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STUDIES ON OSTEOGENESIS AROUND AUTOPLASTIC BONY TRANSPLANTS IN BONY DEFECTS

By

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New bone can be seen growing on fresh cortical grafts relatively soon after their implantation in bony defects.

There has been considerable discussion as to the origin of this newly formed bone. Does it come from the host bone next to which the transplant has been placed, or is it formed by some action of the transplant itself? Slight osteogenesis can also be found on the surface of bony tissue transplanted in the soft parts. Murphy was of the opinion that grafts are only osteoconductors, and that the new bone grows from the host bone to the transplants, over which it gradually spreads. Murphy based his conclusions on animal experiments, in which he noted that although bony tissue transplanted into the soft parts showed signs of osteogenesis, these signs soon disappeared and both the transplant and the new osteoid tissue were absorbed. He therefore concluded that the grafts themselves had no appreciable osteogenetic properties.

Brooks found in animal experiments that osteogenesis on the surface of bony transplants was approximately equally lively all over the transplant. In his opinion, this meant that the new bone on the transplant had not grown over from the host bone but had been formed by the transplant itself. Phemister observed, in a few cases, a relatively profuse growth of new bone on the periosteal surface of the grafts, despite the fact that there was as yet no bony union between transplant and host bone. He concluded that the new bone must have been formed by the graft, since it could not have originated in the host bone. According to studies by Vainios, new bone forms independently on autoplastic grafts which have retained their periosteum and later fuses with osteoid tissue from the host bone. This theory is sub-

stantiated by other animal experiments by Camitz, Holmgren and Johansson. According to Reynolds and Oliver, the new bone on the grafts is the result of osteoid tissue growing from the host bone to the graft.

Opinions thus differ as to whether the new bone on grafts develops through osteoid tissue growing over from the host bone. Like Murphy, I was impressed, when conducting animal experiments for an entirely different purpose, by the insignificance of the new bone growth on the surface of bony grafts transplanted into the soft parts as compared with grafts transplanted into bony defects. It seems reasonable to assume that this means that osteoid tissue from the host bone has grown over to the transplant. However, results of other investigations indicate that this is not the case. I therefore made a number of experiments on rabbits in order to study the question in greater detail. The grafts used were autoplastic cortical transplants retaining their periosteum.

If it is true that the new bone on the surface of transplants represents osteoid tissue originating in the host bone to which the graft is apposed, one would expect to find at a relatively early stage that the osteoid production was greatest at the junction between graft and host bone and that it decreased progressively over the rest of the transplant. In the first three experiments, therefore, I examined the spread of the new osteoid tissue on the transplants, one or both ends of which were apposed to the host bone. I also compared this new bone growth with that on grafts transplanted at the same time into the soft parts.

Experiment No. 1. Two centimeters of the central section of the shaft of one radius were excised extraperiosteally and transected into two equal parts. One piece was inserted in the middle of the radial defect at a distance of 5 mm. from the upper and lower ends of the fragments of the radius. The other part of the excised piece of bone was implanted subcutaneously in the back of the animal. Four weeks later the animal was killed. Histologic examination revealed bony union between both the upper and lower parts of the reimplant and the ends of the fragments of the radius (host bone). The transplant and the host bone were united both by profuse periosteal osteoid tissue and by new bone that filled the entrances to the medullary canals of both transplant and host. New bone was also observed all along the ulnar surface of the transplant, but was thickest at the ends (Fig. 1). There was no new bone on the surface facing away from the ulna. The transplant in the soft parts contained one or two small areas showing signs of scanty subperiosteal osteoid tissue.

In Experiments Nos. 2 and 3, the middle section of the shaft of the radius was excised and reimplanted in the defect, in the same way as in No. 1. The section of the radius below the transplant was then entirely removed in one case and almost entirely in the other, so that the transplant could only become united with the upper fragment of the radius (host bone). As in No. 1, a transplant was also embedded subcutaneously in the soft parts of the back. The animals were

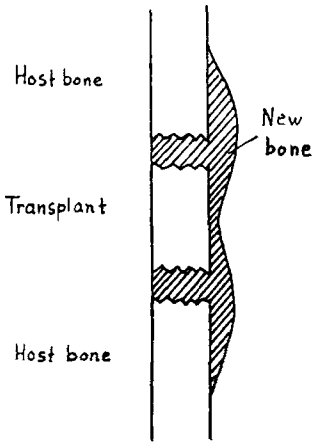

Fig. 1.

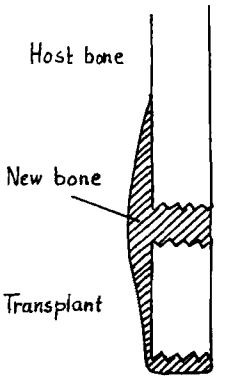

Fig. 2.

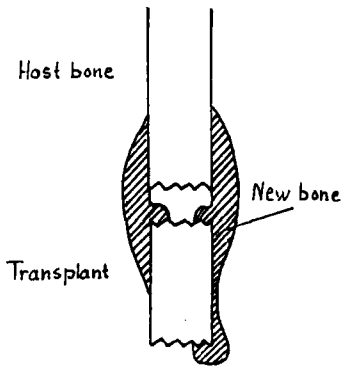

Fig. 3.

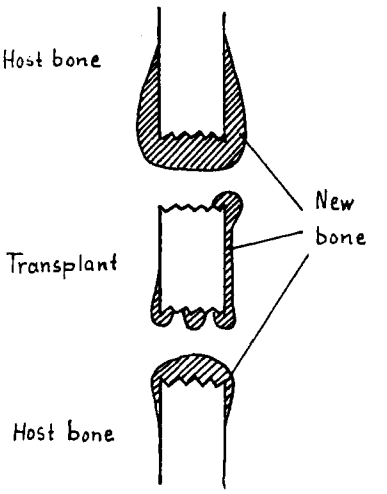

Fig. 4.

killed two or three weeks later. Histologic examination in both experiments showed abundant periosteal new bone, which united the upper end of the transplant with the end of the radius fragment. A tapering carpet of new bone extended subperiosteally from this point along the whole ulnar surface of the transplant (Figs. 2 and 3). In No. 2, the carpet of new bone ran all the way to the lower entrance of the medullary canal of the transplant, which it covered completely. In No. 3, the periosteal new bone expanded at the lower end of the transplant to form a thick mass around the adjacent cut surface of the cortex (Fig. 3). In No. 2 there was no new bone on the surface of the transplant facing away from the ulna, while in No. 3 there were slight signs of osteogenesis. In No. 2 the upper end of the transplant and the adjacent fragment of the radius were united, not only by periosteal new bone, but also by osteoid tissue completely covering the entrances

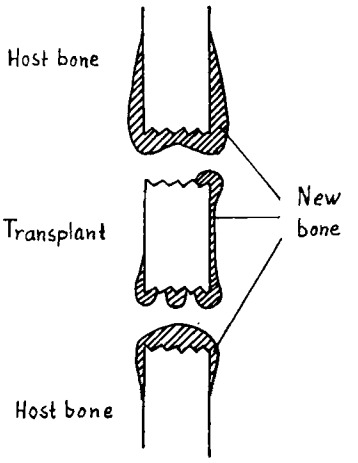

Fig. 5.

to the medullary canal of the host bone and the transplant. In No. 3, on the other hand, the bony union between the upper end of the transplant and the fragment of the radius consisted entirely of periosteal osteoid tissue, there being scarcely any new bone in the entrances to the medullary canals of the host and the transplant. The transplants in the soft parts showed only small patches with signs of very sparse osteoid production.

One or two other experiments similar to Nos. 2 and 3 were made, but had to be rejected as the osteoid tissue on the surface of the transplants united with the parallel bone, thus complicating the evaluation of results. The radius and the ulna are very close together in the rabbit, and the periosteum of the ulna is easily scraped off at excision, with resultant osteoid production which may extend to the transplant.

It appears from the foregoing experiments that there is an appreciable difference in the amount of periosteal osteoid production on bony tissue transplanted into the soft parts and on transplants placed next to living bone. The former showed only signs of exceedingly scanty osteoid tissue in small scattered patches, while the latter exhibited large areas covered by a thick carpet of osteoid production. The new bone was most profuse on the part of the transplant next to the host, from which point it extended unbroken down the periosteal surface of the transplants.

The results of these experiments are quite compatible with the assumption that the proliferation of new bone on the surface of transplants in bony defects arises from osteoid tissue growing from the host to the transplants. That this is not the case, however, is shown by the experiments described below.

In the next two experiments, the transplants were placed at a

somewhat greater distance from the host bone, so that no union between the transplant and the host via newly formed osteoid tissue had taken place when the animals were killed.

In Experiments Nos. 4 and 5, a four-centimeter long section of the shaft of the ulna was excised. The excised piece of bone was transected into two equal parts. One section was inserted in the middle of the defect in the ulna, with the upper and lower ends at a distance of one centimeter from the fragments of the ulna (host). When the animals were killed 18 days later, the transplants in the defects were found to be freely movable, with no bony union either with the ulnar fragments or the parallel bone. This observation was later confirmed histologically.

Thus, in the last two experiments, no osteoid tissue was able to grow from the host bone to the transplant. Nevertheless, a relatively profuse mass of new bone spread over the transplant, particularly its periosteal surface. There was a striking difference in volume between this new bone and the extremely scanty osteogenesis on the transplant in the soft parts (cf. Nos. 1, 2 and 3). Nos. 4 and 5 showed practically the same histologic picture. Osteoid production was more profuse around the ends of the fragments of the host bone than on the transplants. It covered the ends of the medullary canal of the host bone and surrounded the ends of the fragments. Proliferation of new bone was somewhat greater at the ends than on the rest of transplants. It usually appeared as a deposit on the end of the cortex, from which it spread, sometimes as a continuous periosteal osteoid deposit along the transplant (Figs. 4 and 5). In both cases the osteogenesis on the transplants was most pronounced on the side facing away from the parallel bone. Sometimes there was scanty osteogenesis in the middle of the end of the medullary canal of the transplants or along their endosteal surfaces. The osteogenesis on the transplants in Nos. 4 and 5 was somewhat less than in Nos. 1, 2 and 3, in which the transplants showed bony union with the host bones.

Thus, since no osteoid tissue grew from the host to the transplant in Nos. 4 and 5, the osteogenesis in these transplants must have originated as a result of some action of the transplants themselves. The question then arises: Why was the osteoid production around these transplants in bony defects so much more active and profuse than in bony transplants in the soft parts? It must be assumed that the very proximity of the host bone in some way stimulates osteogenesis around transplants in bony defects. Nevertheless it is difficult to explain the mechanism of this action. The pathogenesis of osteogenesis in general is a problem of which we have relatively little understanding. Any attempt to explain how the host bone influences osteogenesis around a

transplant will be purely speculative. It is tempting to assume that the injured host bone gives off substances which stimulate the cells around the bony transplant to osteoid production.

According to studies by Levander, the bone contains extractable substances, which, if injected into soft tissue, give rise to osteogenesis. Levander considered that, as bony tissue of the transplant necroses, substances are released, which, together with the tissue fluids, disperse in the surroundings and have the capacity to activate non-specific mesenchymal cells so that the latter become transformed into bony tissue. Annersten reproduced Levander's experiments and arrived at the same conclusion. He considered that osteoid tissue is formed in fractures as a result of an osteogenetic substance being released from necrotic tissue in the fracture fragments into the surrounding tissue where it stimulates the mesenchymal cells to osteogenesis. Meantime, Heinen, Dobbs and Mason, as well as Lindahl and Orell, investigated this matter by means of experiments with bony tissue extracts, but they were unable to confirm the existence of such substances.

If the substances in question emanate from the necrotic tissue in a bony transplant, it is also conceivable that they stimulate osteogenesis on an adjacent bony transplant (summation), with the result that the osteoid production on two adjacent bony transplants is particularly profuse on the surfaces that face each other. This question was studied in eight experiments (Nos. 6 to 13). Two one-centimeter long transplants, including the entire circumference of the shaft, were excised from the central part of the shaft of the radius. The transplants were attached to each other by Kirschner wires inserted in the medullary canal, so that they lay parallel to and about two millimeters away from each other. They were implanted subcutaneously in the soft tissue of the back. In six of the experiments the periosteum was left on and in two it was whittled off. The transplants were removed for histologic examination ten days to two months later. Some of the specimens showed small scattered areas with signs of insignificant osteoid growth, while the others exhibited no trace of new bone. In no case was there any appreciable continuous osteogenesis and consequently no bone union between the transplants. It could not be proved that the surfaces of the transplants facing each other more often showed signs of osteoid production than other parts. The investigation thus yielded no evidence to prove that substances with a strong stimulating effect on osteogenesis emanate from the bony transplants.

Judging from my experiments, osteogenesis is most pronounced around the host bone and therefore probably originates in that area. It next appears on the part of the transplant nearest to the host, after

which it spreads over the surface of the transplant. Thereafter, the osteoid tissue from the host bone fuses with that from the transplant, on the condition that the transplant is either in contact with the host bone or situated very near to it. As already mentioned, it is difficult to explain the profuse osteoid production around transplants in bony defects as compared with transplants in soft tissues, in view of the fact that osteogenesis is observed even if no new bone has grown from the host bone to the transplant. One hypothetical explanation of the problem is that, as a result of activity by living cells in the injured host bone, a substance is released that first gives rise to new bone at the site it is released and later, when it comes into contact with the transplant, stimulates osteogenesis there also.

SUMMARY

Animal experiments revealed that osteogenesis around autoplastic bony transplants in bony defects was much more profuse and more massive than the extremely scanty new bone on bony transplants implanted in soft parts. This was the case even before bony connection had been established between transplant and host bone. Therefore, osteogenesis on these transplants could not have taken place by osteoid tissue growing from the host bone to the transplant. New bone on transplants in bony defects originated next to the host bone, from which point it proceeded along the transplant. The host bone must in some way have had a stimulating influence on osteogenesis around the transplant.

On the other hand, it was not found that transplants in soft parts stimulated osteogenesis in adjacent transplants.

RESUME

Des essais expérimentaux sur animaux ont montré que les nouvelles formations osseuses dans les transplantations autoplastiques sur un milieu osseux sont beaucoup plus riches et cohérentes que les nouvelles formations osseuses très parcimonieuses qui se forment sur une transplantation osseuse insérée dans des parties molles. Telle est la situation déjà avant qu'il se soit établi une relation osseuse entre la transplantation et l'os qui l'héberge. La nouvelle formation osseuse de la transplantation ne peut donc pas provenir d'une supercroissance du tissu ostéïde de l'os qui héberge. La nouvelle formation osseuse d'une transplantation dans un milieu osseux commence à l'endroit le plus

rapproché de l'os qui héberge et s'étend ensuite à la transplantation. L'os qui héberge doit donc exercer une influence stimulate sur la nouvelle formation osseuse de la transplantation. Par contre, il n'a pas été possible de démontrer que la transplantation isolée dans des parties molles ait exercé une influence sur la nouvelle formation osseuse d'une transplantation adjacente.

ZUSAMMENFASSUNG

In tierexperimentellen Versuchen zeigte es sich, dass Knochenneubildung um autoplastische Knochentransplantate im Knochenmilieu viel reichlicher und mehr zusammenhängend auftritt als dies bei den äusserst sparsamen Knochenneubildungen der Fall ist, die im Anschluss von freier Verpflanzung von Knochen in die Weichteile auftreten. So verhalten sich die Dinge bereits bis etwas knöcherne Verbindung zwischen Transplantat und Wirtsknochen herstellt ist. Daher ist die Knochenneubildung in diesen Transplantaten nicht durch Herüberwachsen von osteoidem Gewebe vom Wirtsknochen entstanden. Die Knochenneubildung beim Transplantat im Knochenmilieu beginnt zunächst dem Wirtsknochen und schreitet entlang dem Transplatate fort. Der Wirtsknochen muss in irgendeiner Weise einen stimulierenden Einfluss auf das Transplantat ausüben. Dagegen gelang es niemals nachzuweisen, dass ein frei in den Weichteilen liegendes Transplantat Knochenneubildung um ein zweites danebenliegedes Transplantat anregte.

REFERENCES

Annertsen: Acta chir. scand. 84, Supplement 60, 1940.
Brooks: Annals of surgery. 66: 625: 1917.
Camitz, Holmgren, Johansson: Acta chir. scand. 75: 1: 1934.
Heinen, Dobbs, Mason: J. Bone and Joint Surg. 21 A: 765: 1949.
Levander: Surg. Gyn. & Obst. 67: 705: 1938.
Levander: Nordisk Medicin 9: 44: 1941.
Lindahl and *Orell:* Acta chir. scand. 101: 136: 1951.
Murphy: Surg. Gyn. & Obst. 16: 493: 1913.
Phemister: Surg. Gyn. & Obst. 19: 303: 1914.
Reynolds and *Oliver:* J. Bone and Joint Surg. 32 A: 283: 1950.
Vainio: Acta chir. scand. 100: 86: 1950.