

## EXPERIMENTAL EPIPHYSEAL TRANSPLANTATION

### Part II

#### *Histological observations*

By

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#### INTRODUCTION AND PROBLEM

In a previous paper I described radiological observations on survival and growth of the autotransplanted proximal end of the fibula to the site of the removed radius and to the thigh of young rabbits. It appeared that *the longitudinal growth of the graft in the respective sites amounted to 2/3 and 1/2 of the normal growth of the fibula.*

The object of the present histological investigation has been to create a basis for estimating the prospects of successful epiphyseal transplantation and the reasons for failure of such a transplantation by studying which parts of the transplant survive, how regeneration takes place, and when and how longitudinal growth is resumed.

#### HISTORY

At *reimplantation* of epiphyseal cartilage, *Enderlen* observed an increase in volume of the matrix in the centre of the cartilage during the first few days. This region degenerated while in the surviving peripheral cartilaginous regions there was abundant cell proliferation followed by continued enchondral new formation of bone. *Obata* and *Heller* (1914) similarly observed primary necrosis of the centre of the cartilage followed by almost complete regeneration with hardly any disturbance of growth. *Haas* (1915, 1916), on the other hand, did not notice any changes in the cartilage during the first two to three weeks after the operation, but thereafter, at the border between the distal and middle thirds of the epiphyseal cartilage, there appeared a zone of lightly staining cells, necrosis, fragmentation and finally a penetration of connective tissue from the periphery resulting in arrest of growth. *Brücke* observed necrotic cartilage remnants in the metaphysis at a distance of 2 to 3 mm. from the epiphyseal line and believed that these marked the site of the

original epiphyseal cartilage which had been "displaced" towards the metaphysis by the resumed new bone formation. He believed that the regeneration of the epiphyseal cartilage emanates from surviving parts of the reserve zone and the columnar zone and that these in turn receive fresh supplies of cells from the perichondrium at the "encoche d'ossification".

At *autotransplantation* to bone, *Enderlen* and *Haas* observed phenomena similar to those seen in reimplantation. In *Obata's* experiments only the peripheral regions of the epiphyseal plate regenerated, while a streak of connective tissue penetrating from the sides in between the proliferation zone and the primary calcification zone cut off the growth zone. *Heller* (1918), the pioneer in this field, observed incomplete regeneration of the epiphyseal cartilage starting about two weeks after the transplantation. He divided the histological development of the transplant into the following stages: (1) Primary necrosis involving varying amounts of the epiphyseal cartilage and occurring shortly after transplantation, (2) regeneration of an irregular cartilaginous mass from a surviving cartilaginous element, setting in as soon as there is renutrition of the transplant which, at transplantation of an epiphyseal plate with thin bone lamellae, took place within 3 to 6 days, (3) reconstruction of the regenerated cartilage to an epiphyseal plate of normal structure, and (4) regained capacity for longitudinal growth. During the first few weeks, *Ring 2* saw only insignificant changes, if any, in the cartilage, but later he noticed eosinophilia of the cells at its centre and penetration of connective tissue into the surrounding matrix as well as calcium deposits in the connective tissue, so that a bony bridge occurred between the epiphyseal nucleus and the metaphysis, after which growth ceased and the epiphyseal line fused.

At autotransplantation to soft tissues, *Axhausen* found regeneration of the border regions of the epiphyseal plate and vascular and lacunar resorption of the necrotic portion of the cartilage proceeding from connective tissue which penetrated, by way of the metaphysis of the transplant, into the epiphyseal plate.

At *homotransplantation* many authors have observed only insignificant regeneration of short duration after the primary stage of degeneration. *Heller* (1918) further noticed secondary degeneration of regenerated cartilage elements and, after the third week, *Ring 3* observed complete degeneration of the entire epiphyseal plate which was replaced by a transverse zone of penetrating connective tissue. *Ring 4* also stated that hardly any radioactive sulfur could be demonstrated in the reserve zone of the transplant, while the sulfur concentration in the columnar zone was normal, and from this he concluded that the cells of the reserve zone did not survive homotransplantation.

Owing to differences in the experimental conditions, the results obtained by different investigators cannot be directly compared. It appears, however, that, in a histological sense, the epiphyseal cartilage is transplantable, at any rate as an autotransplant to bone. An observation made by *Ring 1* indicates that the most essential part of the epiphyseal cartilage for the preservation of a capacity for longitudinal growth is the reserve zone. At selective resection of various parts of the epiphyseal plate with or without adjacent bone, he found

that the plate could seemingly regenerate completely in all cases, but that *growth remained undisturbed only if the reserve zone had been left intact.*

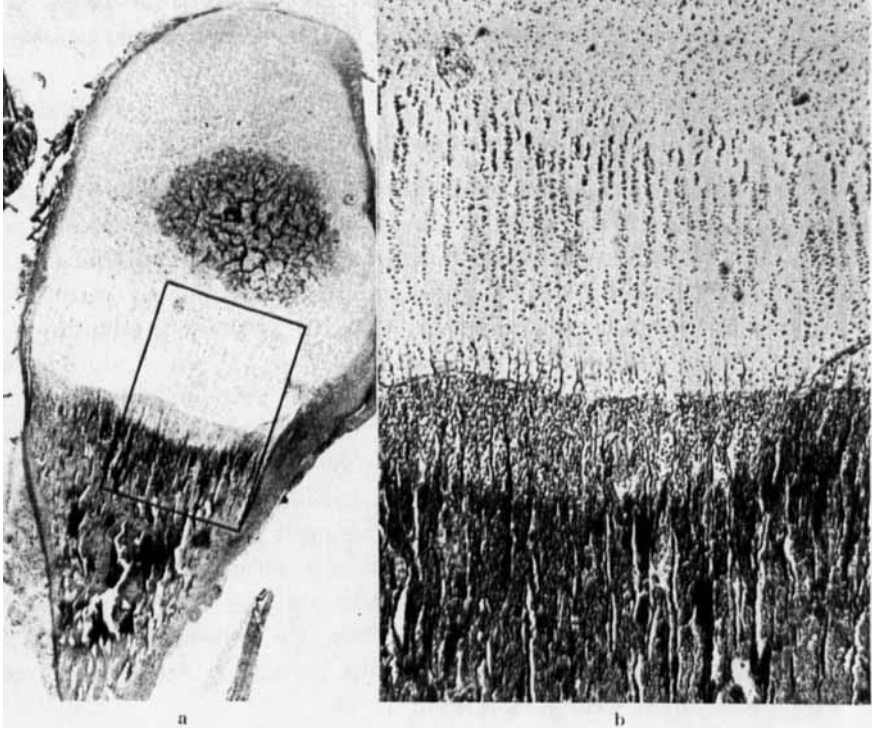
#### METHOD AND MATERIAL

On 34 rabbits, 32 autotransplantations of the proximal part of the fibula to the site of the radius and an equal number to the thigh were carried out. To investigate the dependence of the result of the transplantation on the stage of development of the epiphyseal cartilage, estimated on the basis of the degree of ossification of the epiphyseal nucleus, transplantation was in some cases carried out at the age of 10 days, when the epiphyseal nucleus is not radiologically demonstrable (9 transplantations to the site of the radius and 14 to the thigh), in some cases at the age of 15 days when the epiphyseal nucleus is sometimes radiologically demonstrable (10 to the site of the radius and 12 to the thigh), and in some cases at the age of 21 days when ossification of the nucleus had set in in all cases (13 transplantations to the site of the radius and 6 to the thigh). The animals were killed 2 to 40 days after the transplantation, the extremity in question was examined radiographically, fixed in formalin, decalcified, sectioned and stained with hematoxylin.

#### RESULTS

No certain difference between the different experimental groups could be established. The difference between the results of transplantation to the site of the radius and to the thigh, which was radiographically observed (see part I), must therefore be due to circumstances present after the fortieth day.

*On the second day* after the transplantation, when, radiologically, the transplant was unchanged, it lay in a wound cavity where there was, in places, granulation tissue (Fig. 1a). *In the central parts of the epiphyseal cartilage*, or in those which, in the graft, lay on the side farthest from the ulna and femur respectively, the matrix stained lightly, *the cells were scattered and many of them were vacuolized and stained lightly.* This ill-defined area comprised the major part of both the proliferation zone and the reserve zone and, in slides from the youngest animals, part of the region of the future epiphyseal nucleus. In the metaphysis and the diaphysis no living marrow cells were visible, but the spaces between the primary trabeculae were filled



*Fig. 1.*

Exp. 141. Proximal end of the fibula transplanted to the thigh at the age of 15 days, period of observation 2 days. (b = enlarged detail of a).

- a. The central parts of the epiphyseal cartilage are lightly stained. Next to this part there is a light arcuate zone in the metaphysis, and farther a dark and another light zone.
- b. The nuclei within the lightly stained area are shrunken and sparse. Some distance from the metaphyseal border, in the metaphysis, "packed" detritus may be observed.

with detritus. The latter was divided into *three zones* (Figs. 1 and 2): nearest the borderline between the epiphyseal cartilage and the metaphyseal bone (hereinafter called "the metaphyseal border"), close to the necrotic cartilage region, there was a narrow arcuate zone within which the cell remnants were sparse. There followed a wider, dark zone the periphery of which extended to the metaphyseal border and within which the detrital mass was tightly packed, and, finally a third diffuse zone with more scattered cell remnants.

*On the third to fourth day*, when there were still no radiologically demonstrable changes, a slight accumulation of neutrophil granulo-

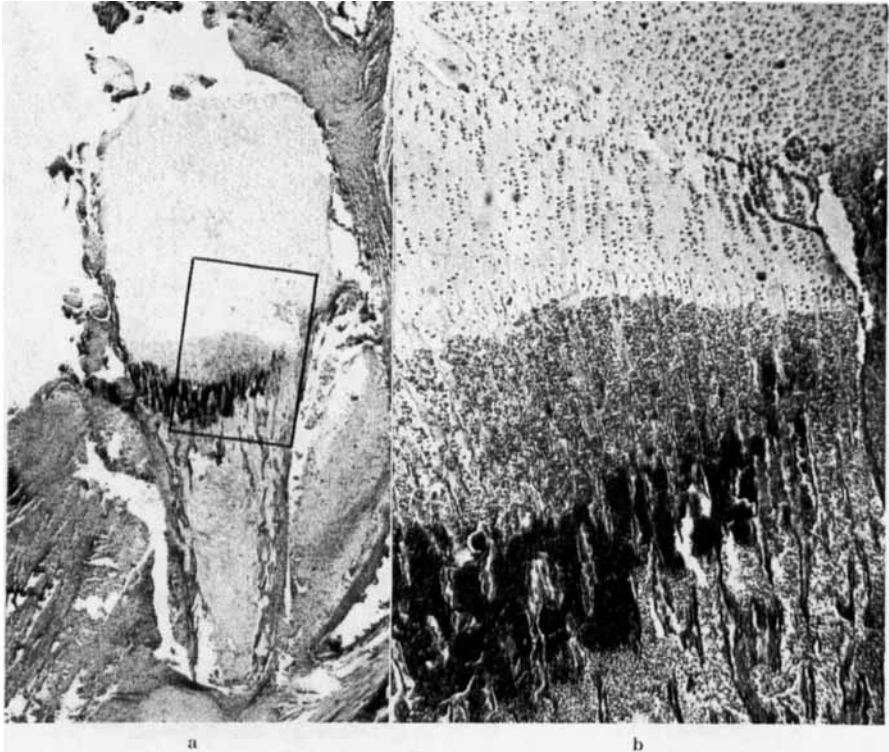


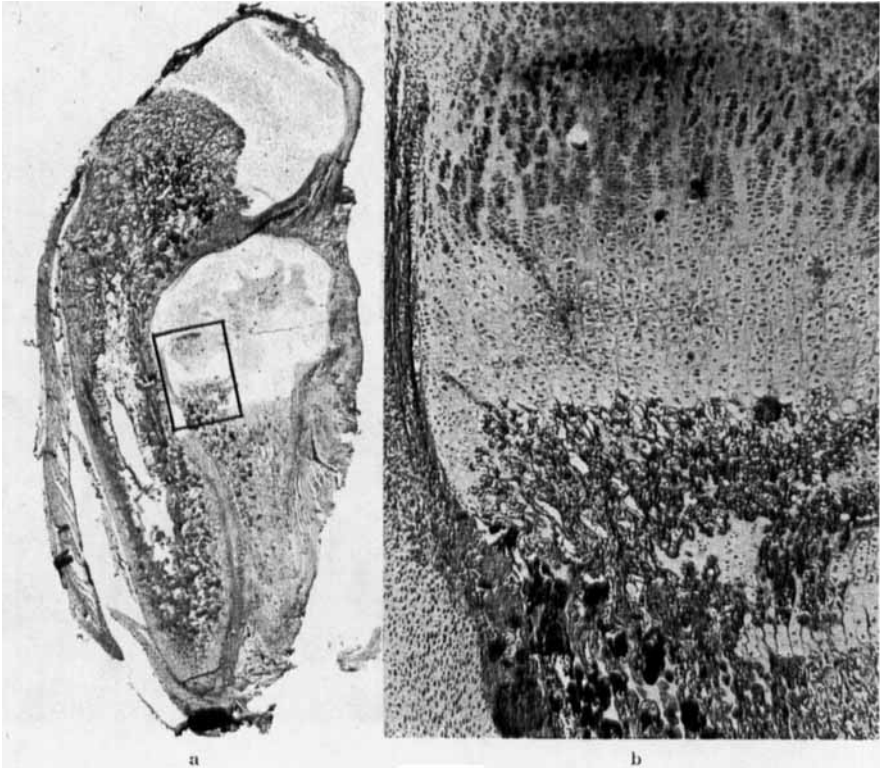
Fig. 2.

Exp. 148. Proximal end of the fibula transplanted to the site of the radius at the age of 15 days, period of observation 3 days. (b = enlarged detail of a).

- a. Only the peripheral regions of the epiphyseal cartilage have stained well. The zonation in the metaphysis is clear.
- b. The metaphyseal trabeculae lack an osteoblast lining and the interspaces are filled with detritus. Below to the right, penetration of histiocytes.

cytes around the transplant was seen and, around its diaphyseal end, granulation tissue, rich in cells, from which streaks of histiocytes penetrated through the marrow cavity in the direction of the epiphyseal plate. A similar penetration through gaps in the cortical layer was seen here and there. No other living cells were seen in either the metaphysis or the diaphysis. The zonal division was sharper in some slides while in others it was more diffuse than on the second day.

The signs of *necrosis of the epiphyseal cartilage* were more distinct than on the second day, and the limits of the lightly staining area were sharper (Fig. 2b). In some slides this area comprised *almost the entire proliferation zone* but, as a rule, *only a small central portion of the*



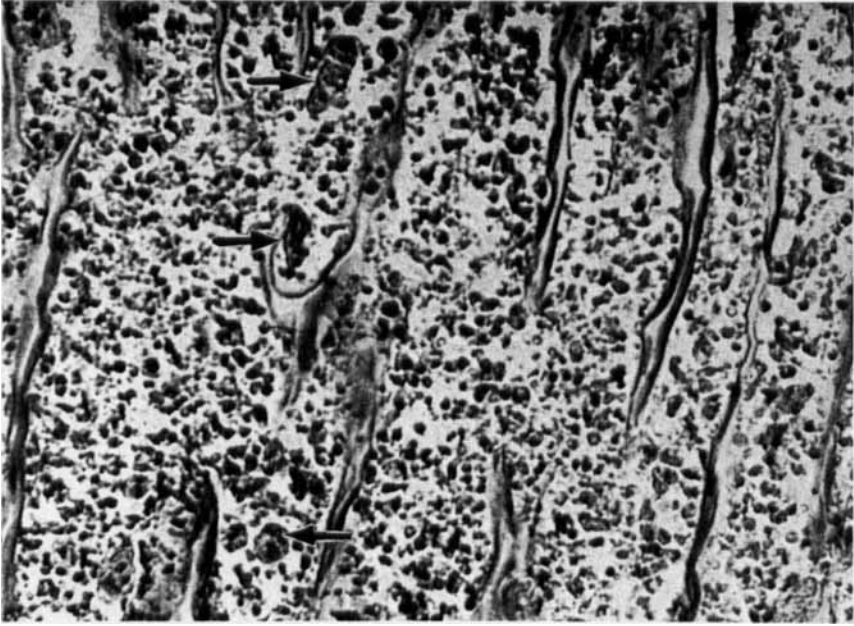
*Fig. 3.*

Exp. 141. Proximal end of the fibula transplanted to the site of the radius at the age of 10 days, time of observation 7 days. (b = enlarged detail of a).

- a. The epiphyseal cartilage has partly degenerated and ossification has commenced, the stepped necrotic portion has been left behind in the metaphysis (right part).
- b. The degeneration area of the columnar zone is abnormally thick. The primary trabeculae are irregular. In the metaphysis, islets of necrotic cartilage tissue are seen.

*reserve zone.* In the preserved peripheral parts of the proliferation zone, those parts of the columns which consisted of degenerating cells were longer than normal and the height of the columnar zone was therefore increased (Fig. 3).

Seven days after the transplantation, when an increase in length of 1/2 to 1 mm. could be measured radiologically although the graft had not yet fused with the ulna or the femur, mesenchymal tissue could be seen between the trabeculae which were lined with osteoblasts or osteoblast-like cells reaching to the metaphyseal border except in the necrotic cartilaginous area. *Close to the latter there was a narrow zone*



*Fig. 4.*

Exp. 147. Proximal end of the fibula transplanted to the thigh at the age of 11 days, period of observation 7 days (highly magnified). The bone trabeculae of the metaphysis lack an osteoblast lining, the interspaces being filled with detritus. The arrows indicate isolated macrophages filled with cell remnants.

*within which there were neither osteoblasts nor living erythrocytes, though other parts of the metaphysis and the epiphyseal nucleus were well nourished. In the metaphysis and the diaphysis isolated osteoclasts were also observed and, in some slides, remnants of detritus and macrophages filled with phagocytized material (Fig. 4).*

The necrotic portion of the epiphyseal cartilage was sharply defined and seemed *laterally compressed, particularly in the columnar zone in which the columns were arched with the convexity towards the necrotic area, but also within the reserve zone (Figs. 3a, 5)*. The mushroom-like necrotic area penetrated 1/2 to 1 mm. into the metaphysis. Within it, columnar cells with slightly stained, yellowish shrunken nuclei could be observed.

*Along the metaphyseal border, there was vigorous ossification except at the transition zone to the necrotic cartilaginous region. The newly formed primary bony trabeculae were irregular and, in places, contained considerable amounts of uncalcified matrix.*

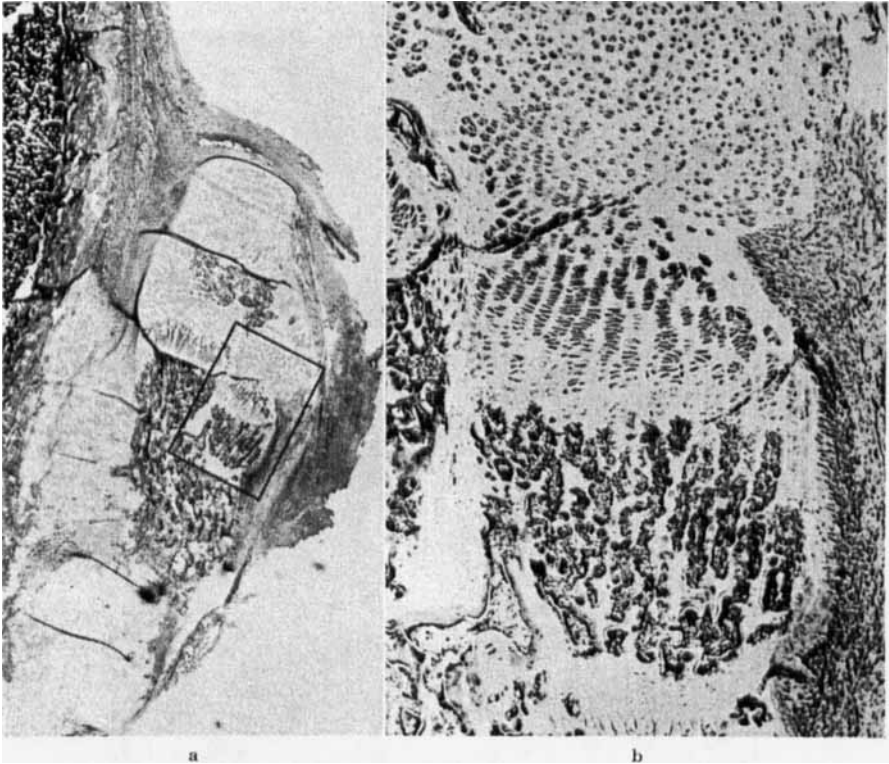


*Fig. 5.*

Exp. 156. Proximal end of the fibula transplanted to the thigh at the age of 21 days, period of observation 7 days. (b = enlarged detail of a).

- a. The necrosed cartilage, which comprised  $\frac{3}{4}$  of the width of the epiphysis, has been replaced from the sides, while it has been left behind in the metaphysis.
- b. The arch shape of the regenerating columns illustrates how they partly cut off the necrotic cartilage which still extends to the epiphyseal nucleus. On the metaphyseal side of the necrotic cartilage the bony trabeculae lack an osteoblast lining and in the interspaces there is detritus.

*On the ninth day*, when no bony contact could yet be demonstrated, while the growth in length of the graft could be radiographically shown to be  $\frac{1}{2}$  to 3 mm., the epiphyseal plate seemed almost normal in some slides, though the *reserve zone appeared to be thinner than normal* in all. In other slides a more or less centrally situated streak of connective tissue was seen, reaching from the epiphyseal nucleus into the epiphyseal plate or through it to the metaphysis. Continuing from this streak there was a *triangular necrotic cartilaginous area* in the metaphysis and *the distance from the base of this triangle to the metaphyseal border was in most cases exactly the same as the longi-*



*Fig. 6.*

Exp. 155. Proximal end of the fibula transplanted to the thigh at the age of 15 days. Period of observation 9 days. (b = enlarged detail of a).

- a. Half of the epiphyseal plate has been left behind, stepwise, in the metaphysis.
- b. Above left, a vascular connective tissue streak is seen growing through the epiphyseal plate, and in its prolongation a triangular necrotic cartilage is seen sunk into the metaphysis. The columns of the regenerating epiphyseal cartilage extend from a common point in the reserve zone.

*tudinal growth of the graft as measured on radiograms.* In some cases the base of the cartilaginous triangle reached to the periphery of the graft (Fig. 6) and in these cases another triangular area with irregular newly formed primary bony trabeculae was observed between the necrotic cartilage, the metaphyseal border and the periphery of the graft (Fig. 6b). In some slides the epiphyseal plate was stepped in shape, the step protruding farthest into the metaphysis being on the same side as the greater part of the eccentrically situated necrotic cartilage triangle (Fig. 6a). The osteoblasts of the metaphysis looked normal



Fig. 7.

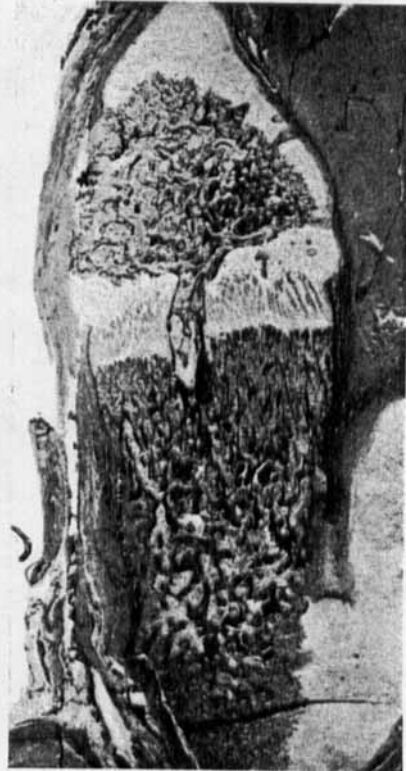


Fig. 8.

Exp. 149. Proximal end of the fibula transplanted to the thigh at the age of 11 days. Period of observation 14 days. The epiphyseal plate looks normal with the exception of a narrow vascular streak growing from the epiphyseal nucleus down into the epiphyseal plate. The diaphysis of the graft has fused with the femur.

Fig. 8.

Exp. 151. Proximal end of the fibula transplanted to the thigh at the age of 15 days. Period of observation 13 days. A broad, partly ossified streak connects the epiphyseal nucleus with the metaphysis, on either side of the streak the epiphyseal plate looks normal. Between the diaphysis of the graft and the femur there is a callous mass, which has ossified enchondrally, yet is without regular columns.

and, in most slides, covered all trabeculae while in other slides *both osteoblasts and living erythrocytes were absent from a narrow zone at the base of the cartilaginous triangle*. In some slides a comparatively large number of osteoclasts were seen.

*From the thirteenth day on, when some transplants had fused with*

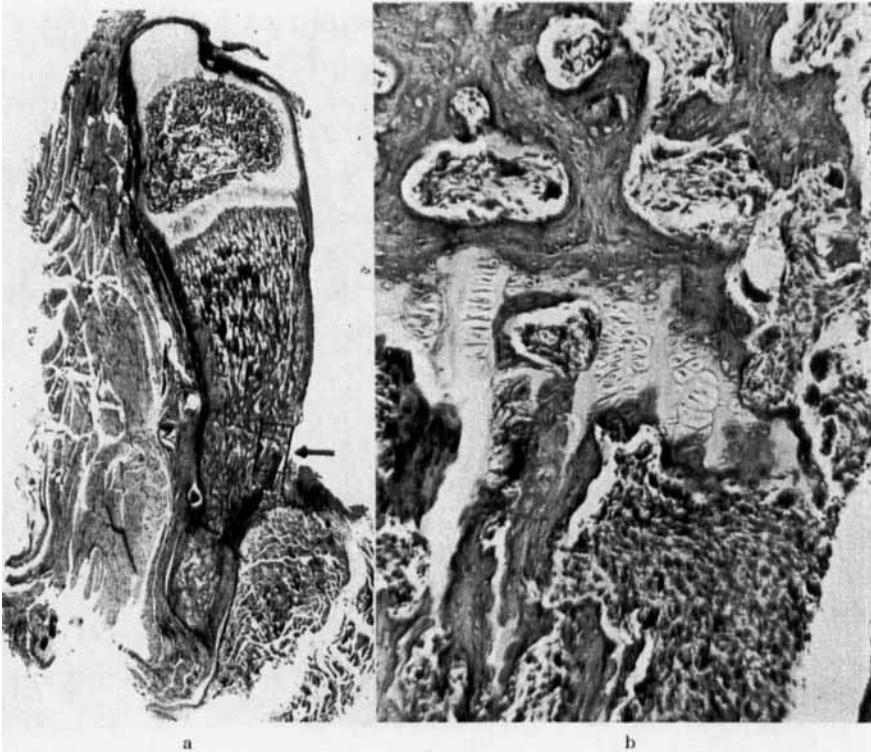


*Fig. 9.*

Exp. 131. Proximal end of the fibula transplanted to the site of the radius at the age of 14 days. Period of observation 14 days. (b = enlarged detail of a).

- a. The epiphyseal plate looks normal except that in the part of the reserve zone furthest from the ulna, the nuclei have stained lightly. The diaphysis has fused with the ulna.
- b. There are islets of necrotic cartilage in the metaphysis. The osteoblast lining of the bony trabeculae extends to these islets and near them there are osteoclasts.

the ulna or the femur, the histological pictures varied more. In some cases the epiphyseal plate looked almost normal and there was a normal relation between the zones, although their continuity was interrupted by a longitudinal vascular connective tissue streak between the epiphyseal nucleus and the metaphysis (Fig. 7). This streak was ossified in some cases (Fig. 8). In other slides a lightly staining area could be seen in the otherwise normal epiphyseal plate within the reserve zone which, in the transplant, lay on the side farthest from the ulna or femur respectively (Fig. 9a). In some slides the reserve zone seemed to be extremely thin and in between this zone and the



*Fig. 10.*

Exp. 96. Proximal end of the fibula transplanted to the thigh at the age of 22 days. Period of observation 23 days. (b = enlarged detail of a).

- a. The graft, which had grown 6 mm., did not fuse with the femur. The epiphyseal plate is regular but the reserve zone in particular is thin. The structure of the metaphysis is regular. 6 mm. from the metaphyseal border a transverse streak is seen (see arrow!).
- b. The transverse streak consists of islets of necrotic cartilage in which the cells are clearly visible. The border regions of the islets are calcified; near them there are osteoclasts.

apparently normal columnar zone, connective tissue cells penetrated from the periphery.

The primary bony trabeculae of the metaphysis were mostly regular, but *up to 23 days after the transplantation islets of necrotic cartilage were still visible*, in which lightly staining columnar cells were identified, and formed a transverse zone across the metaphysis *at a distance of up to 6 mm. from the metaphyseal border* (Figs. 9b, 10 a-b).

In other slides of fibulae transplanted at various ages, only insigni-

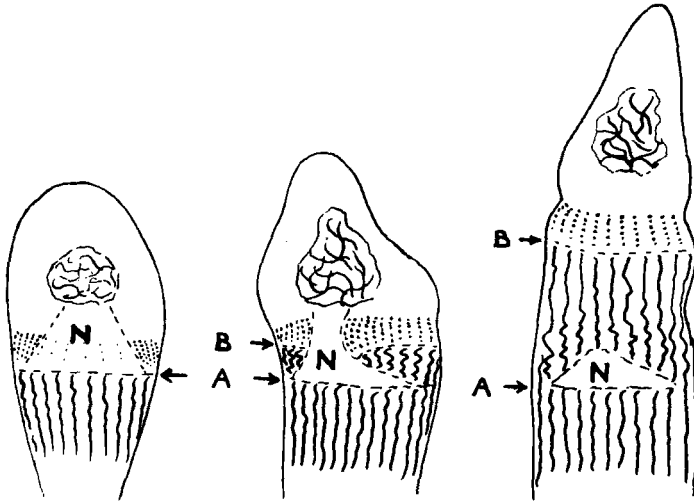


Fig. 11.

Schematic presentation of the cartilage necrosis occurring at transplantation and of how the necrotic area is left behind in the metaphysis (on the basis of sketches of figs. 1a, 5a and 9a). N = necrotic cartilage, A = the cartilage-bone border at transplantation, B = same at the end of the period of observation, the distance A-B = growth after transplantation.

ficants signs of regeneration were observed within the epiphyseal cartilage and there was insignificant new bone formation, if any. These slides had one feature in common, i.e. the area of necrotic cartilage was wide, extending as a broad band to the periphery of the graft from where vascular connective tissue streaks grew into the necrotic cartilage.

#### DISCUSSION

The changes observable within 1 to 2 days after the transplantation are no doubt the result of ischaemic necrosis involving the major part of the columnar zone and a small portion of the central parts of the reserve zone as well as all cell elements of the bone marrow. These latter, the complete destruction of which at bone transplantation had been observed by *Axhausen*, among others, constitute the detrital mass visible in the metaphysis. *The reason for the zonation of the detritus, which I have not seen described in any previous paper, is obscure.* It is conceivable that fluid from an oedematous area in the matrix of the epiphyseal zone caused by ischaemia trickles into the spaces between the bony trabeculae of the metaphysis, compressing

the greater part of the detrital mass into the dark zone, while a smaller part is deposited in the fluid nearest to the metaphyseal border as a light zone. This would explain why *this zone seems to border only on the necrotic cartilage region.*

*The increase in height of the epiphyseal zone*, which was interpreted by *Enderlen* as a result of oedema, is probably also the result of an increase in the height of the columns, which, again, follows continued division of the surviving columnar cells which *undergo the natural degeneration process without being ossified during the first few days.* Ossification does not commence until the osteoblast lining and the capillaries reach the cartilage border. This, which in *Heller's* most favourable experiments on transplantation of epiphyseal cartilage with thin bone lamellae to bony substance took place within 3 to 6 days, occurred in my experiments some time *between the fourth day*, when the first penetrating histiocytes were observed, *and the seventh day*, when ossification was already under way. Whether the osteoblast lining regenerates from isolated surviving cells or from penetrating cellular elements cannot be concluded with certainty. The complete absence of staining cells in the grafts examined on the second to third day supports the assumption that *pluripotential histiocytes have differentiated into osteoblasts.* I am unable to explain the fact that in some slides the osteoblast lining and the penetrating capillaries had not yet reached the metaphyseal border of the necrotic cartilage area by the ninth day.

Apparently the epiphyseal cartilage regenerates from its surviving peripheral parts, as evidenced by the lateral compression of the necrotic part. When renutrition is achieved and ossification of the surviving and regenerated parts of the columnar zone has set in, the normal height of the columnar zone is regained for a short period of rapid but irregular calcification (cf. part I). If regeneration of the epiphyseal cartilage does not reach the centre, a vascular connective tissue streak will grow out from the epiphyseal nucleus to the metaphysis and subsequently ossify, and growth will cease. *By the increased cell proliferation necessary for regeneration of the epiphyseal zone, the reserve zone obviously exhausts its resources, and hence there is a thinner reserve zone than normal in the regenerated cartilage, and early cessation of growth.* Another sign of this exhaustion of the power of the reserve zone to produce new cartilage cells is obviously penetration of the connective tissue streak from the sides, which I, like *Ring*, observed in some transplants.

*The necrotic cartilage does not ossify* and one result of this is that it is overrun by the newly formed metaphyseal bone *and is left behind in the metaphysis*, as was also observed by *Brücke*. The mushroom or triangular shape of the cartilaginous area left behind is partly due to the fact that the necrosis primarily comprised a narrower area of the reserve zone than of the columnar zone, being partly a result of pressure upon the necrotic cartilage by the regenerating epiphyseal plate from the sides. When this cartilage has become cut off from the epiphyseal plate, it is gradually split into cartilage islets, irregular in shape. The same phenomenon has been observed and described in detail by *A. Langenskiöld* and *W. Edgren* as a result of necrosis produced by local irradiation of the epiphyseal plate.

The reason why the necrotic cartilage still does not ossify when, after the ninth day, the osteoblastic lining and the capillaries finally reach it, remains obscure. *Henrichsen*, however, recently showed that the enzyme necessary for calcification, alkaline phosphatase, occurs in the cartilage cell when this undergoes a natural degenerative process, and that calcification cannot take place before this process is completed and the cell is dead. It is therefore conceivable that the cells in the necrotic cartilage which have not undergone natural degeneration, do not contain the amount of alkaline phosphatase necessary for normal calcification. How the necrotic cartilage, after splitting into small cartilage islets, finally disappears is not clearly apparent, but the calcification of the borders of the islets and an accumulation of osteoclasts near the islets, observable in some slides, suggest two different alternatives.

#### CONCLUSIONS

1. Under the given experimental conditions a thin peripheral layer of the columnar zone and a thicker layer of the reserve zone survive autotransplantation. The centre of both these zones and all cell elements of the metaphysis undergo necrosis.

2. The epiphyseal cartilage regenerates from the surviving parts of the reserve zone whose cell-producing capacity is thereby partially exhausted which results in subsequent inhibition of growth. Regeneration proceeds towards the centre of the epiphyseal plate, cutting off the necrotic cartilage region. The marrow cells of the metaphysis probably regenerate from histiocytes penetrating from the surround-

ings. Regeneration begins after about 3 to 4 days, and is completed about 9 to 13 days after the transplantation.

3. As soon as regenerating osteoblast linings and capillaries have reached the metaphyseal border, before the seventh day at earliest, ossification of surviving and regenerating parts of the columnar zone begins and the longitudinal growth of the transplant continues.

#### S U M M A R Y

In 10, 15 and 21 day old rabbits autotransplants of the proximal end of the fibula were made, in some cases to the site of the radius which had been dissected extraperiosteally and removed and in some to the thigh, and were histologically examined after 2 to 40 days.

There was no difference between the results in the different age groups, or after transplantation to the site of the radius or to the thigh.

In the centre of the epiphyseal cartilage there occurred an extensive necrosis (Figs. 1 and 2) which, on the fourth to the thirteenth day was replaced through regeneration from surviving parts of the reserve zone (Fig. 5). All marrow cells of the metaphysis underwent necrosis as well, and in the detritus a characteristic zonation was observed (Figs. 1 and 2), the reasons for which are discussed. The marrow cells regenerated, probably from penetrating histiocytes, between the fourth and ninth days. As soon as the regenerating osteoblast lining and the capillaries reached the metaphyseal border, ossification of the surviving and regenerating parts of the columnar zone began, while the necrotic cartilage did not ossify but was left behind in the metaphysis (Figs. 3, 5 to 10 and 11). The reasons for the non-occurrence of ossification are discussed. Though in successful cases the epiphyseal zone seemed to regenerate completely, this seemed to take place at the expense of the capacity for cell proliferation of the reserve zone, which may be held to explain why the total growth capacity of the transplant is less than that of the normal bone.

#### R E S U M E

Des autotransplantations de l'extrémité proximale du peronée ont été effectuées chez des lapins âgés de 10, 15 et 21 jours, dans certains cas à la place du radius qui a été disséqué extrapériostalement et enlevé et dans d'autres sur la cuisse, et qui ont été examinées histologiquement après 2 à 40 jours.

Il n'y avait aucune différence entre les résultats chez les différents groupes d'âges ou après transplantation à la place du radius ou sur la cuisse.

Dans le centre du cartilage épiphysaire, il s'était produit une nécrose extensive (fig. 1-2) qui, entre le 4ème et le 13ème jour a été remplacée par la régénération de parties survivantes de la zone en réserve (fig. 5). Toutes les cellules de moëlle de la métaphyse ont également subi des nécroses, de même qu'on a observé dans le détritus une division en zones caractéristique (fig. 1 et 2) dont les raisons sont discutées. Les cellules de moëlle régénèrent, probablement par suite de la pénétration d'histiocytes entre le 4ème et le 9ème jour. Aussitôt que la doublure formée par les ostéoblastes régénérés et les capillaires atteint la bordure métaphysaire, l'ossification des parties survivantes et régénérées de la zone colonnaire commence, alors que le cartilage nécrotique ne s'ossifie pas, mais s'affaisse dans la métaphyse (fig. 3, 5 à 10 et 11). Les raisons de la non-apparition de l'ossification sont discutées. Bien que dans les cas heureux, la zone épiphysaire paraît complètement régénérée, cela semble se faire aux dépens de la capacité de prolifération des cellules de la zone en réserve, ce qui pourrait expliquer que la capacité totale de croissance de la transplantation est moins forte que dans un os normal.

#### ZUSAMMENFASSUNG

An 10, 15 und 21 Tagen alten Kaninchen wurden Autotransplantationen des proximalen Endes der Fibula, in einigen Fällen an die Stelle des Radius, der extraperiostal präpariert und entfernt worden war, in anderen zum Oberschenkel vorgenommen. Die Transplantate wurden nach 2 bis 40 Tagen histologisch untersucht.

Kein Unterschied zwischen den Ergebnissen der verschiedenen Altersgruppen oder nach Transplantation zum Radius oder Oberschenkel konnte gefunden werden.

Im Zentrum des Epiphysenknorpels entstand eine ausgedehnte Nekrose (Fig. 1 und 2), die am vierten bis dreizehnten Tage durch Regeneration von überlebenden Teilen der Reservezone erstattet wurde (Fig. 5). Alle Markzellen der Metaphyse wurden ebenfalls nekrotisch und im Detritus wurde eine charakteristische zonenartige Anordnung beobachtet (Fig. 1 und 2), deren Ursach besprochen wird. Die Markzellen regenerierten, wahrscheinlich von eindringenden Histozyten zwischen dem vierten und neunten Tage. So bald die regenerierende

Osteoblastschichte und die Kapillaren die Metaphysengrenze erreichten, begann die Verknöcherung der überlebenden und regenerierenden Teile der Säulenzone, während der nekrotische Knorpel nicht verknöcherte, sondern in der Metaphyse hintergelassen wurde (Fig. 3, 5 bis 10 und 11). Die Gründe für das Nichtauftreten von Verknöcherungen werden besprochen. Obwohl die Epiphysenzonen in erfolgreichen Fällen vollkommen zu regenerieren schienen, geschah dies doch augenscheinlich auf Kosten der Proliferationsfähigkeit der Zellen der Reservezone. Dies kann erklären weshalb die gesamte Wachstumsfähigkeit des Transplantates geringer ist, als die von normalen Knochen.

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