AN IRREGULAR, FAMILIAL CHONDRO-OSSEOUS DEFECT

With Suggestions Concerning the Nomenclature of the Generalised Osseous Dystrophies

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A tiny deformed white woman (Maria), aged fifty-two years, was discovered knitting strenuously in a surgical ward, having lost her left breast (Figs. 2 and 3). She had always been labelled achondroplastic but one immediately had to doubt that diagnosis. She was a bright, intelligent, normal-headed, hunchbacked, knock-kneed dwarf, waddling round the ward with difficulty on short legs and severe club-feet, dexterously manipulating the finest needle and thread with stumpy little fingers attached to short forearms. Her limb joints, particularly the knees and ankles, were swollen and the normal bony contours largely unrecognisable, the disorganisation producing marked limitations of movement (Table I). Gross knock-knee was caused by extraordinary angulation of the right joint. The dwarfism (height 4 feet 1 inch) was partly vertebral with kyphoscoliosis, but mainly of short-limb type, as the measurements in Table I show. Considering her severe deformities and limitation of movement she was remarkably agile. She was able to touch her toes without bending her knees despite complete absence of movement in the lumbar region.

Her brother Daniel, aged fifty-six years, is shown in Figure 4, in which he is seen "standing" as straight as he could. His height in this position was 4 feet. He had similar shortened limbs and fingers, even worse club-foot and much grosser limitation of movement of hips and knees (greatest extension of these joints shown in Figure 5). There was no movement at all at the shoulders except forwards, and Figure 6 shows, as well as the scoliosis, the limit of elevation of the arms. Again, the knees were grossly disorganised and the patellae could be felt laterally (Fig. 18).

FIG. 1

Family history. The black signs indicate the three affected siblings. The ringed figures indicate the number of unaffected offspring.

The eldest sister (Louise), aged sixty-two years, was less severely affected (Fig. 2). She was 4 feet 6 inches tall. She also had gross club-feet and needed crutches to get about, but her limitation of movement was less and her spine was quite straight and clinically normal. Her limbs were short (Fig. 7). Her knees were also swollen and the patellae dislocated laterally (Fig. 8).

Family history (Fig. 1)—These people believed that their deformity had been present since birth—their parents had told them so. Daniel had never been able to walk unaided, but

FIG. 2

The three affected siblings, Maria, Louise and Daniel, photographed with a normal brother.

FIG. 3—Maria.

FIG. 4—Daniel.

Louise could do so until she was twelve years old. No other abnormalities have been found and all three have retained excellent health. Further siblings are four normal brothers and one normal sister. The youngest brother, shown in Figure 2, is 5 feet 9 inches in height, and two

FIG. 5

FIG. 6

Daniel—Note in Figure 5 the flexion deformity of hips, knees and elbow; and in Figure 6 the kyphoscoliosis. The shoulders are abducted to their fullest extent.

FIG. 7

FIG. 8

Louise—Figure 7 shows marked shortening of forearms and hands. Figure 8 shows the gross deformity of both feet. The patellae are displaced laterally.

elder brothers are over 6 feet. The parents (mother 6 feet, father 5 feet 10 inches), grandparents and great grandparents are believed to have been normal, and there have been no affected members in collaterals despite considerable prolixity (Fig. 1). The deformed sibs have never married. There was no consanguinity in any marriage in the family.

The appearance of three abnormal mixed-sex siblings to normal parents suggests a type of inheritance which is either fully recessive or dominant with incomplete penetrance. The latter is unlikely in view of the large number of unaffected ascendants and collaterals and it seems most probable that we are here dealing with a recessive pedigree, despite the absence of cousin marriages and the ratio of affected to unaffected sibs being 3:5 instead of the theoretical 1:3.

TABLE I
PHYSICAL DATA IN THREE AFFECTED SIBLINGS AND ONE NORMAL SIBLING

Body measurements (in inches)	Maria	Daniel	Louise	Normal brother
Height	49	49	54	69
Head circumference	22	22	22	22
Sitting height	31	31	32	36
Crown—umbilical length	23	24	—	24
Umbilical height	26	? { flexed hips }	32	45
Xiphisternal height	30	? { prevent }	—	50
Anterior superior iliac spine—knee joint	15	? { measurement }	15	17–18
Humerus (approximately)	9	9½	8	12½
Ulna (approximately)	5½	7	6	10½
Radius (approximately)	5	6	5½	9
Middle finger (web—tip)	2½	2¾	2½	3¼
Femur (trochanter—knee joint)	12½	11½	12½	16
Fibula (approximately)	10½	11	12½	15
Foot (heel—tip of great toe)	6	7	—	10
Joint movements				
Spine	Excellent lumbar. Nil thoracic	Stiff throughout	Normal	
Shoulders	Mild general restriction	Nil except anterior	Normal	
Elbows	10° limitation of extension	15° limitation of extension	Normal	
Hips	Flexion and extension free	110° extension only (i.e. permanently flexed by 70°)	120° extension only	
Knees	10° limitation of extension	90° extension (i.e. permanently flexed at right angle)	100° extension only	

Radiographic examination (of Maria and Daniel)—The skulls of both Maria and Daniel are normal. The shoulders, elbows, hips and knees show, in general, great irregularity of joint surface and surrounding bone with local hypertrophy and utterly abnormal shapes, diminution of joint space, osteoarthritis and some rarefaction (Figs. 9 to 18). In addition, there are large extraneous calcified bodies near to Daniel's shoulders which are either loose bodies or calcifying chondromas (Fig. 15); because of the total immobility of these joints it was impossible to take further radiographs to settle their exact nature. It appears that the head of his humerus has fused with the acromion process. At the knees the patellae are dislocated laterally, and the lower leg is rotated through 90 degrees so that the fibula comes to lie posteriorly (Fig. 18). The radii of both subjects are bowed; the forearms are short compared to the humeri; the metacarpals and phalanges short and stumpy, but not grossly irregular (Figs. 13 and 17). Both spines show gross kyphoscoliosis; in the case of Maria the appearance in the lateral radiograph (Fig. 10) resembles that of Morquio's disease in its flattened vertebral bodies (platyspondyly) with irregular anterior, superior and inferior

FIG. 9

FIG. 10

FIG. 11

FIG. 12

Maria. Figure 9—Right humerus. Figure 10—Spine showing platyspondyly and osteoarthritis. Figure 11—Right knee, and Figure 12—Left knee, showing irregularity and rotation deformity.

FIG. 13

FIG. 14

Maria. Figure 13—Right elbow and forearm. Note irregularity of elbow joint, short forearm bones and stumpy metacarpals. Figure 14—Hip joints showing gross irregularity of upper ends of femora, with subluxation and degenerative changes.

FIG. 15
Daniel—Left shoulder showing deformity of upper end of humerus and of glenoid and acromion.

FIG. 16
Daniel—Spine showing kyphoscoliosis.

FIG. 17
Daniel—Left elbow and forearm. Note disorganisation of elbow and shortening of forearm bones.

FIG. 18
Daniel—Antero-posterior radiograph of right knee showing rotation deformity and lateral dislocation of patella.

margins not entirely accountable by osteoarthritis, with irregular increase of intervertebral space and rarefaction. But unlike Morquio's disease is the absence of any anterior tongue-like projections. Finally, the fibulae are perhaps shortened and the feet require no comment. In general the bony trabeculation is coarsened and irregular, particularly around the deformed epiphyses, and rarefied in parts.

DISCUSSION

Nature of the dystrophy—After examining these siblings I first tried to fit their condition into a recognised syndrome, but it was soon evident that they represented an irregular chondro-osseous dystrophy, possibly unique. It resembles achondroplasia superficially in its dwarfism, short limbs, waddling gait and brachydactyly; but the normal skull, the articular and vertebral irregularities, the high humero-ulnar ratio, club-foot and the lack of a dominant pedigree (*cf.* Mörch 1940) invalidate that diagnosis.

The resemblance to the Morquio-Brailsford osteochondrodystrophy is closer, with the normal skull, irregular epiphyses and enlarged joints, irregular vertebral bodies with kyphoscoliosis and platyspondyly, coxa vara, short limbs and fingers, generally coarse bony trabeculation and osteoporosis, and the probable recessive nature of the inheritance. On the other hand, the dwarfs did not have the external appearance of the Morquio dystrophy, particularly Louise, with her clinically normal spine yet grossly deformed joints. Club-foot is not a feature of the Morquio dystrophy, and the joint spaces are characteristically increased rather than diminished.

Dysplasia epiphysialis multiplex (Fairbank 1947) is suggested by the short limbs and the stumpy fingers, the epiphysial irregularities with reasonable acetabula, the normal skull and teeth. But in dysplasia epiphysialis multiplex the spine is normal (except in Jansen's case, which is included under this head by Fairbank), there is no club-foot, and the actual appearance of the swollen epiphyses of the present family is not quite like those in published cases of epiphysial dysplasia, even allowing for the osteoarthritis.

The bowed radius is reminiscent of diaphysial aclasis (Keith 1919), while Brailsford (1935) reported a family of four siblings with much grosser radial bowing which he classified, rather doubtfully, as atypical achondroplasia. Lance (1927) reported the single case of a child of sixteen months with platyspondyly and club-foot.

A plea for a simplified classification of generalised osseous dystrophies—The present family represents one of the several "irregular osteochondrodystrophies," each of which has certain unique features although most authors have attempted to thrust their described case or family into a recognised group or to give it another long and confusing name of its own. Gates (1946) suggested that these dystrophies might be due to sectional deficiency in a chromosome causing irregular crossing over and so giving rise to various types of familial deformity. Many of these "irregular dystrophies" are, in fact, in some ways intermediate between two recognised syndromes: for example, between achondroplasia and Morquio's disease such as the cases of Warkany and Mitchell (1934), of Silverskiöld (1925), and the "achondroplasiacs with spinal changes" (Parsons *et al.* 1936); between Morquio's disease and multiple epiphysial dysplasia (Jansen 1934); between dyschondroplasia, achondroplasia and Morquio's disease (Dwyer 1932); between Morquio's disease and gargoylism (Ruggles 1931, Snoke 1933); between the absence of single bones and osteodental dysplasia (cleidocranial dysostosis); between single ivory osteoma and multiple exostoses (type Keith); between osteopetrosis and osteogenesis imperfecta (Brailsford 1935); between osteopetrosis and melorheostosis (Wakeley 1931); between osteostriata and osteopoikilosis (Lindbom 1942); and all the gradations from unilateral enchondromatosis (type Ollier) to multiple exostoses (type Keith).

Certainly there are well recognised time-honoured entities such as achondroplasia and osteogenesis imperfecta in which each new case usually reproduces the classical features.

Nevertheless the suspicion arises that the various osseous dystrophies do not necessarily fall into watertight compartments, but allow of overlapping, the one with the other, in certain cases. This suggestion is strengthened by a brief examination of points of similarity between several of the recognised syndromes. Thus we see the similarity of the spines of Morquio's disease and gargoylism (incidentally the anterior surfaces of the vertebral bodies in Morquio's very first case show both central tongue projection and inferior beaking); the depressed nasal bridge of gargoylism, of achondroplasia and some cases of Morquio's disease; the thick stumpy phalanges and metacarpals in achondroplasia, Morquio's disease, gargoylism and multiple epiphyseal dysplasia; extra metacarpal epiphyses in achondroplasia, Morquio's disease and cleido-cranial dysostosis; the joints of multiple epiphyseal dysplasia, of gargoylism and less severe cases of Morquio's disease; the histological similarity between achondroplasia and dysplasia epiphysealis punctata (Harris 1933); shortening of ulna with bowing of radius which may occur in several types; some cases of Morquio's disease with short thick humeri and femora like those of achondroplasia. Differences in mode of inheritance do not necessarily separate different groups, since the distinction between recessiveness, sex linkage and dominance appears no longer clear cut (Gates 1946). The same gene appears to be able to behave as a dominant in one family, recessive in another, and in a third may cross over to an X-chromosome and become sex-linked. Morquio's disease is probably inherited in all three ways. Certainly there are marked clinical, prognostic and pathological differences between the main chondro-osteodystrophic syndromes, but the attempt to separate out more and more of these as distinct diseases with new and confusing names is, I suggest, not scientifically justifiable. The names already are awkward enough, and frequently do not accurately describe the conditions to which they are applied. Who, from the names, could deduce the difference between: achondroplasia, dyschondroplasia, chondrodysplasia, chondrodystrophy, chondro-osteodystrophy, chondrodystrophia ossificans, chondrodystrophia calcificans congenita, osteogenesis imperfecta, dysostosis multiplex, periosteal dysplasia, osteopsathyrosis, melorheostosis, osteochondropathia, diaphyseal dysplasia and mutational dysostosis?

For these reasons a simplification of classification and nomenclature of the generalised developmental osseous dystrophies seems highly desirable, somewhat on the following lines (the more important clinical syndromes are shown in heavy type):

Cartilaginous Defect (Affecting Cartilage Bone Only)

DIAPHYSAL ONLY (displaced islands of cartilage cells)

Multiple enchondromata (type Ollier)

(Usually not hereditary; mainly unilateral; shortening and enlargement of long bones; with or without multiple haemangiomas)

Multiple exostoses (type Keith).

(Strongly dominant; symmetrical dwarfing; short ulna and bowed radius)

Mixed, incomplete, and intermediate types.

METAPHYSAL DYSPLASIA

Type Jansen (see Fairbank 1948)

(Extremely rare dysplasia, confined to metaphyses).

EPIPHYSAL ONLY

Multiple epiphyseal dysplasia (type Fairbank 1947)

(Dwarfing; irregular mottled epiphyses of limb joints).

Stippled epiphyses (type Fairbank 1927)

(Extreme stippling of multicentric epiphyses; with or without congenital cataract).

? *Intermediate types.*

WHOLE BONE**Achondroplasia***Type Parrot*

(absence of zone of provisional chondral calcification; strongly dominant; present before birth; frequent foetal death; classical features, but normal bony pattern).

Atypical types (e.g., unilateral, types with normal skull, recessive inheritance, the Ellis-van Creveld syndrome, etc.).

Type Morquio (all degrees of severity)

(Recessive or sex-linked; develops after birth; spine is characteristic; coarsened and irregular bone pattern).

Intermediate types (Warkany and Mitchell 1934, Silverskiöld 1925).

Gargoylism*Type Hunter-Hurler*

(Recessive; storage disease; mental defect and corneal opacity).

Incomplete types.

Intermediate types (Ruggles 1931).

Irregular types (present family).

Defect in Ossification (Affecting Cartilage and Membrane Bone)**Osteogenesis imperfecta**

Types Vrolik (early) and *Lobstein* (late)

(? Deficiency of osteoblastic activity (Knaggs 1924); brittle bones; blue sclerotics and otosclerosis; variably combined, with dominant inheritance).

Atypical types (unilateral, cystic, etc.).

Increased bone density (? deficiency of osteoclastic activity)**Osteopetrosis**, or *type Albers-Schönberg I*

(Recessive or irregular dominant inheritance; widespread loss of differentiation between cortex and medulla; association with anaemia, fractures and cranial nerve compression).

Spotted bones, osteopoikilosis or type Albers-Schönberg II

(Dense spots in spongiosa; no disability; with or without dermatofibrosis lenticularis disseminata).

Type Léri ("melorheostosis")

(Bands of dense bone at ends of long bones; usually only one limb affected.)

Osteotriata (type Voorhoeve)

(Generalised streaking of long bones; no disability.)

Irregular or intermediate types.

Intermediate types (e.g., Brailsford 1935)

Osteodental dysplasia (see Jackson 1951)

"*Cleido-cranial dysostosis*" (Marie and Sainton 1897)

(Defect of calcification of teeth, membrane and some cartilage bones; strongly dominant.)

Incomplete types—e.g., with normal clavicles; "*Peripheral dysostosis*" (Brailsford 1944);

"*Cleidal dysostosis*" (Baer 1948).

There are certainly difficulties with a classification of this kind. Osteotriata, for instance, shows certain affinities to Ollier's disease and would possibly be more correctly classified with the cartilaginous diaphysial defect group. The "enchondromata" of Ollier's disease are not neoplasms. Perhaps other syndromes, such as polyostotic fibrous dysplasia and the skeletal types of neurofibromatosis should be included. The grouping is not intended as a complete or final classification, but as a suggestion for clarifying the ordinary person's conceptions, simplifying the general nomenclature and rendering easier the teaching of these conditions.

SUMMARY

Three elderly sibling dwarfs are reported from a large and otherwise normal family. Their condition is an unusual and irregular form of cartilaginous defect, combined with club-feet, and bearing some resemblance to the Morquio type.

A brief consideration of the literature of the generalised developmental bony syndromes shows confusion of thought and nomenclature. A plea is therefore made for simplification and a rational and simple grouping of these conditions is attempted. It seems particularly desirable that many confusing names for particular syndromes should be scrapped (for example, dyschondroplasia, chondro-osteodystrophy), although quite evidently the terms achondroplasia and osteogenesis imperfecta must remain because of their long-standing and general usage. Incidentally I have suggested elsewhere (Jackson 1951) that the name cleido-cranial dysostosis should be dropped, because it tends to lead the investigator away from the clinically more important lesions in the teeth and the cartilage bones of the pelvis and legs. It seems reasonable to confine the nomenclature of these various syndromes to the names used in the above classification, or something on those lines.

I am pleased to express my thanks to Professor Forman and Professor Erasmus for their continued help and interest; to Mr McManus of the Department of Surgery for the photographs; and to the radiologists and radiographers of Groote Schuur Hospital.

REFERENCES

- ALBERS-SCHÖNBERG, H. (1904): *Muenchener Medizinische Wochenschrift*, **51**, 365.
 ALBERS-SCHÖNBERG, H. (1915): *Fortschritte auf dem Gebiete der Roentgenstrahlen*, **23**, 174.
 BAER, R. W. (1948): in *Brennemann's Practice of Pediatrics*, Vol. 4.
 BRAILSFORD, J. F. (1935): *British Journal of Radiology*, **8**, 533.
 BRAILSFORD, J. F. (1944): *Radiology of Bones and Joints*. Third edition. London: J. & A. Churchill Ltd.
 DWYER, H. L. (1932): *American Journal of Diseases of Children*, **44**, 776.
 ELLIS, R. W. B., and VAN CREVELD, S. (1940): *Archives of Disease in Childhood*, **15**, 65.
 FAIRBANK, H. A. T. (1927): *British Journal of Surgery*, **15**, 120.
 FAIRBANK, H. A. T. (1947): *British Journal of Surgery*, **34**, 225.
 FAIRBANK, H. A. T. (1948): *Journal of Bone and Joint Surgery*, **30-B**, 689.
 GATES, R. R. (1946): *Human Genetics*. Two Vols. New York: Macmillan Company.
 HARRIS, H. A. (1933): *Bone Growth in Health and Disease*. London: Oxford University Press.
 HUNTER, C. (1917): *Proceedings of the Royal Society of Medicine (Section for the Study of Disease in Children)*, **10**, 104.
 HURLER, G. (1919): *Zeitschrift für Kinderheilkunde*, **24**, 220.
 JACKSON, W. P. U. (1951): *Acta Medica Scandinavica*, **139**, 292.
 JANSEN, M. (1934): *Zeitschrift für orthopädische Chirurgie*, **61**, 253.
 KEITH, A. (1919): *Journal of Anatomy*, **54**, 101.
 KNAGGS, R. L. (1924): *British Journal of Surgery*, **11**, 737.
 LANCE (1927): *Bulletins et Mémoires de la Société Nationale de Chirurgie*, **53**, 132.
 LÉRI, A., and JOANNY (1922): *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, **3. sér.**, **46**, 1141.
 LINDBOM, Å. (1942): *Acta Radiologica*, **23**, 296.
 LOBSTEIN, J. F. (1833): *Traité d'Anatomie pathologique*. Paris: F. G. Levrault, Vol. 2, p. 204.
 MARIE, P., and SAINTON, P. (1897): *Revue Neurologique*, **5**, 394.
 MÖRCH, E. T. (1940): *Journal of Heredity*, **31**, 439.
 MORQUIO, L. (1929): *Archives de Médecine des Enfants*, **32**, 129.
 OLLIER, L. (1899): *Bulletin de la Société de Chirurgie de Lyon*, **3**, 20.
 PARROT, J. (1878): *Bulletins de la Société d'Anthropologie de Paris*, **3. sér.**, **1**, 296.
 PARSONS, L. G. (1936): *British Encyclopaedia of Medical Practice*. Editor, H. Rolleston. London: Butterworth & Co. (Publishers) Ltd. Vol. 1, p. 135.
 RUGGLES, H. E. (1931): *American Journal of Roentgenology*, **25**, 91.
 SILVERSKIÖLD, N. (1925): *Acta Radiologica*, **4**, 44.
 SNOKE, P. O. (1933): *American Journal of Roentgenology*, **29**, 31.
 VOORHOEVE, N. (1924): *Acta Radiologica*, **3**, 407.
 VROLIK, W. (1849): *Tabulae ad Illustrandam Embryogenesin Hominis et Mammalium, tam naturalem quam abnormem*. Amstelodami: G. M. P. Londonck.
 WAKELEY, C. P. G. (1931): *Proceedings of the Royal Society of Medicine (Clinical Section)*, **25**, 145.
 WARKANY, J., and MITCHELL, A. G. (1934): *Journal of Pediatrics*, **4**, 734.