ACHONDROPLASIA AND HYPOCHONDROPLASIA
CLINICAL VARIATION AND SPINAL STENOSIS

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Forty-eight patients with achondroplasia and 24 with hypochondroplasia have been reviewed in order to clarify the differences between the two disorders and establish the height, body proportions and other clinical and radiological variations within each group. Some of the "classical" findings in achondroplasia are not always present, and hypochondroplasia at its most severe is indistinguishable from achondroplasia at its least severe.

The frequency of spinal stenosis and neurological complications was established in an unselected group of 27 achondroplastic and 12 hypochondroplastic patients aged 10 years and over. Only three of the former were free of symptoms but only three developed serious complications (11 per cent). Measurement of radiographs of the lumbar canal did not in general correlate well with the severity of spinal stenosis symptoms, but it was found that the ratio of interpedicular distances at the first and fourth lumbar vertebrae had some value. Neurological complications were rare in patients with simple narrowing of the spinal canal or with persistence of a thoracolumbar kyphos but when these occurred together there was a high risk of serious neurological involvement.

Achondroplasia has been known for centuries but only for the past twenty years or so has it been appreciated that there are many other types of short-limbed dwarfism. Hypochondroplasia was first reported in the English literature by Beals (1969). The features are similar to those of achondroplasia but are less severe and are usually stated not to involve the skull.

Achondroplasia is well known and there are reviews by Langer, Baumann and Gorlin (1967) and by Bailey (1970). The short stature is due to short limbs with almost normal length of trunk (Fig. 1). The condition can be diagnosed at birth, and the classical features of a bulging forehead, shortness of limbs, principally in the proximal segments, with the later development of lumbar lordosis and genu varum are well known. Radiographic signs include shortness of the base of the skull with a small foramen magnum, and

Figure 1—Achondroplastic patient aged seven years. Limbs are short compared with trunk, the cranial vault is large, with small facial bones. There is marked lumbar lordosis. Figure 2—Hypochondroplastic patient aged seven years. Limb shortening is less marked than in achondroplasia, and the skull and face appear normal.

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reduced size of the spinal canal throughout its length. The long bones have flared metaphyses, the metacarpals are of equal length giving a "starfish" appearance to the hand and the fibula is disproportionately long. The square ilia, narrow sciatic notch and horizontal sacrum are typical, and the fifth lumbar vertebra appears to be set lower than usual between the ilia, as a result of the lumbar lordosis. These are the classical findings, but Rimoin (1979) indicates that there is more clinical and radiographic variation than is generally described.

Hypochondroplasia was reviewed by Walker et al. (1971) and by Meerson, Iukina and Nechvolodova (1976) and is similar to achondroplasia with the exception of changes in the skull (Fig. 2). Clinical and radiographic abnormalities are less severe, some individuals being radiographically normal, the diagnosis being made on the basis of short stature and abnormal body proportions only. Oberklaid et al. (1979) questioned the separate existence of hypochondroplasia, finding considerable overlap in comparison with achondroplasia, but finally concluded that it probably was a distinct condition.

Both disorders are of autosomal dominant inheritance in the great majority of cases, though most individuals in the community present as new mutations. This gives little chance of studying clinical variation within families (Murdoch et al. 1970). Evidence for their separate aetiology is provided by their separate inheritance; hypochondroplastic patients do not have children with achondroplasia and vice versa. However, McKusick. Kelly and Dorst (1973) reported a family in which the father had achondroplasia, the mother was hypochondroplastic and their child was more severely affected than either parent. This suggested two alleles for the achondroplasia locus in a child who was a compound of both disorders. Kelly reported a similar case in 1974 and one other family is known to the authors.

Gardner (1977) estimated the mutation rate for achondroplasia to be $1.4 \times 10^{-5}$, calculating from a total of 242,257 births from the United Kingdom (Edinburgh and Manchester), USA (Jersey City) and Sweden (Uppsala), with a population incidence of mutant achondroplasia of $2.9 \times 10^{-5}$. Oberklaid et al. (1979) from Victoria, Australia, calculated a mutation rate for achondroplasia of $1.93 \times 10^{-5}$, but were unable to estimate a rate for hypochondroplasia because the overlap between this and normality on the one hand and achondroplasia on the other, made ascertainment difficult and inaccurate. There are likely to be many individuals in the population with unidentified hypochondroplasia.

Skeletal growth in achondroplasia has been investigated by Ponseti (1969), Nehme, Riseborough and Tredwell (1976) and Horton et al. (1978). Endochondral ossification is faulty whereas membrane bones develop normally. Nehme and her colleagues noted that the skeletal age was generally below the chronological age until the adolescent growth spurt, at which stage rapid maturation occurred. They pointed out that standard techniques of assessment of skeletal age cannot be applied in achondroplasia. The predicted height for achondroplastic males is 132 centimetres and for females 122 centimetres; the range for hypochondroplastics is from 127 to 152 centimetres.

**Spinal stenosis and neurological complications.** The foramen magnum and whole spinal canal are reduced in diameter in achondroplasia, but less so in hypochondroplasia. Nearly all achondroplastic patients have a disproportionately large cranial vault with a bulging forehead, though hydrocephalus requiring drainage is only an occasional feature. Spinal symptoms with neurological complications are frequently reported, though clearly these are self-selected by the need to attend hospital (Schreiber and Rosenthal 1952; Cohen, Rosenthal and Matson 1967; Nelson 1972; Özzer 1974; Lutter and Langer 1977). Tetraplegia occasionally develops, but upper limb signs are not common. Problems more often arise from narrowing of the spinal canal in the thoracolumbar and lumbar regions, with symptoms of spinal stenosis sometimes progressing to paralysis.

The first aim of the current survey was to review an unselected group of achondroplastic and hypochondroplastic patients in an attempt to clarify the differences between them and to determine the range of abnormality of height and body proportions and of radiographic appearance. The second aim was to establish the frequency of spinal problems and their neurological complications in patients over the age of 10 years, with particular reference to early symptoms and signs.

**MATERIALS AND METHODS**

Seventy-two patients were traced from the records of eight hospitals, 48 with achondroplasia and 24 with hypochondroplasia. Sixty-six were index patients and six were affected relatives. (An effort was made to trace every individual aged 10 years and over at the time of the survey and the records of 58 achondroplastic patients were identified, of whom 27 were examined. Twenty-one could not be traced, three were dead and seven refused to take part in the survey, stating in each case that they were perfectly fit and did not wish to attend hospital.) The records of 20 hypochondroplastic patients over the age of 10 years were identified, 12 were examined, six not traced and two refused to take part in the survey. Many patients in both groups had attended hospital only for the purpose of diagnosis, and had no complaints other than that of short stature.

Patients not at first willing to come to hospital were visited in their homes, and a pedigree and family history obtained. All patients were later examined at hospital and for those aged 10 years and over information was
collected relating to spinal stenosis. Radiographs of the lumbar spine and of the pelvis were obtained, and of other regions if existing radiographs were inadequate for diagnosis.

RESULTS

Genetics and family history. There was only one affected relative (a mother) of 47 achondroplastic index patients. Of 19 hypochondroplastic index patients, three had mothers affected with the same disorder, and in a fourth family the father and one sister were affected. All relatives had the same diagnosis as the index patients, at about the same severity.

There was no instance of consanguinity. Three achondroplastic patients had a twin, all three were dizygous and unaffected. The mean age of fathers in the achondroplastic group of new mutants was $35.61 \pm 0.82$ years. On average the fathers were $4.31 \pm 0.52$ years older than the mothers, significantly older than the normal mean of 2.3 years (England and Wales) or 2.79 years (Edinburgh) ($0.01 > P > 0.005$). In hypochondroplasia the mean paternal age of new mutants was $31.89 \pm 2.41$ years, only $2.75 \pm 0.91$ years older than the mothers. The paternal age effect in achondroplasia was not so marked as in the Northern Ireland survey of Stevenson (1957), where fathers were 7.2 years older than the mothers on average. There was no significant paternal age effect in hypochondroplasia.

There were no other unexpected findings in the family or maternal histories; the proportions of stillbirths and abortions were normal, and there were no associated developmental anomalies of note either amongst the index patients or their relatives.

Clinical and radiographic variation. It is usually stated that the skull is normal in hypochondroplasia, but the radiograph in Figure 4, although not so obviously abnormal as in achondroplasia (Fig. 3), does show a smaller area for the facial bones when compared with the vault than a normal skull (Fig. 5). During childhood, 14 of the 48 achondroplastic patients (29 per cent) had recurrent severe upper respiratory infections, tonsillitis, otitis media or mastoiditis and some residual deafness. This is thought to be due to the decreased size of the nasal sinuses. No hypochondroplastic patient had these complaints. The supposedly typical hand of achondroplasia with its short metacarpals of equal length was seen in only half of the patients (Fig. 6). All hypochondroplastic patients had normal hands. The ilia in achondroplasia probably appear square because of the pelvic tilt and increased lumbar lordosis. The neck of the femur shows a characteristic splayed metaphysis, which is always obvious in the child with achondroplasia, but less obvious in the adult (Figs 7 and 8). The pelvis in hypochondroplasia is almost normal though pelvic tilt and lumbar lordosis may be present (Fig. 9). The characteristically long fibula in achondroplasia and in hypochondroplasia is compared with the normal in Figures 10 to 12. This sign was present in all

Fig. 6
Hand of achondroplastic patient aged nine years. "starfish" in shape with nearly equal length of metacarpals. This is present in only half the patients. Splaying of the radial and ulnar metaphyses is always present, sometimes with cupping.

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achondroplastic patients and three-quarters of those with hypochondroplasia. Marked genu varum was present in 15 per cent of achondroplasts and eight per cent of hypochondroplasts.

Anteroposterior radiographs of the lumbar spine may show the characteristic reduction of distance between the pedicles from the first to the fifth vertebrae (Figs 13 to 15), but this was not found in every patient. Hypochondroplasia at its most severe overlapped with achondroplasia, and at its least severe with normality. Interpedicular distance was measured at the first and the fourth lumbar vertebrae since estimation at the fifth vertebra was difficult and inaccurate. The ratios found are shown in Table I. Normal distances between pedicles have been reported by Hinck, Clark and Hopkins (1966), and their figures agree with those of our control group. About 69 per cent of all achondroplastic patients show narrowing, 41 per cent of normal individuals exhibit widening between L1 and L4, but achondroplastic, hypochondroplastic and normal individuals may all have equidistant measurements between the pedicles.

Two of the 27 achondroplastic patients aged 10 years and over (seven per cent) had developed thoracic scoliosis during the middle years of childhood, one of whom was untreated with a curve of under 30 degrees at the end of growth. The other child required correction with Harrington rod instrumentation.

Table I. The ratio of the distances between pedicles at L1 and at L4 in three groups of patients.

<table>
<thead>
<tr>
<th>Group</th>
<th>1.79–1.10 (narrowed)</th>
<th>1.09–0.90 (parallel)</th>
<th>0.89–0.70 (widened)</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Per cent</td>
<td>Number</td>
</tr>
<tr>
<td>Achondroplasia</td>
<td>33</td>
<td>68.7</td>
<td>15</td>
</tr>
<tr>
<td>n = 48</td>
<td></td>
<td></td>
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<tr>
<td>Hypochondroplasia</td>
<td>4</td>
<td>10.7</td>
<td>20</td>
</tr>
<tr>
<td>n = 24</td>
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<tr>
<td>Controls</td>
<td>0</td>
<td></td>
<td>45</td>
</tr>
<tr>
<td>n = 78</td>
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Fig. 7 — Achondroplastic patient aged five years showing the square ilia, small sciatic notches and normal capital femoral epiphyses with splayed metaphyses. Figure 8—Adult achondroplastic patient with marked lumbar lordosis but no metaphyseal abnormality at the neck of the femur. Figure 9—Pelvis of adult hypochondroplastic patient. There is some lumbar lordosis, but no other abnormality.

Fig. 10 and 11—A long fibula is characteristic of both achondroplasia and hypochondroplasia. Figure 12—Normal knee for comparison.
Lateral radiographs of the lumbar spine show a transition from achondroplasia through hypochondroplasia to normality (Figs 16 to 18). In early infancy one-half of the achondroplastic patients had a thoracolumbar kyphos, but the great majority recovered fully between the ages of two and four years, only five of the 27 examined at 10 years of age and over (19 per cent) having a residual kyphos with wedged vertebrae (Figs 19 to 21). No hypochondroplastic patient was recorded as having a kyphos at any age.

**Height and body proportions.** The heights in achondroplasia and hypochondroplasia are shown in Figure 22. There is overlap between the two groups, though hypochondroplastic patients are generally taller. The male with achondroplasia is taller than the female (Fig. 23) (mean for males 132.2 ± 1.6 centimetres and females 123.9 ± 1.06 centimetres). Limb shortening is shown in Figures 24 and 25 and is less marked in hypochondroplasia than in achondroplasia. The trunk height was almost normal.

**Bone maturation.** Special radiographs were not taken to determine bone maturation, but from existing radiographs it was apparent that few patients showed any significant delay, some being as much as two years ahead of their chronological age. At adolescence more patients with hypochondroplasia showed skeletal immaturity than those with achondroplasia, though this was not apparent at an earlier age. In achondroplasia the epiphyses around the knee most frequently showed delay in maturation. This delay was over two years in six of the 31 patients for whom radiographs were available (19 per cent).

**Spinal stenosis.** For this part of the survey 27 patients with achondroplasia and 12 with hypochondroplasia were studied. They were aged 10 to 34 (mean 20 years). Symptoms were graded as mild (occasional pain or
paraesthesia only); moderate (persistent pain, paraesthesia or weakness); or severe (paralysis). Only three achondroplastic patients (11 per cent) were free of symptoms, nine (33 per cent) had mild symptoms, 12 (44 per cent) moderate, and three, aged 10, 10 and 13 (11 per cent) had severe symptoms. One of the three developed paralysis of the lower limbs between the ages of 10 and 11, and after investigation for spinal stenosis, recovered spontaneously with rest. The second patient developed severe backache between the ages of 10 and 11 with persistent paraesthesiae and weakness of the right leg. The back and leg pain occurred after walking only 10 yards and was relieved by rest. She had no treatment at this stage, but at the age of 18 and again at 19 years of age decompression was carried out. This was not successful and at the age of 24 she is confined to a wheelchair. The third patient developed severe symptoms of spinal stenosis between the ages of 13 and 14 years. Decompression was successful and at 16 he remains free of symptoms.

Eight of the 12 hypochondroplastic patients were free of symptoms, three had mild and only one had moderate symptoms. None had ever had a neurological problem. Symptoms in the upper limb were unusual and minimal in both achondroplasia and hypochondroplasia.

It was hoped that measurements of radiographs of the lumbar spinal canal as described by Jones and Thomson (1968) would correlate with the symptoms of spinal stenosis, but the measurements were difficult to make, particularly on the lateral view, and the trefoil shape of the spinal canal in some individuals must also make for inaccuracy (Eisenstein 1980). The ratio of distances between the pedicles at the first and the fourth lumbar vertebrae is shown in Figure 26. The wide range found in achondroplastic patients contrasts markedly with hypochondroplasia and normal controls, although again, no correlation with the severity of symptoms of spinal stenosis could be found. The more helpful warning sign of potential neurological complication was a narrowed lumbar canal together with a persistent thoracolumbar kyphos. There were five patients over the age of 10 years who had a residual lumbar kyphos with wedged vertebrae. Two of them were free of symptoms at 11 and 13 years (with L1 to L4 ratios of 1.40 and 1.06). One had moderately severe symptoms...
(L1 to L4 ratio 1.40), and the remaining two had serious neurological problems (L1 to L4 ratios 1.59 and 1.30). In the presence of a persistent lumbar kyphos, complications are more likely if the interpedicular narrowing is severe, perhaps with an L1 to L4 ratio of 1.3 or more. It seems to be unusual for either kyphos or narrowing by itself to lead to neurological complications. Only one patient without a persistent lumbar kyphos had serious neurological problems, and he had the highest L1 to L4 ratio found, at 1.79. His symptoms settled with rest, but he is still only 15 years old.

DISCUSSION

It seems likely that achondroplasia and hypochondroplasia are two separate conditions, each exhibiting clinical and radiographic variation. Hypochondroplasia at its most severe overlaps with achondroplasia, and at its least severe with normality. The clinical diagnosis of hypochondroplasia is made on short stature with disproportionately short limbs compared with the trunk. There is no invariable clinical or radiological feature which will distinguish hypochondroplasia from achondroplasia and the only firm evidence for delineation into separate conditions is genetic. The survey confirmed the likelihood of autosomal dominant inheritance. Although most patients were new mutants, when there was an affected first-degree relative he was always of the same type as the index patient. No achondroplastic patient was related to a hypochondroplastic family or vice versa.

Orthopaedic complications in achondroplasia include persistent kyphos (19 per cent of those over 10 years of age), scoliosis (seven per cent of those over 10 years), and genu varum (15 per cent). Hypochondroplastic patients rarely had problems, other than genu varum in eight per cent. No good correlation could be found between measurement of radiographs of the lumbar spinal canal and the severity of symptoms. Measurement by ultrasound, as described by Porter, Wicks and Ottewell (1978) would be of interest. However, it was found that the ratio of interpedicular distances at the first and at the fourth lumbar vertebrae was of some value. Those patients showing a high ratio (marked narrowing at L4) who also had a residual kyphos and wedging of lumbar vertebrae were more at risk of developing neurological complications than those with only one of these signs. If there is already severe narrowing of the lumbar canal, then any further reduction in its diameter is clearly dangerous, and this could be produced by kyphosis, scoliosis, a prolapsed intervertebral disc (not seen in this series) or by any other space-occupying lesion.

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ACHONDROPLASIA AND HYPOCHONDROPLASIA