

THE GROWTH MECHANISM OF THE EPIPHYSEAL CARTILAGE IN THE LIGHT OF EXPERIMENTAL OBSERVATIONS¹

BY

A. LANGENSKIÖLD & W. EDGREN

In an article on Ollier's disease published by *A. Langenskiöld* (*Acta orthop. scand.* 1947, 17, 93) the observation that the cartilaginous foci which appear in the skeleton in this disease develop in a characteristic manner was reported (Fig. 1). In another article (*Acta chir. scand.* 1947, 95, 367) it was suggested that this development is caused by a successive displacement of cellular elements from the central parts of the epiphyseal cartilage to its periphery transversely to the axis of the bone. It was assumed that this displacement occurs in normal bone growth in the layer between the bony epiphysis and the layer of cartilage cell columns. The osteogenic layer of the diaphyseal periosteum probably grows in length by means of a cellular material which is displaced from the interior of the epiphyseal cartilage. As this idea of the mechanism of normal bone growth can explain several phenomena in the pathology of bone growth it seemed desirable to try to elucidate the question experimentally.

The basis of the experiments was the idea, which has been stated previously, that Ollier's disease might be compared to an experiment by nature with "labelled cells" which only partly obey the laws of normal differentiation, growth and resorption. According to this idea it seemed probable that irradiation of limited portions of the epiphyseal cartilages

¹ A preliminary report.

with X-rays might produce foci which would be similar to those of Ollier's disease, and would undergo the same stages of development.

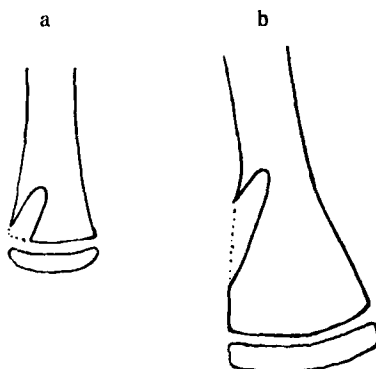


Fig. 1.

Schematic drawings illustrating the development of a cartilaginous focus in Ollier's disease. a) Stage II, b) Stage IV. These drawings were published before the experiments were begun (cf. *Acta chir. scand.* 1947).

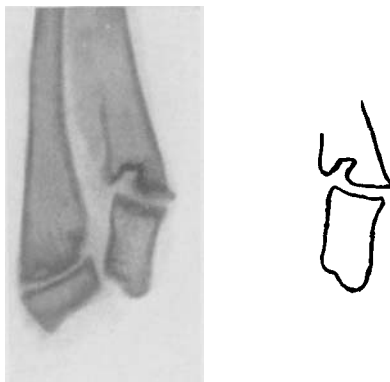


Fig. 2.

Radiograph of the antebrachium of a rabbit 41 days after localized X-ray irradiation. Beneath the radiograph a contour drawing of the ulna. Note the oblique position of the focus in relation to the diaphysis.

In rabbits aged 3-6 weeks, limited portions of the distal epiphyseal cartilages of the radius or ulna or both bones were

exposed to a single X-ray dose of 8000-20000 r. The growth was then followed by repeated X-ray-photography. It was found that ossification slowed down in the part of the meta-

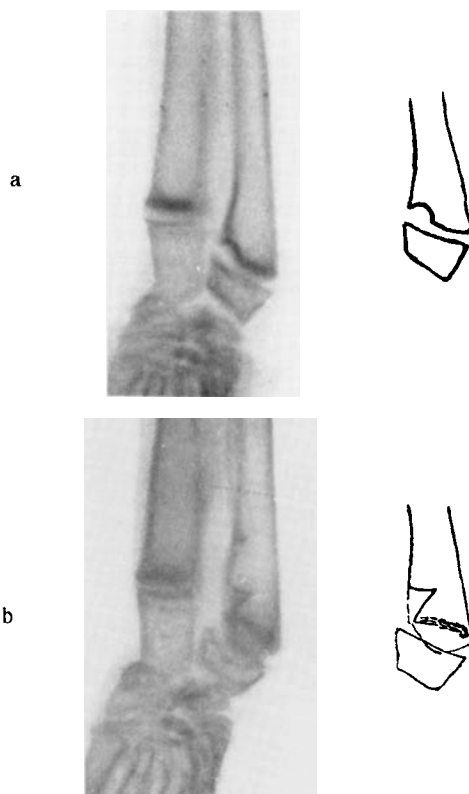


Fig. 3.

Radiograph of the antibrachium of a rabbit. a) 26 days after localized X-ray irradiation, b) the same leg 49 days after irradiation. Beneath the radiographs, contour drawings of the radius.

physis which corresponded to the irradiated part of the cartilage. After 3-5 weeks the roentgenograms showed foci very similar to those seen in Ollier's disease (Fig. 2). These experimentally provoked foci developed with regard to their

shape, in the same manner as the Ollier foci. The epiphyseal end of a focus was gradually displaced towards the periphery of the epiphyseal plate and finally lost contact with it. At this stage the foci also appeared, in roentgenograms taken at a certain angle, as triangular notches in the periphery of the bones (Fig. 3). Perpendicular projections also showed the similarity to Ollier foci.

As the working-hypothesis has been proved correct, these experimental results may support the views on normal and pathological bone growth which were expressed in the articles already mentioned. Several other arguments, which cannot be discussed here, support this view, that in a certain layer of the normal epiphyseal cartilage, a migration of cellular matter occurs transversely to the axis of the bone. This displacement is assumed to play a rôle in any pathological process in epiphyseal cartilage.—In localized X-ray irradiation we may have a useful method for the study of growth processes.—The detailed description of the experimental results with microphotographs and more roentgenograms will be published later in *Acta chirurgica scandinavica*.

S U M M A R Y

Using localized X-ray irradiation of limited areas of the epiphyseal cartilages of growing rabbits, the authors provoked foci, which, with regard to their shape, developed in the same characteristic manner as the foci in Ollier's disease. The results support the views on bone growth which were put forward by A. Langenskiöld in 1947.

R E S U M E

Par application localisée des rayons X à des parties limitées des cartilages epiphysaires des lapins en croissance les auteurs ont provoqué des foyers qui se développent à l'égard de sa configuration de même façon caractéristique que les foyers dans la maladie d'Ollier. Les résultats appuyent les vues sur la croissance de l'os présentées en 1947 par A. Langenskiöld.

ZUSAMMENFASSUNG

Durch lokalisierte Röntgenbestrahlung begrenzter Epiphysenknorpelpartien an wachsenden Kaninchen haben die Verfasser Herde provoziert, die sich in Bezug auf ihre Form in derselben charakteristischen Weise entwickeln wie die Herde bei der Ollier'schen Krankheit. Die Resultate stützen die Ansichten über das Knochenwachstum, die im Jahre 1947 von A. Langenskiöld ausgesprochen wurden.

DISCUSSION

Lütken, Silfverskiöld.

P. G. K. Bentzon, Århus: referred to his publication in *Acta Radiologica* vol. 3 and said that in Ollier's disease one must regard diaphyseal "chondroma formations" as the most important element of the disease. The chondroma lines which can be shown corresponding with the nutrient foramina of the diaphysis can never originate in elements developed from the epiphyseal cartilage since the central parts of the bone are developed from the primary *diaphyseal* cartilage. *Bentzon* showed illustrations of this condition. (*Bentzon* will give a more extensive and detailed account of his view of Ollier's disease at Nordisk Ortopedisk Forening's meeting in Helsingfors 1949).

A. Langenskiöld: With reference to the radiograph shown by Dr. *Bentzon* we have reason to assume that the part of the tibia in which the proximal cartilaginous focus was situated had developed in its entirety from the proximal epiphyseal cartilage. This cartilage is responsible for a good half of the growth in length of the tibia. The oldest part of the diaphysis of the tibia corresponds to a level lying somewhat distal to the mid point of the bone.—The migration of cells which is assumed to occur in the layer of the epiphyseal cartilage which lies between the bony epiphysis and the layer of cartilage cell columns does not normally leave any trace in the structure of the metaphysis or in the central parts of the

cartilage. Only in certain pathological conditions do „oblique lines” occur in the metaphyses. These oblique lines are the traces left behind by the limits between normal and pathological tissues in the epiphyseal cartilage. This can be seen directly in histological sections of bones with foci provoked by localized X-ray irradiation.—Dr. Lütken has pointed out that foci corresponding to the type described in the previous papers as stage I, have not been provoked experimentally. This is true, but none of the conclusions drawn either here or in the previous articles are based on the assumption of the existence of this stage. On the contrary, it was previously emphasized that stage I must be considered hypothetical (*Acta orthop. scand.* 1947), whereas the assumption of the existence of stages II-IV is based on facts. The hypothesis of stage I is based on reports in the literature dealing with enchondromata of a less benign nature than Ollier’s disease.

Tissue migration of a type which may occur in the growth of the epiphyseal cartilage is common in embryonic development. This has been shown by V. Vogt (*Roux’ Arch.* 1929. 120. 384) by excellent experiments with labelled groups of cells. Vogt used vital staining to label round areas of the superficial tissue at the equatorial level of amphibian embryos in the gastrula stage. These stained spots developed into long stripes which gradually migrated from the equatorial level through the blastopore into the interior of the gastrula. Although the analogy between these stained stripes and the stripes occurring in the skeleton in Ollier’s disease and in multiple cartilaginous exostoses is striking, this phenomenon is of course no real additional evidence of the correctness of the conclusions concerning bone growth. It will only serve as an example for the sceptic who has a preconceived opinion that the occurrence of tissue migration is improbable.—For other particulars reference is made to the articles mentioned in the report.