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OLLIER'S DISEASE AND ITS RELATION TO OTHER FORMS OF CHONDRODYSPLASIA

BY

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Ollier described in 1899 two cases of a disease which, according to his opinion, had not been described earlier and which he called dyschondroplasia. The clinical picture in these cases was characterized by a unilateral shortening of the limbs and by thickening of the ends of the long tubular bones. Roentgenologically the cases showed large clear areas particularly in the metaphyses and diaphyses of the long and short tubular bones. These foci were considered as persisting cartilaginous masses. Since the time of *Ollier* several cases of this rare disease occurring in children have been published under different denominations: Ollier's growth disturbance, Ollier's disease, dyschondroplasia, chondrodysplasia, systematized enchondromatosis. Absolute unity has not been reached as to the nature of the disease and its relation to enchondromatosis and multiple cartilaginous exostoses.

In the winter 1946 a case in the Orthopedic Hospital of the Invalid Foundation was observed, which no doubt falls under the heading of Ollier's disease. The first and only case in Finland described earlier and just as typical, was published by *L. J. Lindström* in 1924. Thanks to the courtesy of Dr. *Lindström* an interesting follow-up examination of his case could be made. The examination of both these cases has thrown light on several questions regarding the pathogenesis and development of this disease.

Case 1.

J. R., son of an engine-stoker from Björneborg.

Anamnesis: Born 14.10.1939 (6 years). Hereditarily nothing of interest. The patient started walking a little less than one year old. Some months later the parents observed that he limped. At the same time they noticed that the right leg was somewhat shorter and thicker than the left. This shortening increased gradually and in the summer 1943 (at the age of 3½ years) several physicians were consulted and roentgenograms were taken of the lower limbs in Björneborg (figg. 5 and 7). The roentgenograms showed large clear areas at the ends of the long tubular bones in the right leg and in the pelvis as well as two foci in the left femur. The right femur and the tibia were thickened. In 1943 it was also established that the liver was somewhat enlarged. The diagnosis remained unclear and the prognosis was considered bad.

Apart from the fact that the shortening and thickening of the right leg has constantly increased, the patient has generally been sound and both the mental and the physical development has otherwise been normal. Because of the increasing limping the parents sent the boy to the Orthopedic Hospital of the Invalid Foundation in Helsingfors in the winter 1946 where he was admitted for a thorough examination.

Status praesens (March 1946): (Fig. 1.) Length 113 cm. Nutritional condition satisfactory. Sedimentation rate 3 mm/1 hr. Blood count: haemoglobin 86/94 per cent, red cells 5,070,000 per cmm., colour index 0.93, white cells 5.900 per cmm. Differential count normal. Serum calcium 10.8 mgrm. %. Blood sugar 85 mgrm. %. Except for the right limbs the proportions of the body are on the whole normal. The mental development normal. The nervous system, the circulatory organs and the lungs: nothing noteworthy. The pupils of equal size. The border of the liver, which is even, is palpable 3 to 4 cm. under the right costal arcus, the spleen is not palpable.

The right lower limb considerably shortened, the right upper limb slightly shorter than the left. Limping strongly with the right leg. The degree of the shortening appears from the following table:

	Right	Left
Spina il. ant. sup.—the knee joint space	25 cm.	31 cm.
Tibia	21 „	23.5 „
Humerus	20 „	21.5 „
Ulna	16 „	17.5 „
Foot	17 „	19 „

The lower end of the right femur and both ends of the right tibia distinctly thickened and somewhat uneven. Slight crus varum on the right side. The right gastrocnemius muscle considerably shorter and thicker

than the left. Scoliosis convex to the right, neutralized when the right leg is raised. The crests of the ilia and the scapulae symmetric, no nodules palpable. At the upper end of the right humerus nodules are distinctly perceptible. The right index finger is 4 mm. shorter than the left, somewhat thickened. The middle phalanx nodular to the touch. Otherwise the hands are of equal size. The bone-cartilage limits of the IV, VII

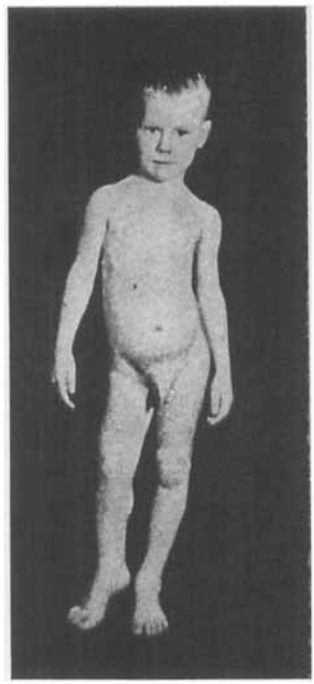

Fig. 1.
Case 1, 1946.

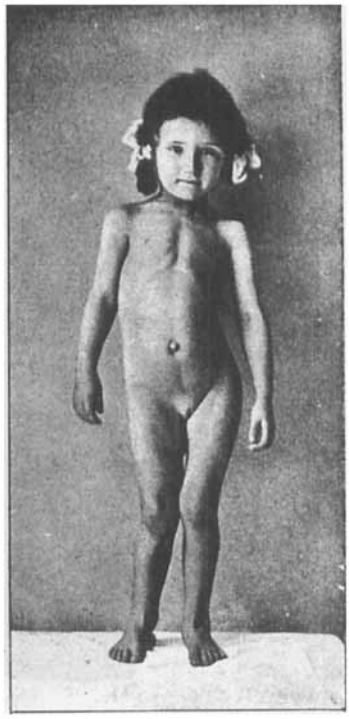

Fig. 2.
Case 2, 1924 (from Lindström's paper).

and IX costae clearly thickened to the right, slight thickening also in other ribs. No Harrison's groove. Brachycephalic. No reduction of the motility of the extremities.

The whole skeleton was roentgenographed. **The roentgen finding** shows changes characteristic of Ollier's disease:

The pelvis and the lower extremities (figg. 6 and 8-12): *Right:* The iliac bone shows fan-arranged and fan-shaped clear areas in the peripheric parts. The pubic bone and the ischium show irregular clear areas, as does also the upper end of the femur. High-grade coxa valga. The

middle part of the diaphysis of the femur is thickened, in the upper end there are superficial foci at which the contour of the cortical bone is missing. At the lower end of the femur and at both ends of the tibia there are extensive longitudinal confluent areas partly separated by dense longitudinal stripes. There are groups of dense spots interspersed indicating calcification processes. At both ends of the fibula

Fig. 8.
Case 2, 1946.

there are areas of the same kind. The epiphyses of the affected bones show distinct irregularities as do also all tarsal bones and metatarsals. In all phalanges of the toes and in the I-III metatarsals there are distinct clear areas. *Left:* The crest of the ilium somewhat irregular. In the upper end of the femur near trochanter minor there is a distinct clear area, and in the lower part of the diaphysis of the femur, more than 5 cm. from the epiphyseal line a longitudinal focus. In the proximal phalanx of the great toe there is a couple of distinct clear areas. In some other phalanges and in thee metatarsals slight changes are surmised.

The upper extremities: (Figg. 13-14).

Both scapulae exhibit changes of the same type as in the iliac bone. In the upper ends of the diaphyses of the humeri there are longitudinal clear areas with scattered dense spots. The contour of the cortical bone is partly missing. The largest focus in the left humerus looks as if a long chip had been gouged out. Areas of this typical form may also be observed in the lower end of the radius on both sides. Distinct foci in the phalanges of the right index finger and in the middle phalanx of the III finger.

Other parts of the body: At the bone-cartilage limits in the V-XI costae on the right side thickenings with dense spots interspersed are seen. Slight thickening of the corresponding costae on the left side. Similar areas are conjectured in the upper right corner of the I and II lumbar vertebrae. Sacral spina bifida occulta. No certain changes in the cranial bones or in the clavicles.

Case 2. (Published by *Lindström* in 1924).

H. F., daughter of a peasant from Malax.

Anamnesis: Born in 1920. A second cousin of the patient has a congenital dislocation of the hip, otherwise hereditarily nothing of interest. *Extract from the record of Lindström* of 1924: "Has not suffered from rachitis or otherwise been ill. ... In the middle of December 1923 the parents noticed that the child limped and it had already some weeks earlier complained of pain in the right leg. About Christmastime the mother noticed a prominence below the right knee."

Status praesens (1924): (fig. 2.) "..... on the right costae IV, VI and IX prominences on the costal cartilage limit. The right leg is 5 cm. shorter than the left." "On the right tibia medial to the tuberosity a prominence is seen. In the lower end of the femur, near the lateral epicondyle a thickening is palpable in the bone. The upper crest of the right ilium is rounded and thickened to the touch. The third finger of the right hand is somewhat clumsier than the others ....." "The girl was wholly roentgenographed. The skull and the spine show nothing abnormal." "Roentgenologically multiple defects appear in the skeleton localized juxta-epiphyseally in the long tubular bones to the right and in the pelvic bones on the same side. The affection is not, however, purely unilateral seeing that there are in the pelvic bones of the left side slight roentgenologically established changes. Clinically and roentgenologically the bone defects seem to consist of cartilaginous tissue confirmed by the histological examination." The treatment at this stage consisted only of a prescription of cod-liver oil and lime. (A more detailed description of the roentgen findings will be found in the article by *Lindström*). Fig. 15 shows the roentgenogram by *Lindström* of the pelvis and the upper ends of the femora. The conformity with the case first described both clinically and roentgenologically is striking.

The course of the disease 1924-1946: In 1933 the patient was sent to the Orthopedic Hospital in Helsingfors because of a highly developed knock-knee on the right side due to an angulation in the upper part of the tibia. The valgus was corrected by osteotomy of the tibia, the healing was free of complications and the formation of callus satisfactory. In 1933 an orthopedic bandage was applied which the patient has carried ever since, and with which she has been satisfied. During the period of growth the shortening of the right leg increased continously and the stirrup under the foot plate of the bandage had to be lengthened several times.

On Aug. 7th 1935 the patient was admitted to the Municipal Hospital of Vasa with the diagnosis malignant *tumor of the right ovary, ascites.* She had herself felt a tumor in the abdomen 4 weeks earlier. Laparotomy 9.8.1935. In the abdominal cavity about 5 litres of ascitic fluid. In the right ovary a firm tumor bigger than a cocoanut. Exstirpation. No metastases could be found. Healing without complications. Unfortunately no histological examination of the tumor was made. 2.2.1938: Condition satisfactory. Walking easy with the bandage.

Follow-up examination at the Orthopedic Hospital of the Invalid Foundation in Helsingfors in March 1946 (at the age of 25): Healthy since 1935. Sometimes pain in the right knee-joint. The patient has not noticed any changes in the skeleton since the end of the growth period.

Status praesens (1946): (fig. 3.) General condition satisfactory. Nothing abnormal in the inner organs or in the nervous system. Face, thorax and pelvis symmetrical. The thorax shows deep, impressed grooves on both sides below the mammae. All costal ends somewhat thicker than normal. Both crests of the ilia feel normal. The right leg is shorter than the left. The lower end of the right femur is thickened, on the medial side a crest-shaped *exostosis* is palpable. Genu valgum about 20° to the right. The motility of the right knee and ankle-joint somewhat reduced as was also the abduction of the hip. The right gastrocnemius muscle is short, but hypertrophic. On the right tibia there is a distinct *exostosis* turned upwards 4.5 cm. above the medial malleolus. On the left side a similar exostosis 7 cm. above the cusp of the medial malleolus. On the medial side of the right heel there are two bluish *haemangiomata* in the skin, one the size of a bean, the other the size of a pin's head. The lower part of the right scapula is distinctly thickened. The medial side of the right humerus somewhat nodular. The right arm is 7 cm. shorter than the left, the basal and the middle phalanx of the index finger, the middle phalanx of the middle finger and the basal phalanx of the little finger are nodular. The prominence on the middle finger is wedgeshaped (the base of the wedge towards the proximal interphalangeal joint). The length of the long tubular bones appears from the following table:

	1924		1946	
Spina il. ant. sup.—the knee	right	left	right	left
joint space	22.5 cm.	29 cm.	37 cm.	49 cm.
tibia	21 „	22.5 „	29 „	37 „
humerus	19.5 „	20.5 „	30 „	34 „
ulna	15 „	15 „	24 „	26 „

The skeleton was roentgenographed. **The roentgen findings** appear from figg. 16-24.

The following facts appearing from the renewed roentgen examination should be particularly observed: The right iliac bone in which there were numerous cartilaginous foci in 1924 (fig. 15) is now unevenly ossified or sclerosed, its form corresponds to that of the left side (fig. 16). Distinct *spina bifida sacralis occulta.* In the long tubular bones on the right side no uncalcified clear areas can be established. These have been replaced by bone with irregular structure and dense spots interspersed as in the pelvis. The lower part of the scapula shows a similar picture. The upper end of the right femur is clumsy in shape with a marked coxa valga, while the lower end is thickened showing a configuration typical of the disease nominated *multiple cartilaginous exostoses* (fig. 17). This is evident also in the side-view (fig. 18). Both tibiae show in the lower ends typical cartilaginous exostoses (figg. 19-20). The costal cartilages display extensive calcifications in the form of dense spots. The only places where distinct clear foci still occur are the phalanges of the right hand and both feet (figg. 22-23). The following places which showed no changes in 1924, are now affected. The upper end of the left fibular diaphysis (thickening, calcified focus, fig. 24). The left tibia (exostosis, fig. 20). The base of the skull (the back part of the sella turcica is in the roentgenogram covered by an uneven bony structure).

ESSENTIAL PROBLEMS IN CONNECTION WITH THE DISPUTED CONCEPT OF OLLIER'S DISEASE

The following quotation from *Ollier* (the quotation is taken from the article by *Stark*) illustrates his own opinion on the disease, so remarkably well described by him: "The disease is characterized by the irregularity and delay of the ossification of the intermediary cartilages. The cartilaginous tissue intended for the growth in length of the bones does not pass through the normal ossification process. It preserves its structure and

persists in the form of more or less regular cartilaginous masses which often need a very long time for the transformation into bone tissue. These abnormally persisting cartilaginous masses are situated either subperiosteally or intra-medullarily thus superficially or deep lying." *Ollier* had noticed small exostoses in one of his cases and he points out that future investigations will make it clear whether the disease described by him possibly is identical with the hereditary exostosis disease.

Witteck who described a case of this disease in 1906 suggested instead of dyschondroplasia the name "Ollier's growth disturbance". He paid particular attention to the marked although not total unilaterality of the disease causing the unilateral shortening of the limbs which also dominates the clinical picture in most cases later described. The roentgenograms of that time were indistinct, likewise the printed reproductions (in *Molin*'s paper, for instance). More attention was probably therefore paid to the simple fact that there were unilaterally localized cartilaginous foci in the bone tissue. *Frangenheim* thus considered *Ollier*'s and *Witteck*'s cases as *enchondromatosis* with principally unilaterally localized foci and did not accept a classification of these cases in a separate group. Thus Ollier's disease was identified with unilateral enchondromatosis which still often happens. Others who considered that Ollier's disease roentgenologically differs considerably from enchondromatosis, stress the typical longitudinal form of the foci and the increasing calcification which has been observed in the few cases followed during several years. This calcification indicates a good prognosis.

The occurrence of enchondromata and multiple cartilaginous exostoses are coordinated phenomena in that complex disease which, in England and America has been called *hereditary deforming chondrodysplasia.* Several authors (*Jones & Lovett* and others) have expressed the opinion that Ollier's disease should be considered identical with this disease. This opinion has not, however, remained uncontradicted.

The opinion of the *prognosis* of Ollier's disease has mostly been parallel to the opinion of its relation to enchondromatosis.

Frangenheim writes on the prognosis of enchondromatosis, to which he and many others assign the cases of *Ollier:* "The prognosis of the multiple enchondromata is grave." "The end of the growth period does not mean the end of the growth of the enchondromata. Regressive changes which could be considered as signs of healing, such as calcification and ossification are rare".

Contrary to the opinion that the prognosis of Ollier's disease is the same as of enchondromatosis are the results of examination in the few really typical cases which have been followed during a number of years. *Bentzon* has described a case which was followed from the age of 7 until 15 years. Of other published cases one has been followed from 2 to 9 years (*Cleveland*) and one from 2 to 7 years (*Richard* and co-workers). There are probably no cases with a longer period of observation described. These authors have all confirmed *Ollier's* observation that the foci contrary to most enchondromata are subject to a delayed ossification or calcification. No typical case of this disease which appears in children has probably earlier been described as re-examined at an age when the growth may be considered finished. This was also established by *Richard* and co-workers in 1934. *Dahl* in 1930 shortly mentions that in *Bentzon's* case the foci at the age of 23 years show a continued tendency of ossification.

Ollier already points out that in this disease partly deep lying and partly superficial foci are found, some of them lying in the metaphysis close to the epiphyseal cartilage and others in the diaphysis itself. He did not, however, explain *how the diaphyseal foci arise and in which relation these stand to the epiphyseal cartilages, and the metaphyseal foci.* Neither has anybody else later given any satisfactory explanation of this question. An attempt to explain the appearance of the superficial foci has been made by *Logroscino* who writes: "When the destruction and the regeneration of the bony tissue do not take place equally quickly, cartilaginous tissue is produced in excess and finally breaks through outwards until it is no longer covered by the bony cortex". It is evident that this statement does not

answer the question, nor does the interesting statement of *Bentzon* that the masses of cartilage follow paths similar to those of the arteries of the bones.

THE DEVELOPMENT OF THE CARTILAGINOUS FOCI IN OLLIER'S DISEASE

When inspecting the roentgenograms of cases of Ollier's disease it can be established that these present certain changes in the tubular bones which must be considered characteristic of this disease. *Bentzon* describes them as follows: "... mainly longitudinal, stripe-shaped, sharply limited clear areas in the bone itself; it looks as if long chips had been taken out of the bone with a gouge". That the clear foci in typical cases consist of common hyaline cartilage with signs of degeneration or calcification in parts has been shown by means of biopsy by numerous authors (*Johansson, Lindström, Cleveland* and others). As the diagnosis in my case without doubt could be made on the roentgen finding biopsy was not necessary.

Ollier's opinion that the longitudinal clear areas in the metaphyses arise through parts of the epiphyseal plate forming cartilage which persists, and does not make way for the normal enchondral ossification, has been accepted by many. It is also proved by the roentgenograms in my case. If the appearance of the lower end of the right femur in case 1 in the roentgenogram taken in 1943 (fig. 5) is compared with the roentgenogram taken in 1946 (fig. 6), it can be established that the upper limit of the clear areas against the not affected part of the diaphysis has almost the same configuration in both roentgenograms. The distance from the upper poles of these clear areas to the foci in the upper end of the diaphysis of the femur is also the same. That the growth in length of the long tubular bones takes place only at the epiphyseal cartilage is of old a well-known fact. The foci in the lower end of the femur have grown several centimeters in length between 1943 and 1946. It can be proved that no expansion upwards in the diaphysis has taken place.

Therefore, the growth of the foci must have occurred at their bases, which in both frontal-view roentgenograms are constituted by the epiphyseal plate. The foci in the lower end of the left femur (fig. 5) and the upper end of the left humerus (fig. 13 b)

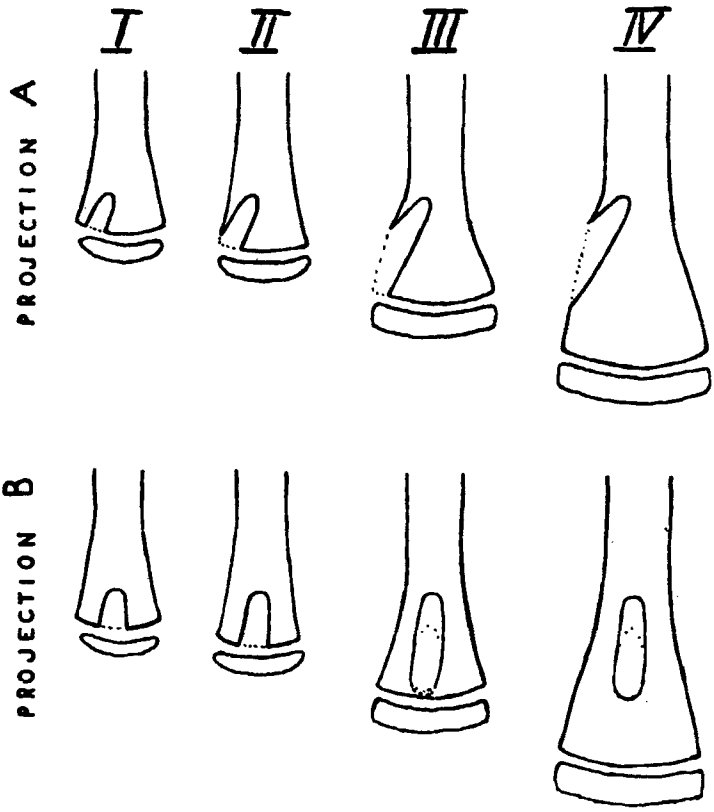

Fig. 4.
Schematic drawing of the development of a metaphyseal focus into a diaphyseal focus in the growth of the bone. Stage I-IV in two projections perpendicular to one another (A and B).

also clearly illustrate such cartilaginous "traces" occurring in growth, when, within a limited area, the epiphyseal plate produces cartilage, which of some unknown reason is not replaced by enchondral bone.

If, however, the focus in the lower end of the femur on the

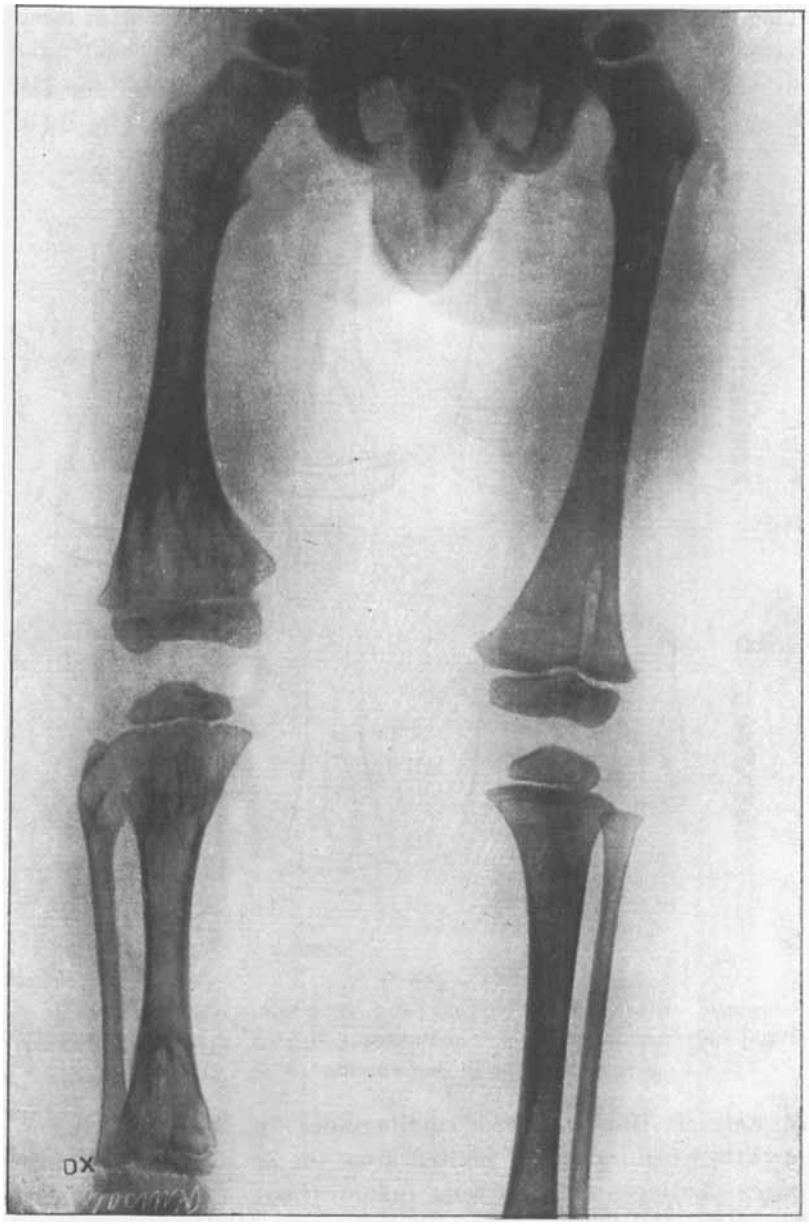

Fig. 5.
Case 1, 1943. The lower extremities.

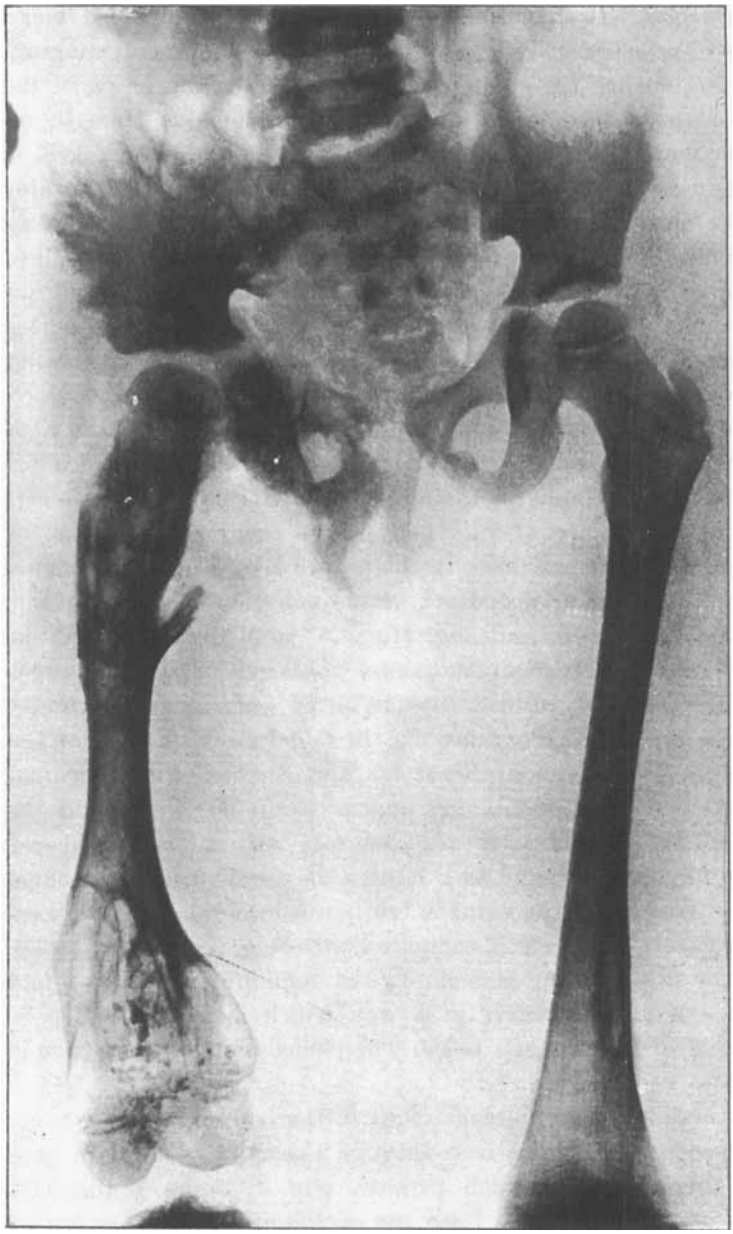

Fig. 6.
Case 1, 1946. The pelvis and the femora.

less affected left side is observed in the roentgenograms, it can be established that this area on the previous roentgenogram (fig. 5) touches the epiphyseal plate, whereas the focus in the later roentgenogram (fig. 6) is situated rather far from it, up in the diaphysis. That it is the question of the same focus is without doubt, the distance from the focus at the trochanter minor being exactly the same in both roentgenograms. This focus has thus developed from a typical metaphyseal focus into a diaphyseal one. In the side-view roentgenogram (fig. 9) we find that this diaphyseal focus in its lower part somehow issues on the surface of the bone. In other words, *corticalis is lacking at the end of the focus which lies closer to the epiphyseal plate.* Upon closer examination of my roentgenograms and those of other authors we shall find that this is absolutely typical of all foci in the diaphyses in this disease. A condition precedent for the appearance of this fact in the roentgenograms is, of course, that these are taken in the proper projection. This phenomenon is particularly distinct in the side-view roentgenograms of the right knee and leg (figg. 7 and 8). It may be established in the roentgenograms published of the phalanges in most cases of Ollier's disease, often even more distinctly than in my roentgenograms, i.a. in *Ollier*'s own cases (in the thesis of *Molin*) and in *Bentzon*'s and *Stark*'s cases. The diaphyseal foci in the phalanges appear particularly often in the form of oblong, obliquely situated foci with the bases nearer the epiphyseal plate and as if issuing on the surface of the bone.

The roentgenograms taken with an interval of 2½ years in my case (figg. 5 and 7 compared with figg. 6 and 8-10), show that the development of metaphyseal foci into diaphyseal foci in Ollier's disease occurs in a way which is schematically illustrated in fig. 4, stage II-IV. The probable existence of stage I will be discussed below.

If there is a cartilaginous focus in the metaphysis of a bone, this focus grows at the base through the epiphyseal plate here producing cartilage which persists (fig. 4, stage I and II). *Simultaneously with the bone the cartilaginous focus grows in length and its base widens. The base of the focus does not, how-*

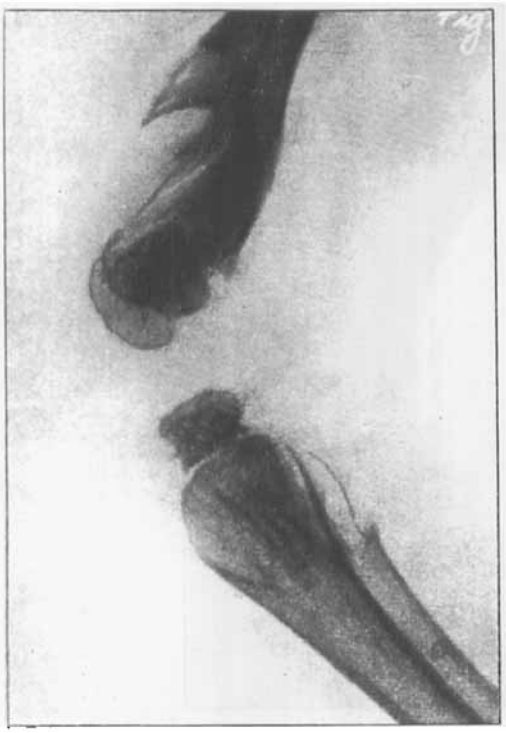

Fig. 7.
Case 1, 1943. Side view of the right knee-region.

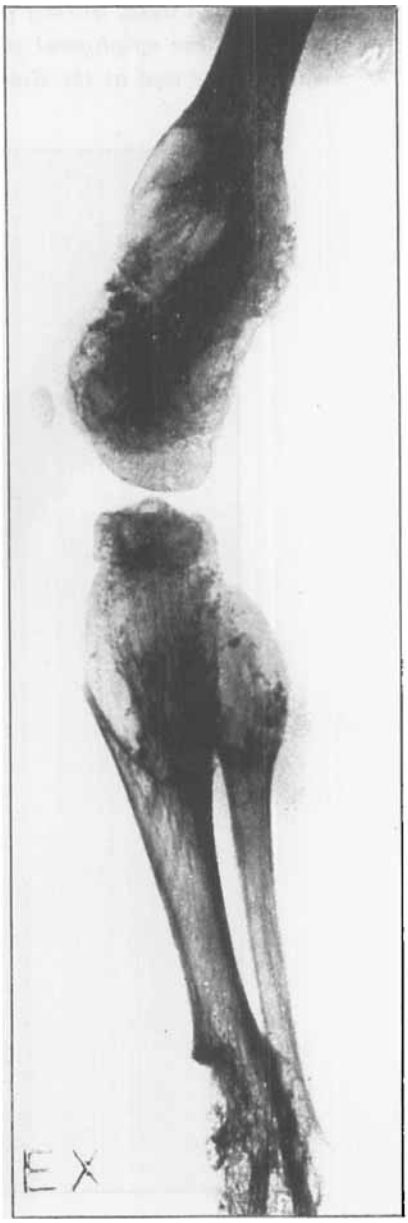

Fig. 8.
Case 1, 1946. Side-view of the right knee and crus.

ever, widen only, during growth it also moves towards the periphery of the epiphyseal plate until the focus at last lies at the edge of the end of the diaphysis (stage II and III). *While both*

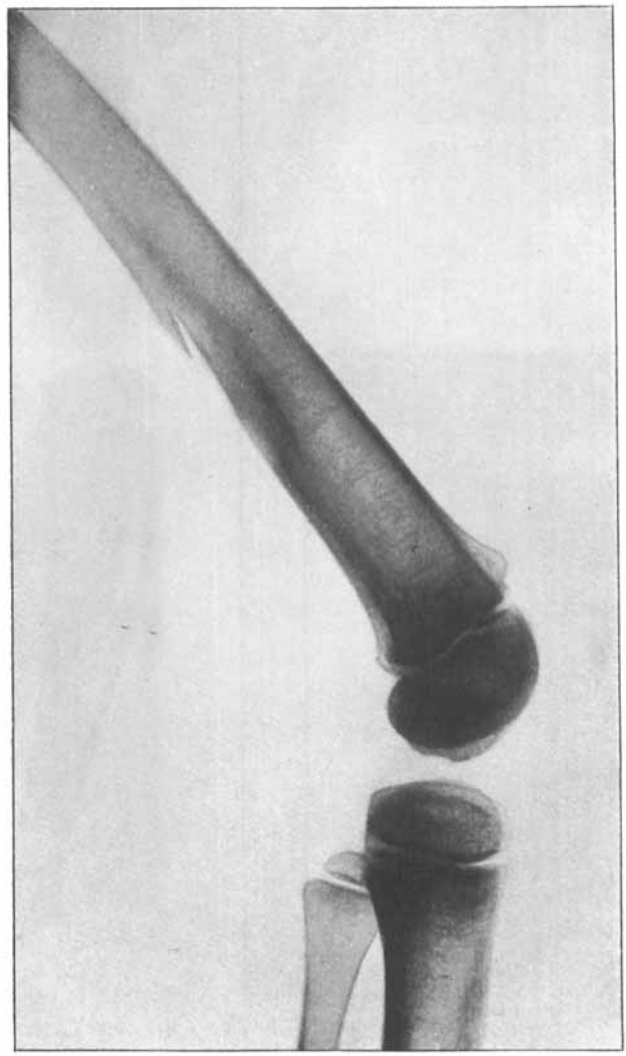

Fig. 9.
Case 1, 1946. Side-view of the left knee-region and the femoral diaphysis.

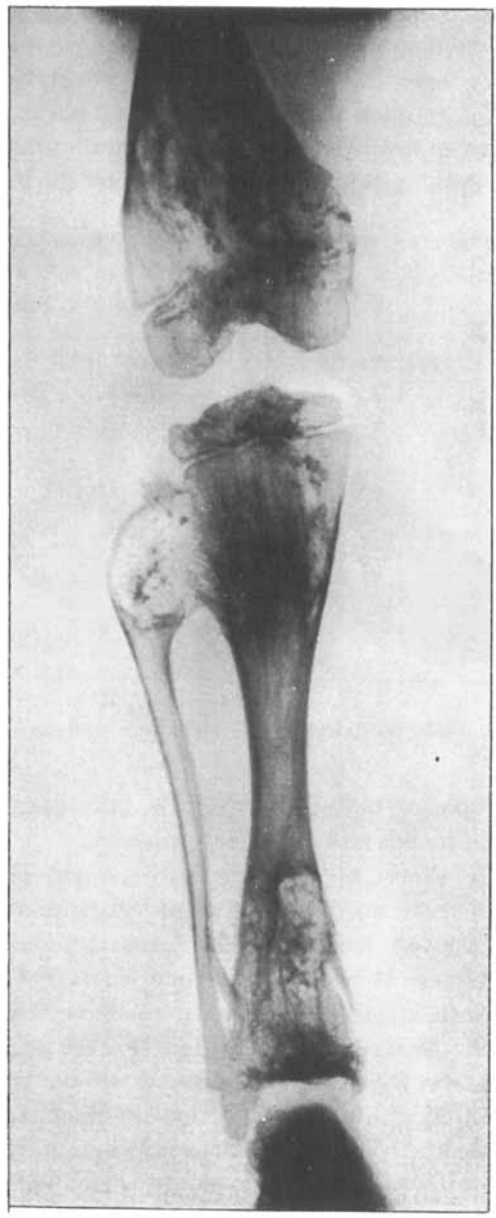

Fig. 10.
Case 1, 1946. The right knee and crus (frontal view).

the bone and the focus grow longer, the base moves towards the periphery of the bone and finally it will lie completely on the surface of the bone (stage IV). At this stage the focus has completely lost contact with the epiphyseal plate. The pole of the focus turned towards the diaphysis maintains during the whole of this development its position in relation to the diaphy-

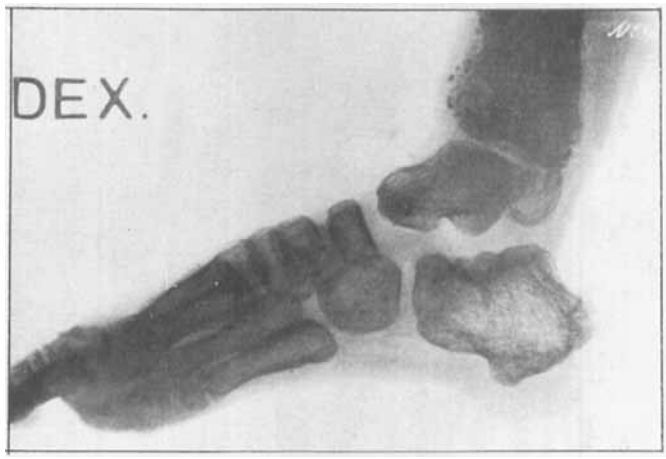

Fig. 11.
Case 1, 1946. Side-view of the right foot and the ankle.

sis, the development taking place in the epiphyseal end of the focus in which its growth principally occurs.

In my case almost all foci are in the stages II to IV. Unfortunately there is no side-view roentgenogram from 1943 of the focus in the left femur described above, judging from the frontal-view picture it was at that time in stage II or III. Its development into stage IV has taken place between the years 1943 and 1946. A necessary condition for the establishing of stage I, in which the base of the focus would lie completely within the epiphyseal plate, thus not touching its periphery, is that a comparatively small focus arising in the centre of a metaphysis with small changes should be found. Other conditions are that the focus be photographed in two projections at an early stage of development. Not even photography in two

projections would with complete certainty guarantee that the base of a focus does not touch the periphery of the plate. It is natural that these conditions are rare and roentgenograms in more than one projection have seldom been published. While the

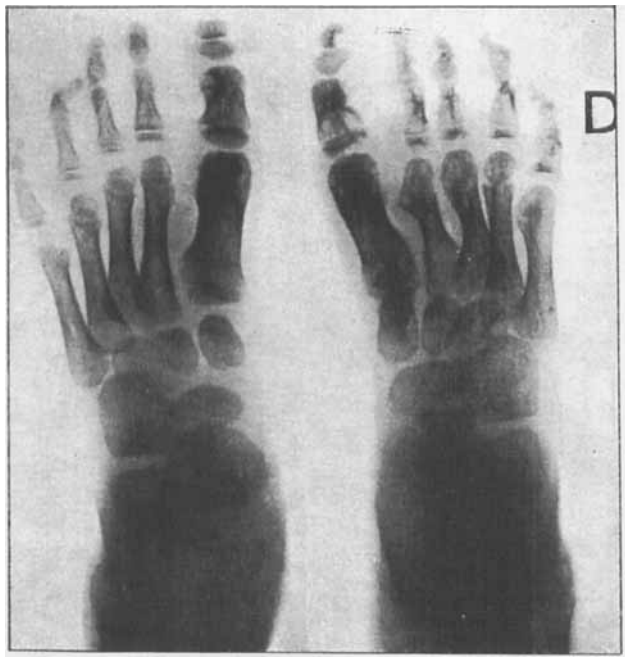

Fig. 12.
Case 1, 1946. The feet.

development from stage II into stage IV has been roentgenologically confirmed, the existence of stage I is not proved with certainty. There is reason to believe, however, that such a stage of foci primarily arising in the central parts of the epiphyseal plate exists. *Stark* quotes *Ollier* as follows: "These tumors are mostly localized to the surface of the bone, often found in the axial part of the bone." Foci already in their earliest stage reaching the periphery of the epiphyseal plate will probably also later in their entirety be more superficial (cf. fig. 13, the right humerus).

That the different stages of development of the foci have not been described by other authors probably depends on several circumstances: If the changes in a metaphysis are very large (for instance the right knee, fig. 10) the result is a typical yet

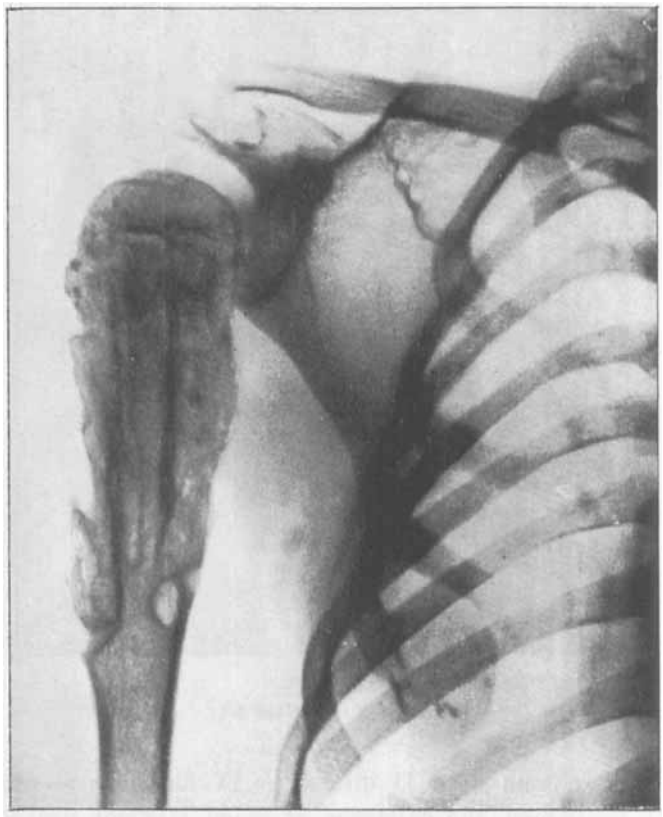

Fig. 13 a).
Case 1, 1946, right.

somewhat different picture than if they are limited (the left femur and humerus, figg. 5 and 13 b). In the bones with large changes the growth of the bone is much delayed and a continuous calcification changes the cartilage before an embodiment of clear foci in the diaphysis can take place. Small foci, on the

other hand, have seldom been photographed in several projections.

Several authors have mentioned that the foci in Ollier's disease pierce the cortical bone. In fact there has been from the

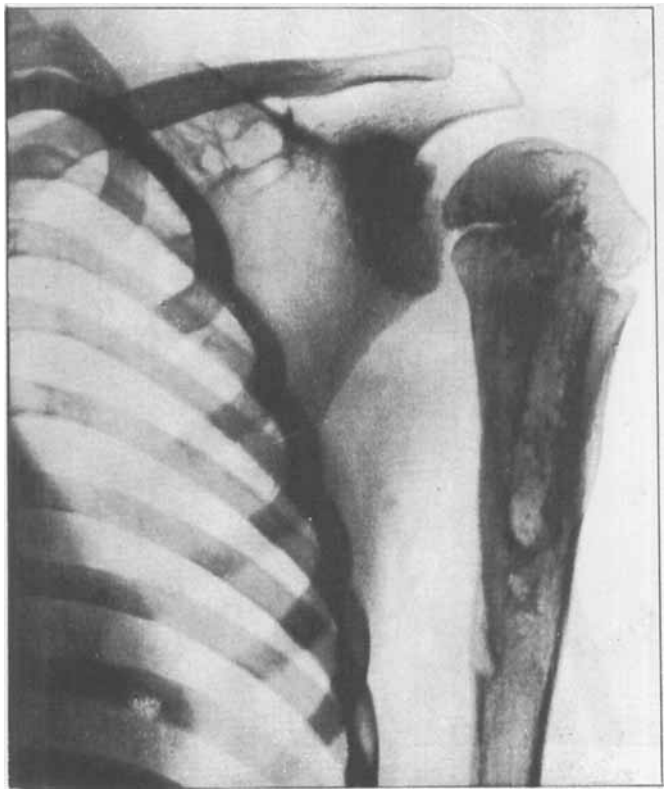

Fig. 13 b).
left.

beginning a defect in the cortical bone in these places. That this defect owing to the normal resorption and modelling of bones at the surface later may increase or secondarily be covered by bone does not alter this fact. These cortical defects do not arise in the same way as the secondary defects produced by autonomously growing enchondromata.

That the foci develop in the manner described above is also confirmed by the study of the roentgenograms of other authors.

Growth disturbances and congenital anomalies develop on the basis of partial arrest or other disturbances of

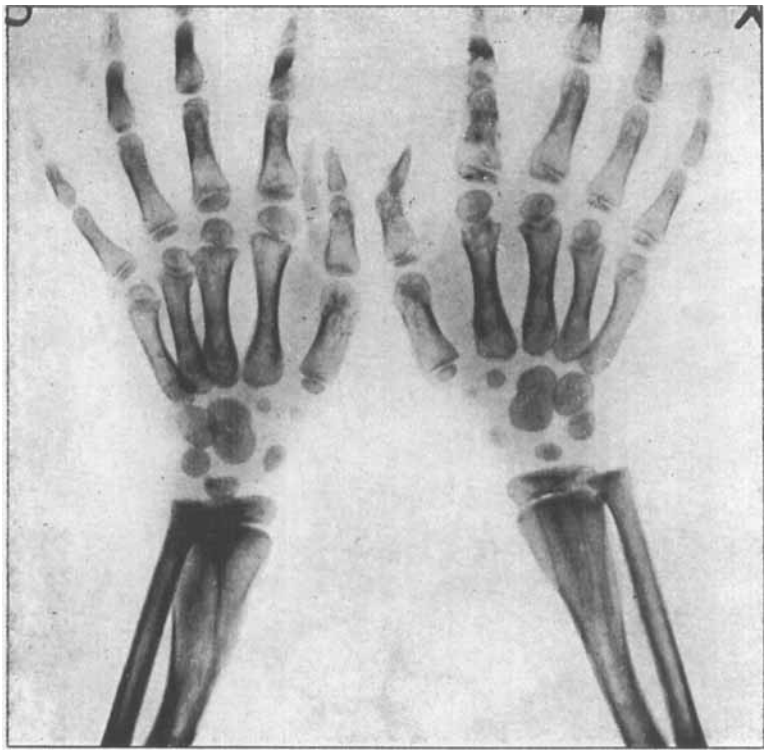

Fig. 14.
Case 1, 1946. The forearms and hands.

the normal process of development. A condition for fully understanding the genesis of disturbances in the development is that the course of the normal development in the regions in question is known. On the other hand disturbances in the development may give us valuable information on the course of the normal development. That the development of the foci in Ollier's disease macroscopically takes place as described above must be

considered proved, but the question of the histogenetical basis of this development is a problem the consequence of which goes far beyond the problem of the pathogenesis of this rare disease.

It is evident that there is a disturbance in the histogenetical development at the limit between the epiphyseal plate and the periosteum and that this may be of importance to the develop-

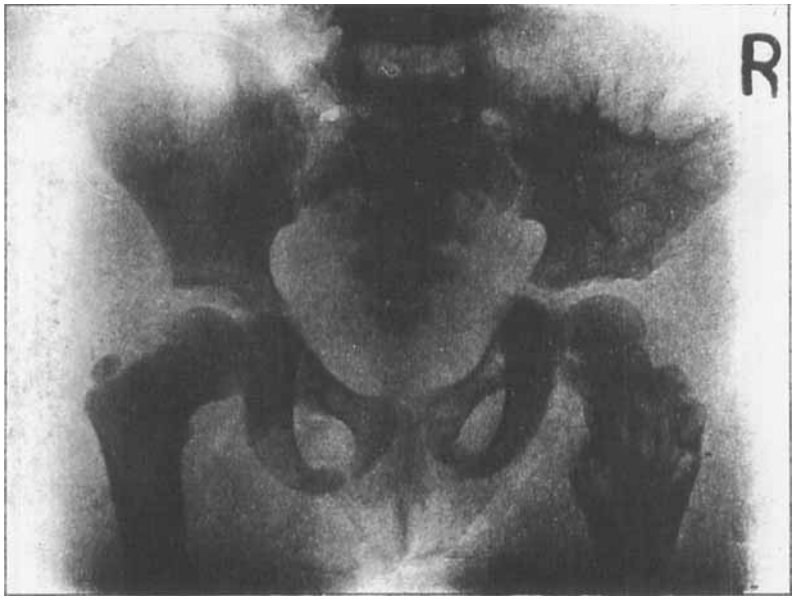

Fig. 15.
Case 2, 1924. Roentgenogram of the pelvis (from Lindström's paper).

ment of the metaphyseal foci into diaphyseal (cf. fig. 4). In the places where the metaphyses exhibit changes in the stages II-III the corner between the epiphyseal plate and the outer surface of the metaphysis does not consist of bone but of cartilage. In stages I-II the base and growth zone of a focus is considered a limited portion of the precartilaginous connective tissue of the epiphyseal plate, giving rise to cartilage which of some unknown reason is not replaced by enchondral bone. *In Ollier's disease the base of a focus during growth successively moves past the angle between the epiphyseal plate and the sur-*

face of the bone. This gave rise to the thought that the undifferentiated layer of the epiphyseal plate may successively move from the inner parts of the plate to the surface of the bone. This lead to the question whether in normal postembryonic bone

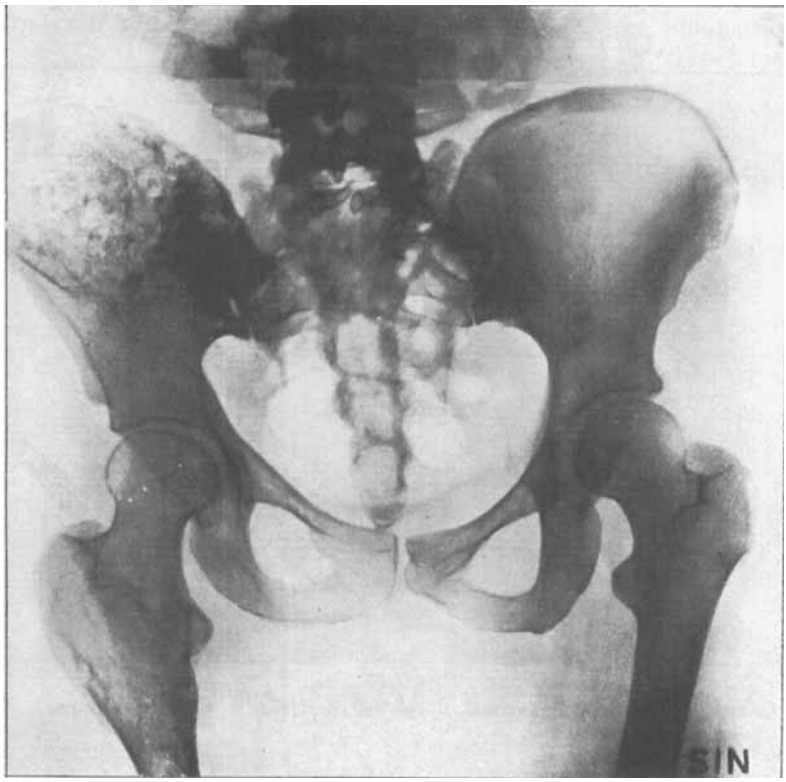

Fig. 16.
Case 2, 1946. Roentgenogram of the pelvis.

growth the undifferentiated connective tissue within the epiphyseal cartilage may be responsible for the formation of the osteogenic layer of the periosteum. A study of the literature on the normal bone growth showed that the histogenetical development in the transition zone between epiphyseal cartilage and periosteum has not been subject to thorough investigations since *Ranvier* in 1889 investigated this zone.

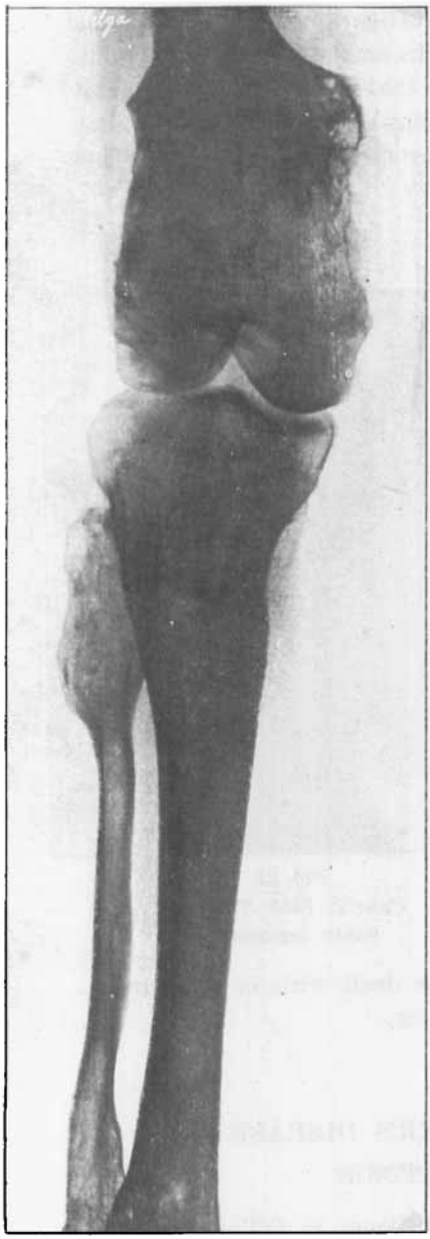

Fig. 17.
Case 2, 1946. The right knee and leg.

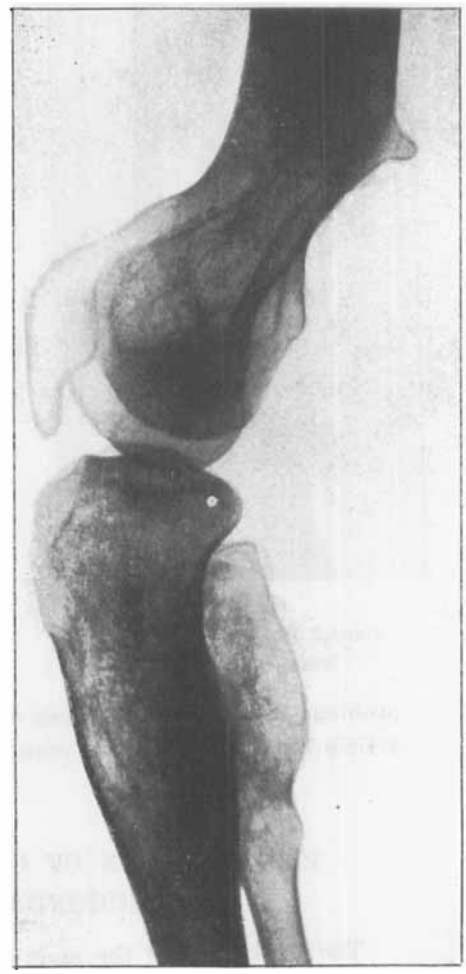

Fig. 18.
Case 2, 1946. Side-view of the right knee region.

Ranvier, whose histological investigations in general seem to have been left unobserved in works on the pathological conditions of bones, drew the conclusion that the osteogenic layer of the periosteum of the normal growing bone probably originates in cells primarily lying within the epiphyseal cartilage. This

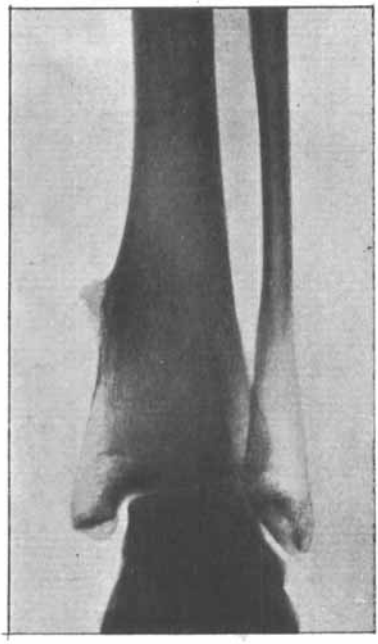

Fig. 19.
Case 2. 1946. The right ankle (exostosis).

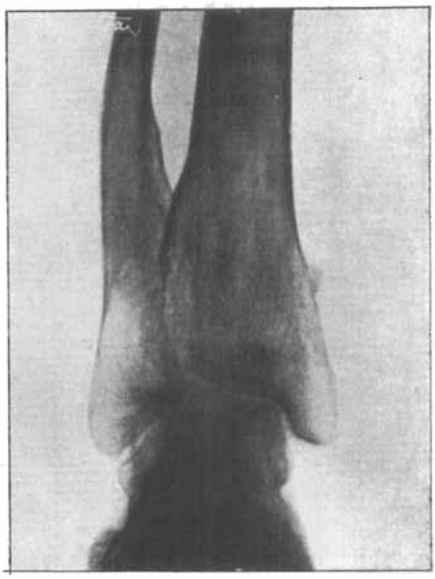

Fig. 20.
Case 2. 1946. The left ankle (exostosis).

problem and its consequences will be dealt with in a separate article in Acta chirurgica scandinavica.

THE RELATION OF OLLIER'S DISEASE TO ENCHONDROMATOSIS

The thickening of the ends of the bones in Ollier's disease is a consequence of the development of the foci. The car-

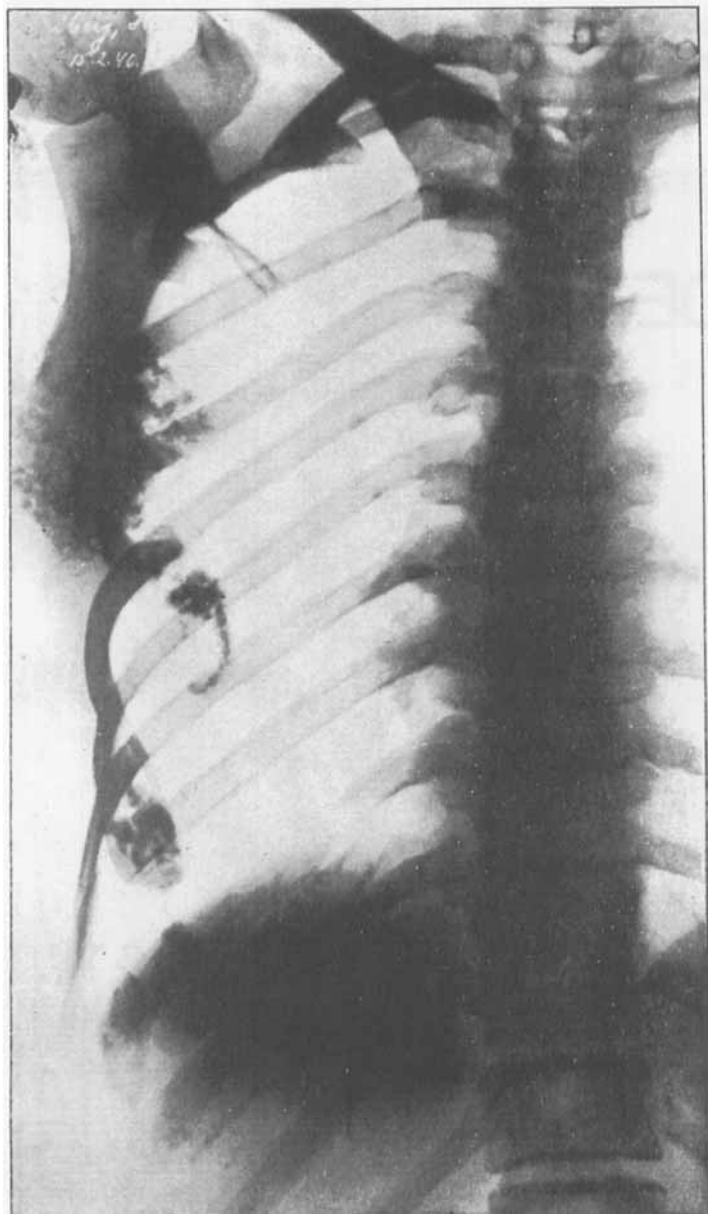

Fig. 21.

Case 2. 1946. Calcified foci in the right scapula and ribs.

tilaginous tissue in the foci is not resorbed at normal speed in order to give way to the enchondral ossification. Neither can the resorption from the surface which should take place in

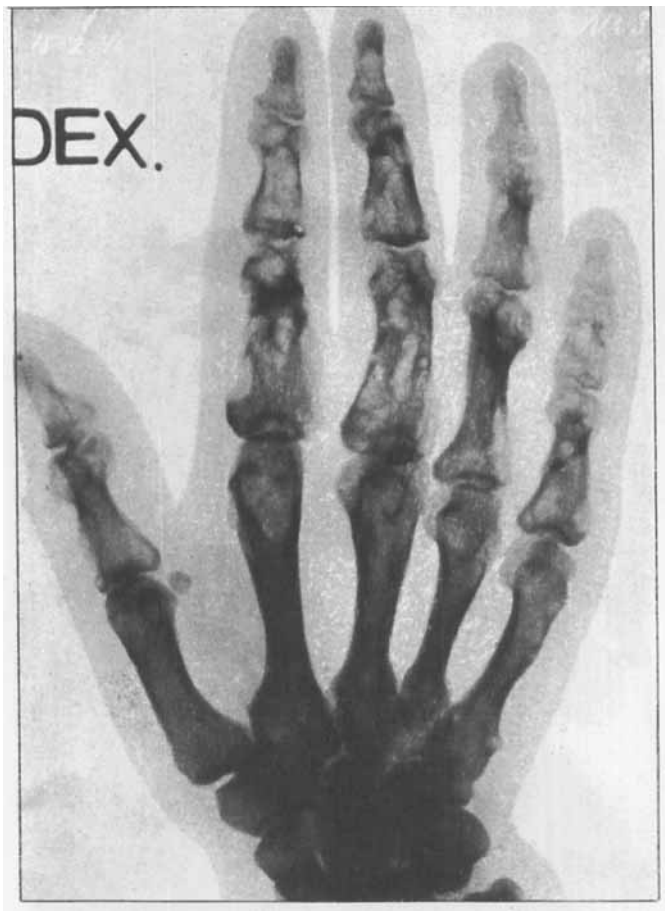

Fig. 22.
Case 2. 1946. The right hand.

order to allow the end of the growing bone successively to merge into the narrower diaphysis (the tubulation), follow normally. Thickening and apparent tumors may thus develop without any true neoplastic growth of cartilage.

In literature about ten cases which do not completely correspond to the above described, may be found partly under the name Ollier's growth disturbance, partly under enchondromatosis. Among these *Hackenbroch's*, *Thiemann's* and *Weiss'* cases may be mentioned. All these exhibit multiple cartilaginous foci

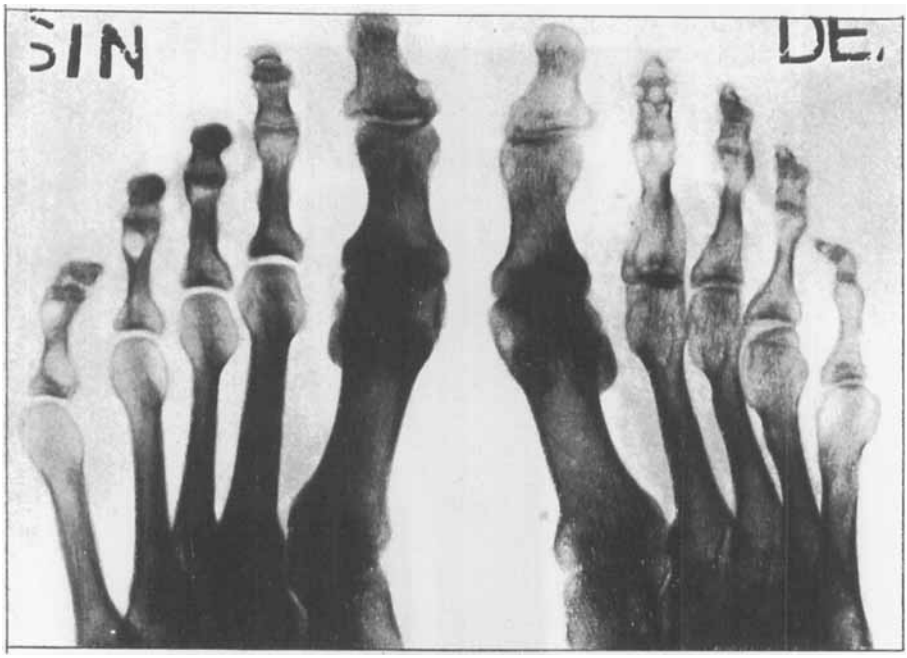

Fig. 23.
Case 2, 1946. The toes and metatarsal bones.

in the metaphyses and diaphyses of the tubular bones. They are ranked by these authors in the same category as other cases of "Ollier's growth disturbance". If the roentgenograms of these cases are examined, it may nevertheless be noticed that they differ considerably from those of *Johansson, Bentzon* and *Lindström,* for instance. Most of the foci are not of the typical longitudinal shape, but are either round or oval, partly consisting of conglomerates of small round clear areas (*Weiss'* case). Further these cases show in the fingers tumors of such a size that they must be considered real enchondromata with consider-

able neoplastic power of growth. It is hardly accidental that these cases with predominant round and oval foci exhibit tumors of considerable size and that many authors describing such cases, deny Ollier's disease as a roentgenologically definable group. The resemblance between the group represented by the cases of *Hackenbroch, Weiss* and *Thiemann* and that represented

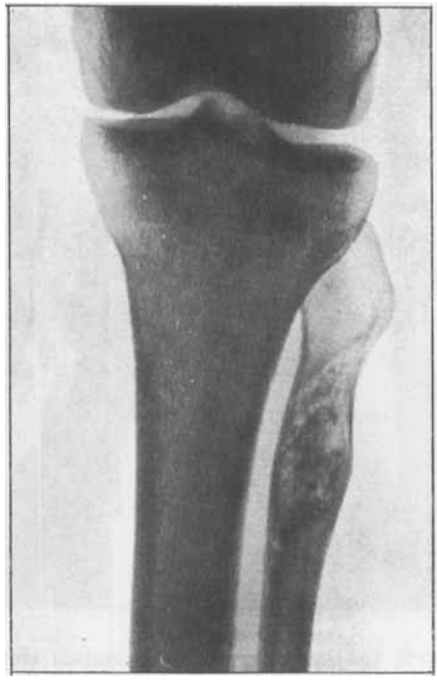

Fig. 24.
Case 2. 1946. The left knee-region.

by the cases of *Johansson, Bentzon* and *Lindström* is, however, so great that it cannot be a question of a difference in the nature of the process but of a difference in degree.

The after-examination of *Lindström*'s case gives no doubt valuable information for the elucidation of these problems. The examination at the age of 25 shows that practically all foci, with the exception of those in the toes and fingers, have ossified or

calcified respectively. In the cases of *Hackenbroch, Weiss* and *Thiemann* the case is considerably different. In the adult patient extensive uncalcified tumors with a tendency to continuous growth were still observed. It is evident that the shape of the foci is a circumstance closely connected with the prognosis in these cases seeing that the round foci are a sign of neoplastic growth. The shape of the longitudinal foci, however, is due to their growth being principally appositional, setting out from the epiphyseal cartilage. In my case (case 1) a certain growth in the breath of the foci may, it is true, be noticed. Interstitial growth is, however, a quality possessed also by normal cartilage and in my case the expansive growth was not great enough to alter the primary longitudinal shape of the foci.

Lindström quotes *Borst* as follows: "However inclined we are to consider the process of the constitution of tumors as completely different from all other growth processes, we cannot disregard the fact that apparently many and inappreciable transitions exist leading from the range of hyperplasia to that of the autonomous tumors." The follow-up examination of *Lindström*'s case shows that the prognosis in a case of Ollier's disease with the typical striped foci and gouged-out areas differs from the prognosis in typical enchondromatosis. A comparison with other published cases, however, shows that the transition between these diseases is extremely indistinct. Analogous phenomena often occur in pathology. New foci arising during the growth as in the case of *Lindström,* hardly change the prognosis, as also these foci calcify after completed growth. In this case the tumor of the ovary which was found and removed can hardly be considered in direct connection with the skeletal disease but sooner as a parallel occurrence of the same category as the hemangiomata.

When *Ollier* described and defined the disease which he called dyschondroplasia he no doubt chiefly stressed the typical roentgenological finding. Later attention principally turned to the mainly unilateral distribution of the process due to a great extent to the statements by *Witteck* and *Frangenheim.* The unilaterality is of no value in defining the disease as bilateral

cases with symmetric occurrence of the typical longitudinal cartilaginous foci have been published (*Müller*).

In many branches of pathology where the transition between hyper- and dysplasia respectively on one hand and autonomous tumorous growth on the other is indistinct, we are entitled and compelled to give the extreme cases different names and definitions. This is both of theoretical and practical importance as far as Ollier's disease and enchondromatosis are concerned, because of the great differences in the roentgenological finding and the prognosis in typical cases. *Considering Ollier's classical description there is a reason to leave the possible unilaterality of the process out of account, designating as Ollier's disease cases with typical longitudinal striped cartilaginous foci which have an evident tendency to calcification, qualities which are closely connected with the favourable prognosis of these cases. Under the denomination enchondromatosis we may collect the cases in which the foci of principally round form and continous growth at adult age constitute a sign of a really autonomous neoplastic growth.*

In the re-examination of the case of *Lindström* uncalcified but comparatively small foci were still found in toes and fingers. Neither did this phenomenon escape *Ollier:* "They remain very distinct in the phalanges of the toes, but especially so in the fingers." These persisting foci in toes and fingers in this case are mostly round. That a tendency towards the development of foci with a certain tumorous growth is present in typical cases of Ollier's disease hardly deprives us of the right to separate this group from the typical enchondromatosis. This question will be further dealt with below.

THE RELATION OF OLLIER'S DISEASE TO MULTIPLE CARTILAGINOUS EXOSTOSES

Ollier, Bentzon and *Logroscino* i.a. noticed exostoses in their cases, but as far as I know there has been no real case of Ollier's disease with so typical cartilaginous exostoses as those

discovered in the follow-up examination of *Lindström's* case. In typical cases of multiple cartilaginous exostoses, on the other hand, longitudinal cartilaginous foci have often been found in the bones (*Kienböck, Milani* and others). The general tendency has lately been to consider Ollier's disease, enchondromatosis and multiple cartilaginous exostoses as three different groups under the common heading of chondrodysplasia. The above facts and viewpoints must be considered as supporting this classification. The use of the designation chondrodysplasia as a common heading for all these affections speaks against the use of the term dyschondroplasia.

The fact that *exostoses, enchondromata and cartilaginous foci of the Ollier-type may be found in the same case* and in the same bones has in many quarters lead to the opinion that a division of the concept chondrodysplasia is not justified. *It is, however, evident that in most cases one of the three manifestations predominates. This difference with regard to the predominating form of foci seems somehow to be connected with differences both in heredity and in the tendency to a unilateral distribution.* Multiple cartilaginous exostoses present a picture of a disease with dominant inheritance (*F. Langenskiöld* and others). In typical cases of Ollier's disease no hereditary factors have ever with certainty been established, a circumstance which has induced some authors (*Logroscino*) to doubt the close connection between the exostosis disease and Ollier's disease and the character of genetically conditioned disease of the latter. Literature provides, however, so many examples of the close connection and indistinct transitions between enchondromata, multiple cartilaginous exostoses and Ollier's disease that their at all events partly common etiology can hardly be doubted. We may consider the possibility of different gene combinations causing differences both in heredity, in the form of manifestation and in localization (unilaterality) and that diseases depending on gene factors may arise through mutation.

The tendency towards unilateral localization is a quality which may occur in all three principal forms of chondrodys-

plasia. It is a rule with rare exceptions in Ollier's disease, unusual in typical enchondromatosis and still more rare in multiple cartilaginous exostoses. Certain inheritance has never been established in cases of typical Ollier's disease, provable inheritance is common in enchondromatosis and a general rule in multiple cartilaginous exostoses.

The pathogenesis and the origin of enchondromata and the rise of multiple cartilaginous exostoses are much discussed questions. The establishing of the different stages of development of the foci in Ollier's disease furnishes some viewpoints on these problems which shall be dealt with in another article in Acta chirurgica scandinavica.

DIAGNOSIS. CLINICAL CHARACTERIZATION. THERAPY

The above investigation shows that it is difficult to present all cases in literature which can be considered Ollier's disease. When metaphyses and diaphyses exhibit typical gouged-out areas the diagnosis is easily established by one who knows the disease, but in cases where all affected metaphyses show great changes (*Cleveland*'s and *Cole*'s cases for instance) the diagnosis is more difficult. Here the longitudinal stripes and the typical dense spots are, however, reliable indications. Intermediary cases between Ollier's disease and enchondromatosis or multiple cartilaginous exostoses, where none of the three manifestations predominates, may be designated by the common name of chondrodysplasia.

Ollier's disease in its typical form is rare, the number of published cases hardly exceeding 100. Several cases have been described in journals with limited distribution, many have not even been reported in the great medical journals, and are therefore not available for the forming of an opinion. This article is based on the information obtained of the following 46 certain cases: 1) Available in the original: *Burchard* (2 cases), *Bojesen, Johansson, Cameron & Trethovan, Bienert, Johannesen, Bentzon, Lindström, Jansen, Cole, Müller, Cleveland, Flotow*

(3 cases), *Hessenthaler, Blount, Bromer & John, Heidbrinck, Levin, Bonola* (3 cases), *Boppe & Lièvre & Franco, Richard & Depuis & Roederer & Froyez* (2 cases), *Hunter & Wiles, Zikeef, Logroscino, Sanderson & Smyth, Stark, Passarge, Hellner* (1940), *Fritzsch,* case 1 in this article. 2) Available in reports which make an estimation possible. *Ollier* (2 cases, described in *Molin*'s thesis), *Nové-Josserand & Destot* (in *Molin*'s thesis), *Koehler, Witteck, Kummer, Fairbank, Massart & Ducrouquet & Chauveau, Barrin, Beuing.*

The following cases should be considered intermediary forms between enchondromatosis and Ollier's disease: *Thiemann, Hackenbroch, Weiss, Dahl, Schrattenbach, Fernbach, Hellner* (1936), *Gäde, Holldack, Dahle.*

In some cases congenital defects such as spina bifida (*Logroscino*) and microdactylia (*Bromer & John*) have occurred in the same family. The first symptom has usually been limping owing to unilateral shortening of the limbs (a few symmetric cases excepted). This shortening has sometimes been discovered at birth (*Cole*), generally at an age of 1-2 years, in several cases not before the age of 5 years. The further course of the disease has been characterized by increasing shortening and by bending and thickening of the ends of the long tubular bones during growth. The degree of the growth disturbance seems to be related to the degree of development of foci in the metaphyses, most important to the growth, and to the point of time of their occurrence. The deformities, on the other hand, are related to the localization of the foci, large lateral foci leading to a valgus position, medial foci to a varus position etc. All authors who have followed their cases during a number of years have drawn the conclusion that the prognosis is good, and my re-examination of a case at adult age confirms this opinion. In literature two cases are described (*Chrysospathes, Carter*) which probably show final stages of Ollier's disease. There are, however, no roentgenograms from childhood. *Carter*'s case shows that the prognosis at a more advanced age may be deteriorated through the rise of autonomously growing tumors in the skeleton.

A surgical operation consisting of an exstirpation of the cartilaginous masses with or without bone grafting is evidently of little benefit to the patient with Ollier's disease, at least during the growth period. *Passarge* assumes that the bone-graft in her case caused calcification in unremoved adjacent foci. Experience shows that the foci in question would probably have calcified in spite of all operations. For the correction of deformities surgical therapy in the form of osteotomy is of inestimable value. Experience shows that healing after osteotomy is good. The unilateral shortening of a lower extremity may suitably be corrected with a bandage of the type which was used in *Cleveland*'s case.

SUMMARY

The discovery of a new case of Ollier's disease caused a follow-up examination of a similar case which was published by *Lindström* in 1924. These two cases of this system disease of the growing skeleton are described. Roentgenograms have been taken in one case at the age of 3½ and 6 years, in the other at 4 and 25 years. These roentgenograms illustrate several circumstances in the pathogenesis and development of the disease.

In Ollier's disease longitudinal cartilaginous foci occur principally in the metaphyses and diaphyses of the tubular bones and in the pelvis. The roentgenograms of one of the described cases confirm the opinion of *Ollier* that the foci arise through parts of the epiphyseal plates forming a cartilage which persists and which is not replaced by enchondral bone. The origin of the diaphyseal foci and their relation to the metaphyseal foci has so far been unclear. *A metaphyseal focus develops gradually into a diaphyseal focus by its base and growth zone during the growth of the bone gradually moving out of the epiphyseal plate to the outer surface of the bone* (*cf. fig. 4*).

The roentgenograms of the adult patient show that the cartilaginous foci after the end of the growth period have os-

sified or calcified everywhere except in the toes and fingers which is generally not the case in typical enchondromatosis. In the same case typical cartilaginous exostoses occurred. The study of other described cases shows that the transition between Ollier's disease and enchondromatosis is indistinct. The longitudinal shape of the cartilaginous foci is caused by appositional growth indicating a satisfactory prognosis (Ollier's disease). Round foci indicate an additional expansive growth and a less good prognosis (enchondromatosis). The investigation supports the opinion that Ollier's disease, enchondromatosis and multiple cartilaginous exostoses are all different forms of disease depending on in some ways different genetic factors and classified under the common heading chondrodysplasia.

The elucidation of the different stages of development of the foci in Ollier's disease furnishes some viewpoints on the normal bone growth and the pathogenesis in the other forms of chondrodysplasia. These points of view will be published in Acta chirurgica scandinavica. (1947. *95*. 367.)

ZUSAMMENFASSUNG

Die Entdeckung eines neuen Falles der Ollier'schen Krankheit veranlasste eine Nachuntersuchung eines ähnlichen Falles, der von *Lindström* im Jahre 1924 veröffentlicht wurde. Diese zwei Fälle von der Systemerkrankung des wachsenden Skeletts werden beschrieben. Röntgenaufnahmen sind von dem einen Falle im Alter von 3½ und 6 Jahren gemacht worden, von dem anderen im Alter von 4 und 25 Jahren. Diese Aufnahmen sind geeignet, mehrere Umstände in der Pathogenese und Entwicklung der Krankheit klarzulegen.

Bei der Ollier'schen Krankheit treten vor allem in den Metaphysen und Diaphysen der Röhrenknochen und im Becken längliche Knorpelherde auf. Die Röntgenaufnahmen von dem einen beschriebenen Falle bestätigen die Auffassung Olliers, dass die Herde dadurch entstehen, dass gewisse Teile der Epiphysenscheiben einen Knorpel bilden, welcher persistiert und

nicht von enchondralem Knochen ersetzt wird. Die Entstehungsweise der Diaphysenherde und ihr Verhältnis zu den Metaphysenherden waren bisher unklar. *Ein Metaphysenherd entwickelt sich almählich zu einem Diaphysenherde dadurch dass seine Basis und Wachstumzone bei dem Zuwachs des Knochens successiv aus der Epiphysenscheibe auf die Aussenfläche des Knochens verschoben wird* (*vgl. Fig. 4*).

Die Röntgenaufnahmen des erwachsenen Patienten zeigen dass die Knorpelherde nach Ende der Wachstumsperiode überall ausser in Zehen und Fingern ossifiziert oder verkalkt worden sind, was bei der Enchondromatose im allgemeinen nicht der Fall ist. Bei demselben Falle wurden typische cartilaginäre Exostosen gefunden. Das Studium anderer publizierten Fälle zeigt dass die Grenze zwischen der Ollier'schen Krankheit und der Enchondromatose fliessend ist. Längliche Form der Knorpelherde wird von appositionellem Wachstum bedingt und deutet auf eine gute Prognose hin (Ollier'sche Krankheit). Runde Herde deuten auf expansive Wucherung und schlechtere Prognose hin (Enchondromatose). Die Untersuchung stützt die Auffassung, dass die Ollier'sche Krankheit, die Enchondromatose und multiple cartilaginäre Exostosen alle verschiedene genbedingte Krankheitsformen unter der gemeinsamen Rubrik Chondrodysplasie sind.

Der Nachweis der verschiedenen Entwicklungsstadien der Herde bei der Ollier'schen Krankheit bietet gewisse Gesichtspunkte auf das normale Knochenwachstum und die Pathogenese bei den anderen Formen der Chondrodysplasie dar. Diese Gesichtspunkte werden in der Acta chirurgica scandinavica veröffentlicht werden. (1947. *95*. 367.)

RÉSUMÉ

Le découverte d'un nouveau cas de la maladie d'Ollier fut la cause d'un examen posterieur d'un cas semblable, publié par *Lindström* en 1924. On décrit ces deux cas de maladie attaquant les squelettes d'enfant. Des images radiologiques furent prises

du premier à l'age de 3 ans ½ et de 6 ans, du second à l'âge de 4 et de 25 ans. Ces images sont de nature à éclarcir plusieurs faits de la pathogénie et du développement de la maladie.

Dans les cas de la maladie d'Ollier on trouve surtout dans les métaphyses et les diaphyses des os tubulaires et dans les os pelviens, des foyers cartilagineux longs. Les radiographies d'un des cas décrits confirme l'avis d'Ollier selon lequel les foyers naissant parce que des parties des cartilages de conjugaison formant du cartilage qui persiste et n'est pas remplacé par os enchondral. La naissance des foyers des diaphyses et leur relation avec les foyers métaphysaires n'etaint que très peu clairs jusqu'ici. *Un foyer métaphysaire se développe par degrés en un foyer diaphysaire, sa base et sa zone de croissance se déplacant successivement par suite de la croissance de l'os, de la cartilage de conjugaison jusqu'à la superficie exterieure de l'os* (cf. fig. 4).

Les radiographies de la patiente adulte montrent partout, aprés la fin de la période de croissance, l'ossification et la calcification des foyers cartilagineux, à l'exception des doigts de pied et des doigts, ce qui n'est d'habitude pas le cas pour les enchondromatoses. Dans le même cas on trouve des exostoses cartilagineuses typiques. L'examen d'autres cas publiés montrent que la différence entre la maladie d'Ollier et les enchondromatoses n'est aucunement nette. La forme longue des foyers cartilagineux est due à un accroissement appositionnel et fait prévoir un bon pronostic (maladie d'Ollier). Des foyers ronds indiquent un accroissement expansif additionnel et font prévoir un pronostic moins favorable (enchondromatose). L'examen confirme l'avis selon laquelle la maladie d'Ollier, l'enchondromatose et les exostoses multiples cartilagineuses sont tous des formes maladives congénitales différentes réunies sous la même dénomination de la chondrodysplasie.

Le fait de pouvoir indiquer les différentes phases de développement des foyers de la maladie d'Ollier donne certaines indications quant à la croissance normale de l'os et a la pathogénie pour les autres formes de la chondrodysplasie. Ces indications seront publiées dans les Acta chir. scand. (1947. *95*. 367.)

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