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HEREDITARY MULTIPLE EPIPHYSEAL DISTURBANCES

(Chondro-osteo-dystrophia Brailsford)

BY

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During recent years a large number of publications have appeared, treating cases which, while differing considerably from one another, nevertheless have had multiple disturbances of the epiphyses in common. Many authors have observed these changes in more than one generation, others have found several cases within the same family, while some have not published more than one single case.

The clinical and roentgenological symptoms in the different cases have been just as varied as the hereditary circumstances.

This being so, it is not astonishing that the cases in question have been given different names by different authors. Naturally, they have as a rule tested if and to what extent their own cases have corresponded with those published, but the majority of authors seems to have found the differences greater than the similarities.

The most important and best-known authors in this field are *Brailsford, S. Ribbing* and *W. Müller.*

I have here neither the possibility nor the call to give even a short survey of the main trend of their works.—I shall only make some few observations to give a background for the following discussion and to make this paper easier to follow.

Like the other authors, *Brailsford* ascribes most importance to the roentgenological symptoms. He is of the opinion that they

"indicate degenerative changes in the cartilage and defective ossification." B. divides the disease into 4 degrees of severity: "the dystrophy may affect the spine only, the spine and proximal joints, or the whole skeleton." In the more severe cases the patients become dwarfs, owing to the spinal changes. In the most severe cases it is, says B., "doubtful if such children reach maturity."

It should be observed that, according to B., changes in the smaller joints only occur in the more severe cases. In this connection I should also like to draw attention to B.'s description of the appearance of the changes in the hip joints: "the ossification is irregular, so that islands of ossified cartilage are seen developing throughout the epiphysis and on the ends of the diaphysis. The joint spaces are wider than normal. The neck of the femur and the epiphysis for the head may fail to ossify." Regarding the hereditary circumstances B. says: "a familial distribution has been noted in several cases. Two of the author's cases were sisters." B. considers such cases as described by *Morquio, Dale* and *Wahren*, for instance, to be of the same type as his own.

Ribbing classifies the cases of *Brailsford* and the other authors under the term "Achondroplasia atypica," and thinks that his own cases might possibly come under the highly varied symptomatic picture. If so, R.'s cases must be considered very mild. However, R. finds it most correct to distinguish his own cases from the others, on account of dissimilarities in the patients' build, musculature etc. In this connection R. points out that "Röntgenbilder des Skelettes ähnliche oder sogar übereinstimmende Symptome auf Grund unterschiedlicher Faktoren aufweisen können. Deswegen darf man nicht allein auf Grund einer Gleichheit im röntgenologischen Bild annehmen, dass ein und dieselbe Krankheit vorliegt." As to heredity, R. supposes that the disease in his cases "durch ein recessives Gen, welches als Mutation entstanden ist und zufallsweise eine gewisse Verbreitung erhalten hat, bedingt wird."

W. Müller is of the opinion that "Chondro-osteo-dystrophia

(Brailsford), "Hereditäre multiple Epiphysenstörungen (Ribbing) and the various cases of so-called "Achondroplasia atypica" are in fact variants of the same disease, and proposes as the most descriptive term "Familiäre multiple Störung der Epiphysenverknöcherung."

Contrary to *Brailsford,* M. maintains that the epiphyseal cartilages are normal. It is only a question of "eine reine Störung der Knochenentwicklung." According to M. there is "ein mangelhafter Ersatz der knorpeligen Gelenkenden durch Knochengewebe. Das normale Hereinwachsen von Knochengewebe in die durch das Knorpelgewebe gegebene Gelenkform ist gestört." M. is mostly concerned with the milder forms, and stresses that these are probably relatively common, which is why they are of greater practical importance than the fairly rare severe forms. M. tries to differentiate various types of roentgen picture among the mild forms: "Typus des muldenförmigen Defektes," "Typus der niedrigen aber scharf begrenzten Epiphyse'" "Typus der Mikrosepiphyse."

"Erblichkeit und familiäres Auftreten stellen ein Hauptmerkmal dieses Krankheitsbildes überhaupt dar," says M., but points out that "es ist auffallend, wie häufig bei dieser Erkrankung gerade das Auftreten bei mehreren Geschwistern wiederkehrt, während die früheren Generationen nicht verändert befunden wurden." It is this circumstance that has made M. prefer the term "familial" to "hereditary" when giving a name to the disease.

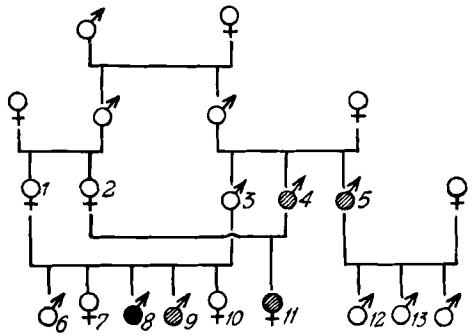
My intention is to describe some cases which I consider to belong to the disease, or group of diseases, in question. The cases come from two different families; the cases in family A. differ considerably from those in family B. both as to roentgenogram and hereditary circumstances. I shall therefore analyze each family separately.

FAMILY A

My investigations started with case E.G., No. 8 in the genealogical table appended. The roentgen findings in this case

prompted me to subsequent roentgenological examination of all the members of the family in so far as this has been possible. As to the remaining members, my data in the genealogical table depend solely on oral communications. All members except No. 8 have been clinically and subjectively free from symptoms.

GENERALOGICAL TABLE A



○ = free from symptoms.
● = affected.
◍ = uncertain symptoms.
The figures denote the persons who have been examined roentgenologically.

No. 1. A.G., born 1905.

Roentgen examination 8.11.41. Pelvis, hip joints, lumbar and lower dorsal spine, finger joints, toe joints, right shoulder, right elbow, right knee: normal.

No. 2. S.G., born 1902.

Roentgen examination 3.1.42. Pelvis, hip joints, dorsolumbar spine, finger joints, toe joints, right shoulder, right elbow, right knee: normal.

No. 3. P.A.G., born 1898.

Roentgen examination 18.11.41. Lumbar and lower dorsal spine: slight scoliosis. Pelvis, hip joints, finger joints, toe joints, right shoulder, right elbow: normal.

No. 4. L.O.G., born 1902.

Roentgen examination 12.11.41. Pelvis and hip joints: slight signs of arthritis in the ileo-sacral joints. Dorsolumbar spine: scoliosis and slight spondylosis deformans. Right shoulder, right elbow, wrists, right knee, finger joints: normal. Toe joints: heads of the first and second metatarsals of the left foot considerably flattened and broadened with markedly irregular joint contours. The spongy structure slightly irregular. Joint space slightly broadened. The roentgen picture corresponds in the main with that found in a so-called Morbus Köhler II.

No. 5. Alb.G., born 1908.

Roentgen examination 8.11.41. *Lumbar and lower dorsal spine:* slight kyphosis in the upper part of the lumbar spine. The vertebral bodies here broad and flat, slightly wedge-shaped. High intervertebral disks. Pelvis, hip joints, right shoulder, right elbow, right knee, toe joints: normal. *Finger joints:* head of the second right metacarpal lacks nearly 1/3 of the ulnar part of the joint surface.

No. 6. R.G., born 1928.

Roentgen examination 1.3.41. Pelvis, hip joints, dorsolumbar spine, finger joints, toe joints, shoulder joints, left elbow: normal.

No. 7. E.G., born 1930.

Roentgen examination 1.3.41; 8.11.41. Pelvis, hip joints, dorsolumbar spine, finger joints, toe joints, right shoulder, right elbow, wrists, right knee: normal.

No. 8. EG., born 1933.

The patient has always been clumsy. He did not begin to walk until at the age of 2, showed bad balance, and fell over readily. He did not like to play with the other children. When the patient began going to school, the symptoms from the legs increased. He limped somewhat with the right leg, most markedly when he came home from school in the afternoon. Improved

after rest.—The patient was admitted to the Karlskrona Hospital Dec. 27, 1940.

General *condition* not satisfactory; somewhat sickly and pale. Mantoux 0.1 mg: negative.

Right hip: definite atrophy of the muscles. In extension to midposition a shortage of 20°, flexion possible to 90°. Rotation as well as abduction completely inhibited. Adduction limited. Movements apparently painless.

Left hip: defect extension as in the right hip. Rotation limited, though less so than in the right hip.—

From the journal 9.4.41. Considerably improved mobility in the hip joints. Abduction and rotation inwards of the right hip still completely inhibited. External rotation 25°, adduction 15°. Left hip: rotation less limited. Painless movements.

6.5.41. Status quo. Discharged to be cared for at home.

Roentgen examinations (30.12.40, 3.3.41, 2.5.41, 8.11.41, 10.11.42 and 2.11.43):

Pelvis: the alae ilei are broad and strong. The true pelvis somewhat hypoplastic. The sacro-iliac joints somewhat wide. No protrusio acetabuli. *Hip joints* (se fig.s 1-2): the femoral neck is enormously thickened. Marked coxa vara, especially on the left side (110°). The epiphyseal border is very irregular, with several small thinner areas distal to it. Above the much protracted epiphyseal border there are, at the site of the epiphysis, a number of small irregular bone islands, whose osseous structure is only vague. A regular external outline, "joint surface," is only found in a small part of the left hip. The distance from this even outline to the acetabulum is considerably greater than the height of the normal joint space. The acetabulum is shallow and the roof sloping. The upper-lateral circumference of the neck and some bone islands in the epiphysis of the head lie outside the lateral acetabular border, which is most marked in the right hip joint. During the 3 years of observation, the bone islands in the femoral epiphyses increased, and merged into larger islands, though without forming any complete external outline, "joint surface." A clear but irregular spongy structure appears. The distance to the acetabulum is very varying in dif-

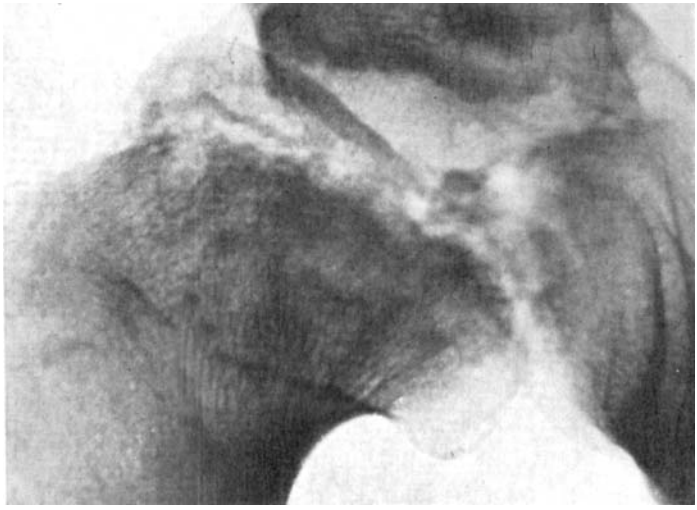


Fig. 1.

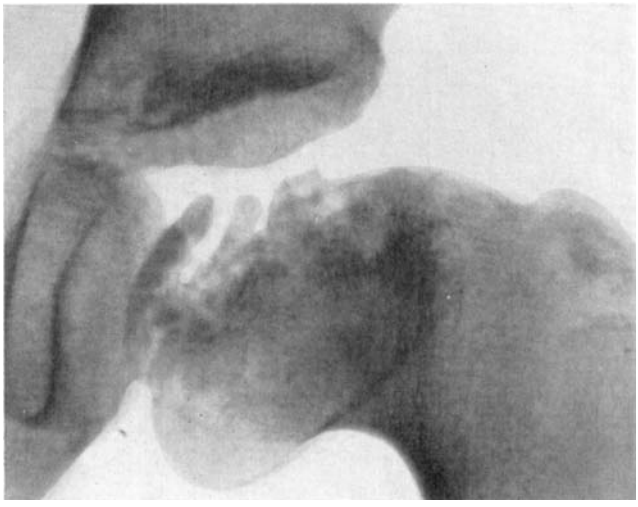


Fig. 2.

ferent places, but is in the main more than normal (see fig.s 3-6).

Dorsolumbar spine, skull, shoulder joints, elbows, wrists, finger and toe joints: normal.

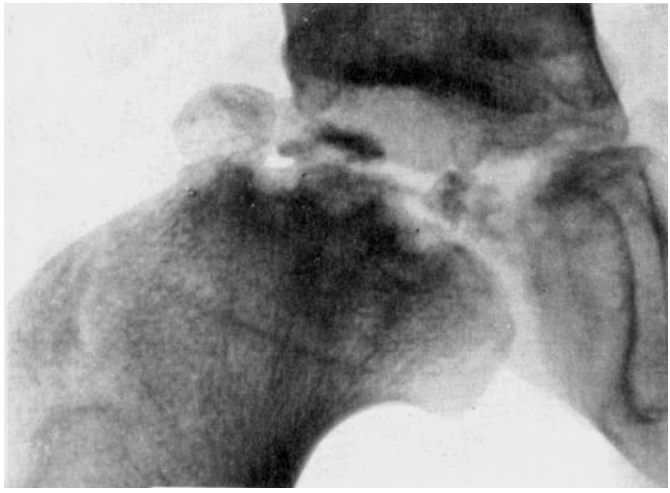


Fig. 3.

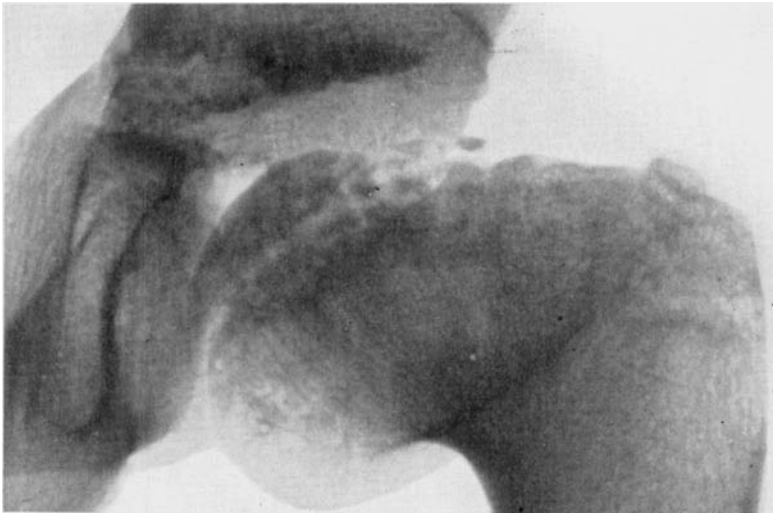


Fig. 4.

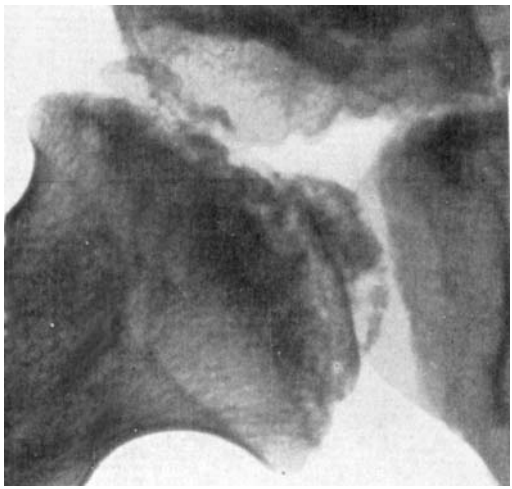


Fig. 5.

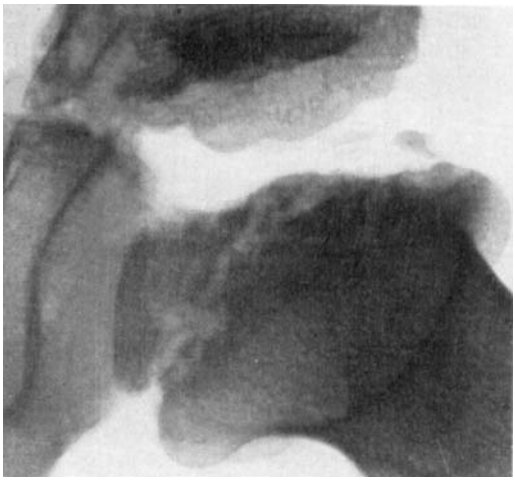


Fig. 6.

No. 9. F.G., born 1935.

Roentgen examinations (1.3.41, 8.11.41, 26.1.43):

Pelvis and hip joints: some irregularity in the central part of the "joint surface" of the head, mainly stationary.—*Dorso-lumbar spine:* small defect in the lower part of the anterior surface of the vertebral body observable in the eleventh dorsal seg-

ment. Left shoulder, left elbow, wrists, finger, knee and toe joints: normal.

No. 10. U.G., born 1938.

Roentgen examination 1.3.41; 10.11.42. Pelvis, hip joints, dorsolumbar spine, wrists, finger and toe joints, left shoulder, right knee: normal.

No. 11. K.G., born 1934.

Roentgen examination 1.3.41: 3.1.42. *Dorsolumbar spine:* in the upper part of the anterior outline there is a little notch in the lower lumbar vertebrae, thus making the body slightly defective.—Pelvis, hip joints, finger and toe joints, right shoulder, right elbow, right knee: normal.

No. 12. P.G., born 1931.

Roentgen examination 27.11.41. Pelvis, hip joints, dorsolumbar spine, finger and toe joints, right shoulder, right elbow, right knee: normal.

No. 13. E.G., born 1934.

Roentgen examination 27.11.41. Pelvis, hip joints, dorsolumbar spine, finger and toe joints, right shoulder, right elbow, right wrist, right knee: normal.

In this family roentgenological and clinical interest is directed exclusively towards one case, No. 8, E.G. We have here a case of pronounced changes in both hip joints, consisting in a considerable disturbance in the development of the femoral epiphysis and of the superior part of the femur as a whole. The roentgen picture corresponds fairly well with that described by *Brailsford* in chondro-osteo-dystrophy. The changes are most pronounced at the time of the first roentgen examination, when the patient was 7 years old, but the improvement during the 3 years of observation is little and slow. The case history suggests that the disturbance in development was present from birth or from earliest infancy. It is especially noteworthy that neither the spine nor the other joints show even the slightest sign of disturbed development. This does not, therefore, agree with *Brailsford*'s notion, according to which the spine is always engaged if the hip joints are affected.

As to the other members of the family, it is chiefly No. 4, L.O.G., a 39-year old man, whose roentgen pictures are of interest in this connection. The changes in the heads of the second and third metatarsals in his left foot do not differ from the roentgen picture in so-called Morbus Köhler II. Nos. 5, 9 and 11 show some slight disturbances, which do not allow of any very definite conclusions as to their connection with the disease, or group of diseases, in question. But, for the sake of completeness, even small deviations from the normal have been noted. As it is extremely important, when judging the hereditary circumstances, that the roentgen examinations be thorough, I have noted in detail what was examined in the different subjects, even in cases where the findings have been normal.

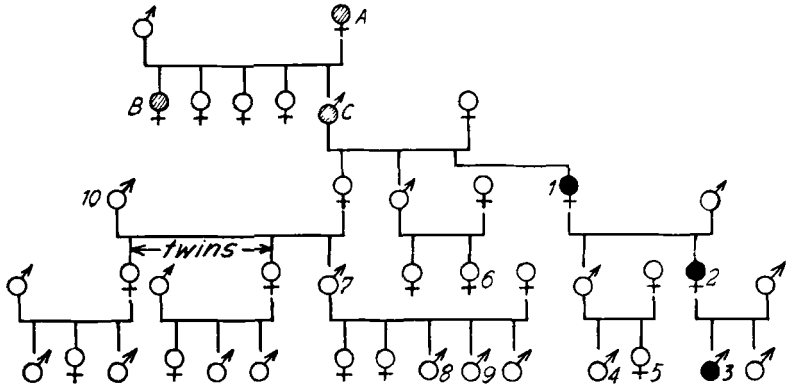
The disease in the hip joint, found in case E.G., can of course not be labelled familial. But neither are there any sure proofs of its being hereditary. If heredity is involved, it must probably be recessive, as both parents are absolutely free from symptoms, and all obtainable data indicate that such was the case in the preceding generation, too. From the point of view of heredity it is also of interest that not only the parents of the sick boy E.G. are closely related, but also the parents of No. 11. In spite of the fact that the father of No. 11, i.e. No. 4, shows the above-mentioned marked changes of Köhler-type in the metatarsals, only quite insignificant disturbances are found in No. 11 himself. If the changes in the metatarsals are of the same nature as the hip disease in question, we should be justified in expecting more definite signs of a disturbed development in No. 11.

FAMILY B

The starting-point of my investigations of this family was the boy K.J.K., No. 3 in the genealogical table. As at the present time nearly all the members of the family live in Stockholm, I have been able to continue my investigations of the family only thanks to the kind assistance of colleagues resident there.

I want here to express my sincere thanks to them for their great helpfulness and understanding.

GENEALOGICAL TABLE B



○ = free from symptoms.
● = affected.
◍ = uncertain symptoms.
The figures denote the persons who have been examined roentgenologically. A, B, C = persons with clinical symptoms, who have not been examined roentgenologically.

I have been able to collect the following data concerning the oldest members of the family, long since dead; they have been denoted with the letters A, B and C in the table.

A., born 1820.

She had severe trouble from the lower extremities, probably mostly in the hips, and was, at least during the latter part of her life, so disabled that she had to use a bath-chair.

B. Eldest daughter of A.

Suffered from so severe trouble in her hips that she was

nearly incapacitated; had to lean on two sticks when walking. She is also said to have had trouble in the fingers, where she had small "nodes." No trouble in the feet. She was rather short of stature.

C., born 1841.

Son of A. He was very short in build. Suffered since youth from severe trouble in the back, interpreted as a form of tuberculosis. No very marked trouble in the hips. Probably no trouble from the other joints.

No. 1. H.W., born 1877.

Moderate trouble in the hip joints from early youth. Walks clumsily. She does not willingly confess to any symptoms, however, and dissimulates quite plainly.

Roentgen examination 18.11.44. Pelvis: normal.—*Hip joints:* in the upper pole of the femoral heads a thinner area, within which the normal structure is nearly effaced. Some smaller, thickened bone trabeculae can be observed there. The border line towards the surroundings consists of a thin band-shape zone. The outline of the head outside the changed area is irregular and less sharp than normally. The acetabulum is well-developed but slightly irregular. Slight sclerosis in the roof. Small cyst formations in the roof of the left hip joint. The joint space is slightly narrowed, more in the left joint. Moderate deforming bone deposits (see fig. 7). Knee joints: marked arthrosis deformans, otherwise nothing abnormal. *Skeleton of the hands* and wrist areas: heads of the metacarpals, especially the fourth metacarpal, markedly flat, broad and clumsy. Some of them show small bone deposits on the border of the joint surface.—Otherwise nothing abnormal. Dorsolumbar spine: considerable spondylosis deformans of the typical kind. No signs of any disturbed development.

No. 2. M.K., born 1906.

Everything that has been said of the mother (No. 1) holds good in this case, too, though the trouble from the hips is

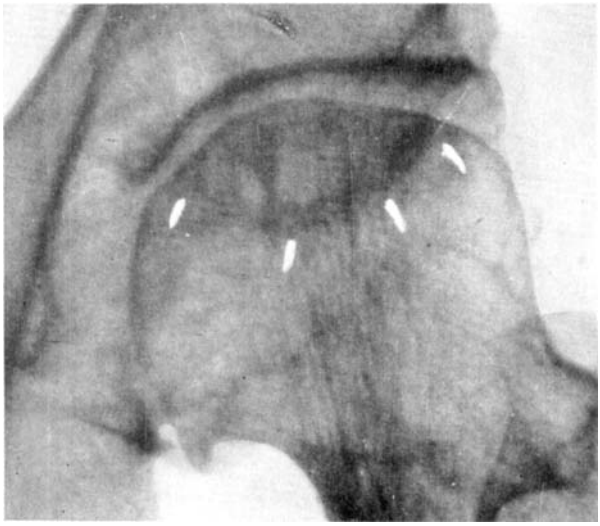


Fig. 7.

clearly more serious here. The patient has repeatedly gone to doctors, and been treated for a long time by a medical gymnast. The similarity in gait of the mother and daughter—both waddle —is evident to their neighbours.

Roentgen examination of *pelvis and hip joints* 12.5.30 and 23.3.43 (it was unfortunately impossible to make the patient consent to further investigations). Pelvis normally shaped.—The femoral heads flatter than normal. The central part of the joint surface deformed; furthermore, blurred in the left joint. In the changed part of the joint surface the right femoral head shows a slight, and in the left a marked change in structure: the calcium density is diminished, and the spongy structure scarcely observable. In the left head a denser zone, well over 1 mm broad, marks off this changed area, which is nearly triangular, with its base corresponding to the deformed part of the joint surface.—The femoral neck is somewhat short and thick. The joint space proximally slightly wider than normal (see fig. 8).

The examination in 1943 showed that the deformation and flattening of the femoral heads had increased markedly. Signs of arthrosis deformans could now be observed.

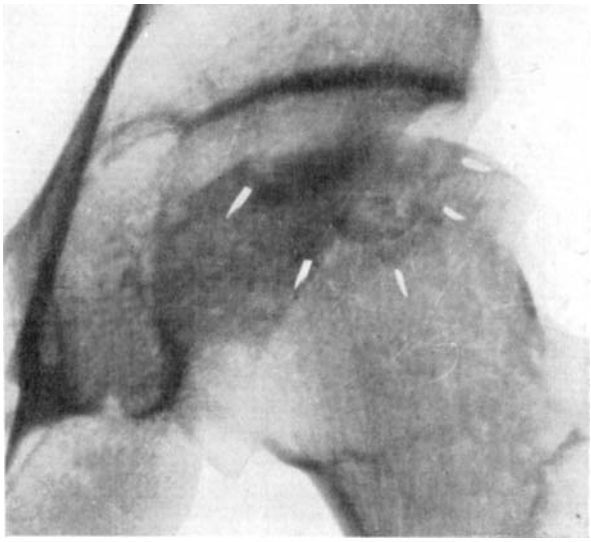


Fig. 8.

No. 3. K.J.K., born 1928.

The boy was brought to the Surgical Policlinic of the County Hospital in Karlskrona on Jan. 24, 1941. At that time he had limped since the age of two years with the left leg; he was himself of the opinion that his left leg was shorter than the right. He had an arch-preserver in the left shoe and walked better when using it.

Extract from the journal: "When examining the patient in a standing position the pelvis is observed to be oblique (the right crista ilii is considerably higher than the left). No measurable shortening of the leg. Hip and knee joints normal."—The patient was not submitted to any treatment, but adviced to seek an orthopaedist.

After that time the patient has been treated at different times at the Orthopaedic Department of the St Göran Hospital in Stockholm. The following clinical data are collected from the extract of the journal, which has kindly been lent to me by the Senior surgeon Dr Orell.

"Treated at the Orthopaedic Department 7.4.-14.10.43 on the

diagnosis: osteo-chondritis cox. juvenilis amb.—Anamnesis: has walked badly since the age of 11. Increasing limp with marked lumbar lordosis during the last few years. Has not been able to take part in gymnastics at school since autumn 1941. The examination revealed a strong flexion contracture, especially in the right hip, amounting to 50°. Very poor external rotation in both hip joints, and 10° abduction.—Tenotomy of flectors and adductors in the right hip was performed on April 13, 1943, and the hip put in plaster. The improvement was only slight, however. A subtrochanteric osteotomy of the right femur was therefore performed on June 18, 1943. After that the gait improved and the lumbar lordosis diminished, but the patient's gait without sticks was still not very satisfactory."

Roentgen examinations 24.1.41, 23.12.41, 26.8.42, 23.3.43 (as a rule only of the pelvis and hip joints):

Pelvis: somewhat oblique. The true pelvis hypoplastic, the alae ilei on the other hand broader and stronger than normal. No protrusio acetabuli.

Hip joints (see fig.s 9-12): femoral neck long, but not increa-

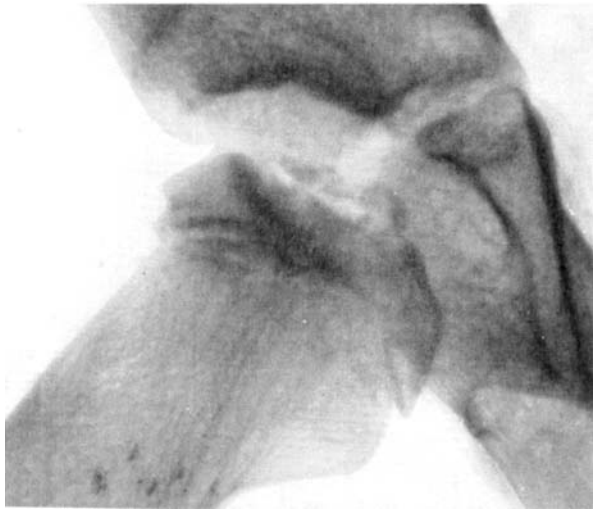


Fig. 9.

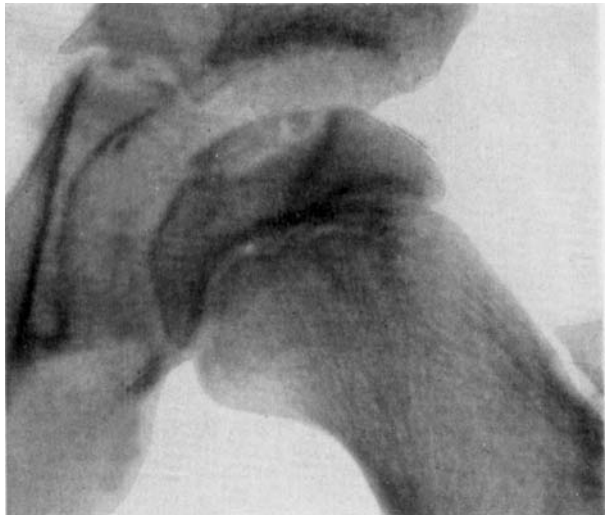


Fig. 10.

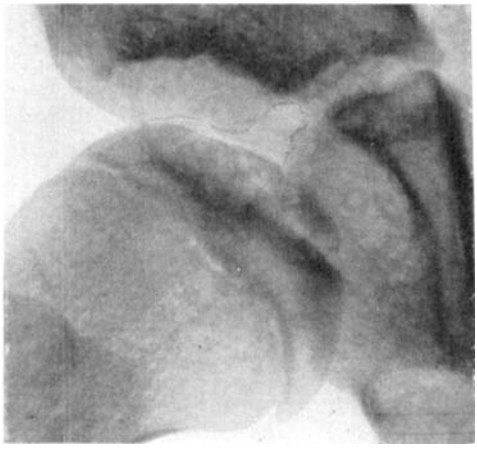


Fig. 11.

sed in width. The bone nucleus in the trochanter major slightly hyperplastic. Epiphyseal borders normal.—The bone nucleus of the epiphysis of the head considerably diminished in height. Its peripheral parts show normal structure and normal "joint surface." The central area presents an unusual picture. Its super-

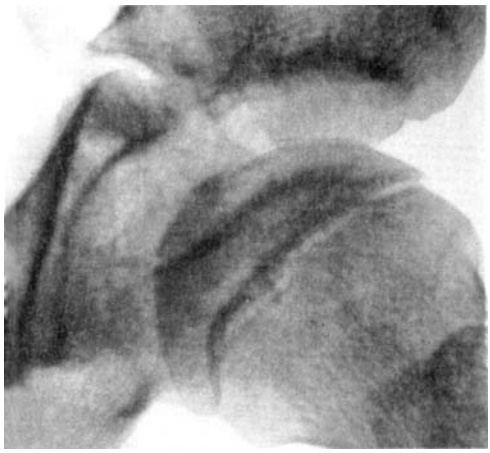


Fig. 12.

ficial part is divided into a number of fragments, some of which show only a blurred bone structure. Calcium content slightly diminished. The fragmentation is somewhat more marked in the right femoral head. The border zone between the fragmented part and the more central parts of the epiphyseal nucleus are seen on the roentgen picture as a bone- and calcium-free "space" with a band-shaped denser zone outside it. Some of the fragments are slightly but clearly higher than the rest of the "joint surface" of the epiphyseal nucleus.—The joint space is moderately widened, mostly in the inferio-medial parts.—The acetabulum is shallow and sloping. The change in shape is especially marked in the acetabular floor, mostly in the right hip ("Ischium varum").—

The roentgen picture of the femoral heads did not change essentially during the more than 2 years of observation.

Spine: the anterior part of the vertebral bodies in the lower dorsal and upper lumbar segments is swollen and club-shaped. —7th dorsal segment: a fairly marked defect on the anterio-inferior circumference. 12th dorsal and 1st lumbar segment: small defect on the anterio-inferior circumference.

Shoulder joints: neck of the scapula hypoplastic.—Elbows: considerably increased calcium density of the epiphyseal nucleus

of the head of the radius, its form normal.—Wrists and hand skeleton: slight irregularity in the shape of the radial epiphysis. A very well-appearing pseudo-epiphysis on the distal end of the first metacarpal. Knee joints normal.—Foot joints: tibial epiphysis moderately irregular in shape.

No. 4. E.W., boy, clinically free from symptoms.

Roentgen examination 6.12.43. Pelvis, hip joints, hand skeleton and wrists: normal.

No. 5. H.W., girl, clinically free from symptoms.

Roentgen examination 6.12.43. Pelvis, hand skeleton and wrists: normal.

No. 6. M.L.B., born 1914.

Very short of stature. Has had trouble in her back and been treated by a doctor. (I have unfortunately not been able to obtain any clinical data from her medical man.)

Roentgen examination 13.12.39. Dorsolumbar spine, pelvis, hip joints, and knee joints: according to testimonial by Dr C. Sandström there were no signs of disturbed development. Scoliosis and a suggestion of spondylosis deformans (I have unfortunately not been able to see these roentgen pictures myself).

Roentgen examination 26.3.43 (pelvis, hip joints, lumbar spine): no indication of disturbed development.

No. 7. B.H., born 1901.

Clinically free from symptoms.—Roentgen examination 28.12.43. Pelvis, hip joints and hand skeleton: normal.

No. 8. Bj.H., born 1932.

In 1936 the boy had temporarily trouble from one hip, and was examined by roentgen. Since then he has been quite free from symptoms. Roentgen examination 23.6.36, 4.7.36, 29.12.43. Pelvis and hip joints normal.—29.12.43: hand skeleton and wrists: normal.

No. 9. C.H., born 1934.

Clinically free from symptoms.—Roentgen examination 29.12.43. Pelvis, hip joints, hand skeleton and wrists: normal.

No. 10. K.B.H., born 1872.

Clinically free from symptoms.—Roentgen examination 12. 10.42. Spine, pelvis and hip joints: slight arthrosis deformans, otherwise normal.

In this family we may perhaps look first at the *hereditary circumstances*. It is evident that there is a *roentgenologically significant disturbed development of the femoral epiphyses in 3 generations* (Nos. 1, 2 and 3 in the genealogical table). The individuals in question also show definite subjective and clinical symptoms, which have got worse from generation to generation. The disease is thus *clearly hereditary,* and it is also evident that the heredity is *dominant*. On the other hand, there is no familial prevalence. The individuals examined by roentgen as controls show no signs whatever of any disturbances in development which might have been induced by the genes in question. No. 6 showed some symptoms, which I at first strongly suspected to be due to disturbances of the type in question. The roentgenological examination showed, however, that such was not the case. The other now living members of the family are free from symptoms. It seems on the other hand to be fairly certain that another 3 cases of the epiphyseal disturbances here discussed have occurred in the preceding two generations. In this family there is thus very probably a *dominant hereditary epiphyseal disturbance in 5 generations*. As far as I can elicit from the literature this is the largest hereditary series, carefully checked by roentgen, of the kind to date.—From the point of view of heredity it is of great interest that the disease has in all the cases first made itself felt at the *same age,* viz. earliest youth. As has been pointed out by other authors, too, this indicates that the initial age is *determined by genotype* in the family in question.

Case No. 3 is the most interesting from the point of view of *the roentgenological symptoms*. The roentgen picture of the femoral head is extremely characteristic. As far as it is possible to judge, it has exactly the same appearance as in the cases published by E. *Freund* and by *R. Romanus*. This is further corroborated by the similarity between the sketches which both

authors made of their roentgen pictures. If I were to draw the roentgen picture in case No. 3, it would also look just the same. *Romanus* calls these changes "perifoveal necrosis." *Freund*'s patient was 15 years old, *Romanus*'s only 7. My patient's age was between these two.

My two *adult* patient also show central perifoveal changes in the femoral heads. In these cases, no more or less separate fragments can be observed. The two cases correspond fairly well. Their roentgen pictures also correspond rather well with those of the adult patients in *Romanus*'s material. The similarity between these cases and *Ribbing*'s cases is also considerable, which *Romanus* himself affirms. *Ribbing* considers the differences in the roentgen picture between the adult patients and the children to be probably due to the difference in age; *Romanus* seems to consider this self-evident. It is not possible to make a decisive pronouncement on this point until one has had the opportunity of following the development of a case from childhood to adult age. However, all experience collected up to now argues to a certain extent in favour of this theory of the importance of age in such cases. It should, nevertheless, not be forgotten, that both in *Romanus*'s and in my material the most serious roentgenological and clinical symptoms were found in the youngest patient, who precisely on account of his clinical symptoms had gone to a doctor. It is therefore probably necessary to consider these cases as more serious than the others can have been at the same age. The multiple milder disturbances in the spine and the smaller joints in case No. 3 in my "family B." also point in that direction.

Four cases of ephiphyseal disturbances in the femoral head have now been described in this essay, viz. 1 case in the first and 3 cases in the second family. The roentgen pictures show considerable differences, which can partly be explained by the different age of the patients at the *examination*. This explanation is not sufficient, however. A still more important factor when judging the cases is the patient's age at the time when the *first symptoms* of the disease appeared. In conformity with

earlier experiences in this field, we find that the earlier the disease appears the more serious are the symptoms.

Theoretically, it is not astonishing that, in the early cases, a severe disturbance in the development of the epiphyseal nucleus causes a secondary disturbance of the epiphyseal border and even of the metaphysis as a whole, as in my case No. 8 in family A. Thus, a primary disturbance of the last-mentioned parts of the skeleton need not necessarily be present, but such a disturbance is naturally difficult to exclude in any one case.

It is less easy to discover the reason for the very great differences in the roentgen pictures of the epiphyseal nucleus itself. Case No. 8 in my family A. is a good example of what *Jaffe* and *S. Hirsch* call "eccentrochondroplasia," ("the epiphysis does not develop from a central nucleus of ossification, but from the multiple eccentric centers of ossification so clearly shown in the roentgenograms").

On the other hand, the division of the epiphyseal nucleus in the femoral heads in case No. 3 in family B. is probably not primary. Neither is there any reason to suppose any eccentrochondroplasia in the remaining cases. *Romanus* calls the changes which are exemplified by my case No. 3 in family B. "perifoveal necrosis;" other authors in this field, e.g. *Ribbing*, are also of the opinion that there is an aseptic necrosis in cases with similar structural changes.

As regards my *adult* patients, finally (Nos. 1 and 2 in family B.), we may suppose that the changes in the femoral epiphyses during growth had about the same appearance as in No. 3 in family B., even if the changes have probably never been quite so serious. Thus, there does not seem to be any remaining fragmentation of the femoral epiphyses in my cases. This is remarkable in view of the fact that some cases of the disease in question are described (e.g. by *Stören*) where the roentgen pictures of adult individuals more or less suggest *osteochondritis dissecans*. In such cases an identical roentgen picture is found in both femoral heads; in some of them other joints, especially the knee joints, also show changes of osteochondritis dissecans type. This has made *W. Müller* declare that he does not doubt that

"zwischen der erblichen multiplen Störung der Epiphysenverknöcherung und den multipen Formen der Osteochondritis dissecans engste Beziehungen bestehen in dem Sinne, dass beide nur graduelle Unterschiede oder auch vielleicht verschieden einsetzende Etappen ein und derselben Störung darstellen." If, however, a careful examination is made of all the cases which the literature has called osteochondritis dissecans in the femoral head, definite differences are found between the multiple or at all events bilateral cases on the one hand, and the "common" cases, localized at one femoral head only, on the other. This is the reason why, in an earlier essay, I have differentiated between the latter group of cases, which I called "primary osteochondritis dissecans in the femoral head," and the first-mentioned cases, which I collected under the heading "secondary osteochondritis dissecans in the femoral head,"—if, indeed, which I doubt, the term osteochondritis dissecans should be used at all for these cases.

As I have mentioned in the beginning of this paper, *W. Müller* is of the opinion that there is "eine reine Störung der *Knochen*entwicklung" in the hereditary multiple epiphyseal disturbances, and that "die *knorpelige* Form des Gelenkes an sich *ungestört* ist." In my opinion it is, however, fairly evident that in the cases with typical "eccentrochondroplasia," as in my case No. 8 in family A., there must have been a disturbance of the epiphysis *even before the beginning of the ossification.* Otherwise we should not find, in the beginning of ossification, any such pronounced malformation of the epiphysis (and even of the metaphysis) as here. *W. Müller* explains the deformation of the epiphysis by saying that in the severe cases "auch das *Knochen*wachstum an den Metaphysen ist offenbar beeinträchtigt." From the above it is clear that I do not find this explanation satisfactory.

In accordance with e.g. *Ribbing* and *Romanus* I, too, maintain that there really is a form of aseptic necrosis in the cases with roentgen pictures, corresponding with those found in aseptic necrosis. Concerning the cases with roentgen pictures suggesting osteochondritis dissecans, finally, I believe that here, as

well as in "primary osteochondritis dissecans in the femoral head," the roentgen picture is obtained on the basis of an aseptic necrosis + a secondary pathological fracture within the changed and insufficiently reorganised area.

As clearly appears from this essay I agree with *W. Müller*'s opinion of the connection between the different forms of the epiphyseal disturbances, but as the formation of both cartilage and bone structure is engaged in the early cases, I think that *Ribbing*'s term ought to be accepted for them all, viz. "hereditary multiple epiphyseal disturbances."

SUMMARY

The author describes some cases of hereditary multiple epiphyseal disturbances, and analyzes the hereditary and roentgenological circumstances.

ZUSAMMENFASSUNG

Der Verfasser beschreibt einige Fälle von hereditärer, multipler Epiphysenstörung, und legt die hereditären und röntgenologischen Verhältnisse klar.

RÉSUMÉ

Description de quelques cas des lésions héréditaires multiples de l'épiphyse et analyse des circonstances héréditaires et radiographiques.

LITERATURE

Brailsford: Radiology of bones and joints, 1934.
Freund: Fschr. Röntgenstrahlen, 41, 1930.
Hermodsson: Acta Radiol., XXV, 1944.
Hirsch: J. of bone and joint surg., 19, 1937.
Müller: Zschr. f. Orthop., 69, 1939.
Ribbing: Acta Radiol., suppl. XXXIV, 1937.
Romanus: Acta Orthop., XI, 1940.
Stören: Acta Chirurg., LXXIV, 1934.