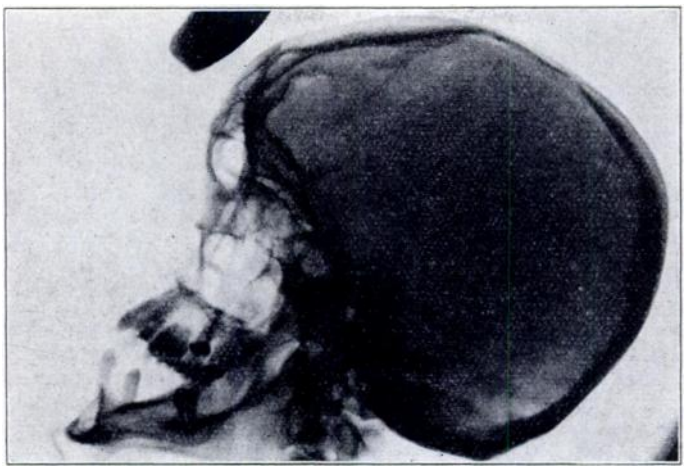

FIG. 3.—Skull showing characteristic shape and shortened base.

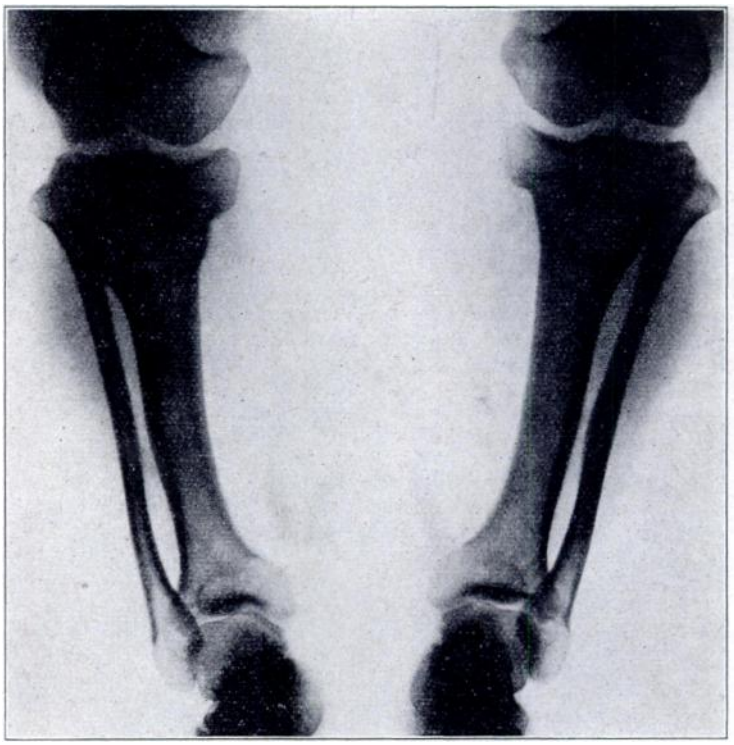

FIG. 4.—Legs showing shortened thickened bones.

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The central nervous system is normal, the blood picture and urine are normal and the E.E.G. shows no abnormality.

CASE 4.—Male, born 20.v.1917.

The father, who was born in 1879, died in 1942; the mother, born in 1881, is alive; both parents were of normal stature. The family history shows no record of psychosis or mental defect. There was neither consanguinity nor miscarriages, and the patient is an only child. His milestones were retarded and he did poorly at school. On leaving school he obtained employment as assistant to a cowman on a farm where his family have had lifelong associations He has held this job ever since, is registered as a disabled person and receives £3 per week, about half the average wages for this type of employment.

He is feeble-minded; his Raven Matrices score on individual test is 19, with normal scatter, which places him in the 8–9-year level. His general knowledge and comprehension are poor. His mother manages his financial affairs as he is only able to give simple change. When questioned as to the simple technicalities of his daily work he failed to reply satisfactorily. He performs simple routine tasks under a degree of supervision. Physically he is 4 ft. 1 in. in height and weighs about 6 st. The head is large, the occipito-frontal diameter 19 cm., the biparietal 16 cm. The nasal bridge is sunk, the lower jaw prognathous. His arms are shortened and the trunk well developed, with some lordosis. The legs are short and bowed externally. There are no neurological signs. Examination of the blood and radio-diagnosis were refused.

CASE 5.—Female, born 11.iv.1914.

She is illegitimate; her mother, who was born in 1893, is feebleminded with an I.Q. of 60 on the Terman Merrill scale Form L, and was admitted to a certified institution in 1948. The putative father died of progressive muscular atrophy in 1931. Two elder sisters are illegitimate and defective with I.Q's. on the Terman Merrill scale of 54 and 40 respectively. Before being ascertained under the Mental Deficiency Acts one of these gave birth to an illegitimate daughter, who was admitted to a certified institution in 1951 and has an I.Q. of 67. All the known relatives are of normal appearance and examination reveals no evidence of chondystrophy.

She was admitted to a children's home in 1924 with a diagnosis of bilateral congenital dislocation of the hips, and later underwent osteotomy to remedy her genu valgum. She was treated with pluriglandular tablets for dwarfism. Her I.Q. was found to be 64 on the Binet scale, and she was certified and admitted to an institution in 1931. She is feeble-minded, scores 25 on Raven Matrices, has a Burt's reading age of 10–11 years and a mental age of the Terman Merrill Form L of $10\frac{5}{12}$ with an I.Q. of 78. Definition of abstract words and comprehension are relatively good. She works steadily and well with supervision and encouragement, but lacks confidence and initiative, is shy and withdrawn and normally associates with the imbecile group.

Physically she is 4 ft. ½ in. in height and weighs 6 st. 2 lb. The head is of normal appearance, the occipito-frontal diameter is 18 cm. the biparietal 14 cm. There is a slight depression at the root of the nose. Her palate is high and arched. The arms are short with limited extension, the chest broad, the trunk of normal length and there is a marked lordosis. Pubic hair is of masculine distribution. The legs are short and severely bowed both antero-posteriorly and laterally. There is a patch of chronic eczema on the left leg and an area of pigmentation on the left thigh. The central nervous system exhibits no abnormality, but the tendon reflexes are generally brisk. The blood picture is normal and the W.R. is negative. Radiological examination of the spine and pelvis shows typical changes. The E.E.G. report is mildly unstable, but not specific; no focal disturbances are apparent.

DISCUSSION.

Mörch (1941) concludes that the incidence of living achondroplasic dwarfs is one per 44,000 of the population, and Haldane (1948) estimates that there are about 1,000 in Britain. Our total of sixteen patients born in this area is

compatible with these figures, and the incidence of mental defect in this small sample is striking. The remainder of the cases surveyed includes two men belonging to the dull group with I.Q's. of 84 and 76 respectively. The first has never been able to earn an adequate living, has served a sentence for indecent assault and is a semi-permanent inhabitant of county homes; the second has lived a sheltered life with poor but indulgent relatives and has only held simple employment for three months in his lifetime. A total of two males and six females, whose intelligence is within the normal range, have been examined and assessed psychometrically. Access to one male patient was denied.

Parsons (1950) postulates that achondroplasia and Morquio's disease are merely different manifestations of chondrodysplasia, while Warkany and Mitchell (1934) tend to substantiate this by describing an intermediate form. Early writers believed Morquio's disease to be associated with normal intelligence, but more recently cases have been reported with mental defect (Ruggles, 1931; Farrell *et al.*, 1942; Benda, 1952). A close relationship between Morquio's disease and gargoylism has long been recognized, and indeed Washington (1940), Ullrich (1943) and de Rudder (1943) express the opinion that the conditions are similar if not identical.

We suggest therefore that achondroplasia, gargoylism and Morquio's disease are different forms of chondrodysplasia. All three may be familial and hereditary, and the features may vary in different generations of the same family (Böcker, 1942; Parsons, 1950). Vertebral changes are a common factor, and occasionally the process is confined to only some bones, while intermediate types have been described. Mental defect may be evident in any of these disorders, but in Morquio's disease and achondroplasia the mental condition is static, while in gargoylism a progressive deterioration may be superimposed on an existing defect of intelligence as the abnormal metabolite accumulates in the neurones (Ellis *et al.*, 1936; MacGillivray, 1952). Oligophrenia in achondroplasia probably results from the hydrocephalus present in this disorder, which has been discussed above. We were, however, unable to observe any correlation in our cases between the diameters of the skull as measured directly, and the intelligence.

Summary.

The literature on achondroplasic dwarfism is briefly reviewed. The aetiology, pathology and clinical features are discussed. Five mental defectives are reported from a sample of sixteen patients.

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