

**THE REPAIR OF BONE.**

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DURING the past few years many of the views on inflammation and repair in bone, which had been accepted by generations of histologists and surgeons, have been subjected to searching investigation. The result has been that some of the old beliefs have been rudely shaken and wide differences of opinion have developed on points of fundamental importance. So necessary is it, from a surgical standpoint, that at least the simpler underlying pathological principles be perfectly understood, that the writers have found it necessary to undertake for themselves a thorough investigation of the subject, and, from the study of a series of experiments, to attempt to formulate opinions which can be safely applied to the ordinary practice of surgery.

**THE PERIOSTEUM.**

Much of the recent study has been devoted to the periosteum. This structure is a strong membrane, firmly united to the bone in the region of the epiphyseal lines, but elsewhere more loosely attached through the medium of a delicate areolar tissue. When the membrane is gently reflected it can be seen that part of this areolar tissue clings to the periosteum and part to the bone. When examined histologically the periosteum is seen to consist of a dense white fibrous tissue in which are many elastic fibres close to the internal surface. It contains many blood-vessels which are rapidly subdividing before entering the bone. In the interstices of the areolar tissue which connects the fibrous membrane with the cortex are many large cells which have been shown to be osteoblasts. In children and adolescents these cells are present in large numbers, but in healthy adult life they are only present at intervals and are sometimes difficult to find. Until recently histologists have uniformly considered these osteoblasts as part of the periosteum, constituting its cambium layer. This view has been questioned by Maccewen, whose work, *The Growth of Bone*, appeared in 1912. He maintained that the periosteum has no osteogenetic function, and that it must be considered to be purely a limiting membrane, much the same as the connective-tissue capsules of the muscles and abdominal viscera. This view was based on a series of experiments which consisted of the raising of periosteal flaps and the subperiosteal resection of the bone. It was found that after these operations new bone practically never developed from the periosteum. He explained the rare instances in which small nodules of new bone did develop by supposing that, in the reflection of the periosteum, a flake of the subjacent cortex had been raised with it.

In order to test the soundness of these contentions, the writers repeated many of the experiments described in *The Growth of Bone*, and obtained results in each case exactly similar to those of Maccewen. These experiments were described in detail in the *Canadian Medical Association Journal* of January, 1914. (*Experiments 1 to 12.*)\*

As a further test, a series of experiments was performed in which grafts, two inches in length and composed of half the thickness of the bone, were removed subperiosteally from the radii of dogs, and, after they had been divided into equal parts and one part boiled for five minutes, were replaced in their bed and covered with the reflected periosteum. The specimens were recovered at intervals of one week, and were then

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\* A description of all experiments mentioned in this paper will be found in the Appendix.

sectioned longitudinally. In the case of the unboiled grafts, new bone always appeared on the surface; but in the case of the boiled, no such change occurred. (*Exps.* 50, 51, 52, and 32 to 41.) Similarly, another series was performed, in which the sections of bone removed from the dogs' radii were replaced by bone removed from a living cat, and the same results were obtained. No new bone appeared between the periosteum and the heterogenous grafts. (*Exps.* 46, 47, 48). (*Fig.* 237.)

In answer to the criticism that, in such experiments, the dead, heterogenous, or foreign materials placed beneath the reflected periosteum may inhibit new bone formation, may

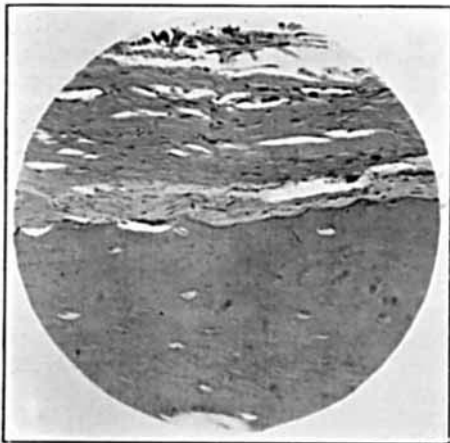


FIG. 237.—High-power photomicrograph of specimen of cat's bone transplanted into the radius of a dog, taken two and a half weeks after the operation. The graft was covered with the dog's periosteum. The photograph shows the periosteum practically normal, the bone dead, and the lacunae either empty or occupied by the shrunken remains of the cells. Between the periosteum and the bone there is no sign of osteoblasts or of absorption or new bone formation. (*Exp.* 47.)

be cited the gross and microscopic appearances following the implantation of living autogenous tissues beneath the periosteum. Such operations were performed on children suffering from infantile paralysis, and consisted in the conversion of the tendons of paralyzed muscles into ligaments which would prevent the development of deformity resulting from the contracture of unopposed groups of muscles. An incision, two and a half inches long, was made in the periosteum, and the membrane raised for an eighth of an inch on either side. A trough was then cut in the bone with a gouge, sufficiently deep and wide to accommodate the tendon. The tendon was drawn taut and laid in the trough, and the periosteum sewn over it with No. 1 catgut. The wound was then closed, and a plaster splint applied. On four occasions we were able to examine the area of the operation many months afterwards, once because of the death of the patient from an acute infectious disease, and three times because of the necessity to perform a second operation. In each case the tendon was found to be buried in the bony trough and

covered with periosteum, but without any covering of bone such as might have developed if the raised periosteum had been osteogenetic.

Whilst these experiments show that the periosteum is not the important structure it was formerly supposed to be, they do not in any way modify our views of the function of the subperiosteal osteoblasts. These cells can be readily shown to have very active powers of proliferation and of bone production. This was demonstrated in a series of experiments in which small segments of the shafts of the radii of dogs were removed with the saw and, with the periosteum undisturbed, buried in neighbouring muscles. The specimens were recovered at the end of one week, two weeks, and so on, and showed the various stages of new bone formation under the periosteum. (*Exps.* 13, 16, 20, 24, 26, and 27.) Similarly, small segments of bone from which the periosteum had been gently removed were buried in muscles, and, after the lapse of similar periods of time, showed very similar results. The presence or absence of the periosteum on these grafts seemed to have no appreciable influence on osteogenesis. (*Figs.* 238 and 239.)

Clinically, in pathological conditions, we are accustomed to see marked evidence of the activity of the subperiosteal osteoblasts. Thus, in osteomyelitis the involucrum results from their proliferation and bone-forming properties. Similarly, following the subperiosteal hæmorrhage of infantile scurvy, new bone forms both on the surface of the shaft and under the periosteum. The explanation of the bone formation under the periosteum in these cases is probably, as Macewen pointed out, that during the period immediately preceding the stripping of the periosteum, the inflammation in the subjacent

tissues leads to a rapid proliferation of the osteoblasts which normally lie on the surface and in the open mouths of the Haversian canals. The result is an enormous increase in the number of these cells, and, when the stripping occurs, some cling to the periosteum and some to the bone. When the inflammation subsides, the osteoblasts begin to produce new bone, with the result that a shell of cancellous tissue appears under the periosteum as well as over the shaft. Again, in the repair of fractures the subperiosteal osteoblasts take a very active part in providing the ensheathing callus. They proliferate rapidly, forming with the new blood-capillaries a granulation tissue about the seat of the fracture,

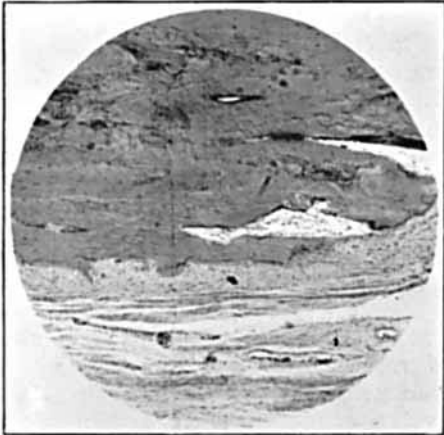


FIG. 238.—Low-power photomicrograph of the periosteal surface of autogenous graft transplanted into muscle after the removal of the periosteum. Specimen recovered three weeks after operation. It shows the formation of layers of new bone on the surface and in the surrounding fibrous tissue practically the same as if the periosteum had not been removed. (*Exp.* 21.)



FIG. 239.—High-power photomicrograph of same specimen as shown in *Fig.* 002. It shows crowds of osteoblasts engaged in absorption of the old bone and in laying down new bone on the surface. (*Exp.* 21.)

which ultimately changes to bone. It was on such evidence as this that the popular idea was based that the periosteum is the important structure in the formation of new surface bone. Macewen has shown, however, that if a fracture is produced in the shaft of a bone after the removal of the periosteum in that area, not only does ensheathing callus develop but its quantity is actually increased. This finding has been corroborated by us in two experiments in which transverse fractures were produced in the radii of dogs. In the first the periosteum was undisturbed, and in the second it was removed for half an inch on either side of the fracture. In both cases the bones were perfectly fixed by the application of a thin steel plate. The specimens were recovered at the end of two months, and the dog from whose radius the periosteum had been stripped undoubtedly showed the greater amount of ensheathing callus.

From these considerations it is evident that the old view which maintained that the periosteum consists of two layers, a fibrous and an osteoblastic, and that in virtue of its osteoblastic layer the periosteum is osteogenetic, can no longer be accepted. While there can be no dispute as to the existence of the cells known as the subperiosteal osteoblasts, or as to their bone-forming properties, to state that this layer of cells constitutes part of the periosteum will lead only to the erroneous idea on the part of the surgeon that the periosteum, as he understands it, can be depended on for osteogenesis. Such an idea is sure to lead to surgical disasters. Although it cannot be denied that operations have been performed on animals and on patients in which reflected periosteum has produced new bone, it can be confidently stated that such results are decidedly rare. Even those who most strongly maintain the osteogenetic theory point out that to ensure any certainty

that new bone will form from the reflected periosteum, it is necessary to scrape the subjacent bone with a sharp-edged instrument in order that the osteoblasts may be reflected with the fibrous membrane, and even with this precaution failures are frequent. There is no reason to doubt that when the periosteum is reflected by ordinary operative means the great majority of the osteoblasts remain on the surface of the bone, and that it is rare for a sufficient number to cling to the fibrous membrane to be of any clinical value in the production of new bone. It would seem better, therefore, to abandon the old idea that the subperiosteal osteoblasts belong anatomically to the periosteum, and to take the view that they really belong to the bone. In reality they have the same relation to the bone as the cells which line the medullary surface and the walls of the Haversian canals.

**Treatment of the Periosteum.**—Apart from the above discussion, which is of interest only in arriving at a definition of periosteum, there are several points of practical surgical interest which demand attention. (1) *Should the periosteum be left attached to the graft when bone is being transplanted?* (2) *How freely may the periosteum be reflected without endangering the circulation and vitality of the bone?* (3) *What measure of restoration of the shaft of a bone may be expected after subperiosteal resection?* (4) *What is the best method of dealing with the periosteum at the end of a bone during an amputation?*

1. The first of these questions has been answered already by experiment. The series of specimens obtained from animals in which bone had been transplanted into the muscles, with and without the periosteum *in situ*, showed no difference in the amount of new bone formation occurring on the periosteal side of the graft. This fact, in conjunction with the mass of published experimental evidence indicating the inability of the reflected periosteum to produce new bone, makes it clear that the transplantation of the periosteum with the graft is not essential. This view has been corroborated clinically to our satisfaction in a long series of bone transplantations in which we have been unable to detect any difference in the clinical results following transplantations with and without periosteum. In recent years it has been our practice to reflect the periosteum before cutting the graft, and to use the reflected membrane to close the gap left by the removal of the bone. The advantages of this method are that it prevents the formation of post-operative hæmatoma; it restores and preserves the correct anatomical outlines of the bone; and it reduces the tendency to adhesion of the scar to the deep structures.

2. The second question is of the utmost importance in these days, when osteomyelitis produced by gunshot wounds is almost universal. It must be remembered that practically the whole of the blood-supply of a bone comes through its periosteum, and therefore, that the reflection of this membrane must interfere with the circulation of the underlying bone. This fact was forcibly demonstrated to us at an autopsy on a patient who had died of an infectious disease about three months after a severe attack of infantile scurvy which had been successfully treated by the proper change in diet. When first seen, the child had enormous swellings extending the whole length of the diaphyses of the femora and tibiæ, and there was separation of several of the epiphyses. Soon after the commencement of treatment the œdema subsided, and after a month the only evidence of the disease consisted of long fusiform swellings on the bones, which extended from one epiphyseal line to the other. The *x* ray showed the swellings to be composed of cancellous bone. At the autopsy the shafts appeared normal, but when the bone was decalcified and sectioned at various levels we were surprised to find that the middle third of each shaft was dead, as evidenced by the absence of bone-cells from the lacunæ. Sections cut at intervals of a quarter of an inch along the shaft showed the bone to be normal in the third nearest to the epiphysis, where the periosteum still remained attached, but approaching the middle third the cells in the lacunæ became fewer and fewer until they completely disappeared. The sections showed the circulation throughout the shaft to be perfect, having been restored, as we shall point out, in the same manner as it is restored in bone transplants, but the fact remained that the central portions of these bones were dead as a result of the previous damage to the circulation. Under ordinary circumstances in scurvy this dead bone would be absorbed and replaced by new bone by the osteoblasts which invade

it from the surface, and no clinical evidence of the necrosis would ever be seen. But if a similar necrosis had occurred in the presence of sepsis, the clinical result would have been very different, as long-continued osteomyelitis and sequestration of necrosed bone would be sure to follow. Similarly, while simple fractures unite without clinical evidence of necrosis, infected compound fractures are practically always complicated by sequestration of bone from which the periosteum has been extensively stripped. Owing to the free anastomosis of the blood-vessels throughout a bone it is easily understood that the removal of the periosteum over a small area, in a sterile operation, will have no ill effect. But when one is performing operations which depend for their success on the vitality of the bone, the source of the circulation should be remembered, and extensive stripping of the periosteum avoided. Neglect of this rule accounts for some of the cases of delayed union which occur after operations upon simple fractures. There is often ruthless reflection of the periosteum from the terminal three or four inches of the fragments before the application of a Lane plate, and in spite of the perfect adjustment of the bones, union is slow. This free stripping of the periosteum also accounts in part for the necrosis and sequestration which occur in septic stumps following re-amputation. Similar results are seen after operation for the removal of sequestra in chronic osteomyelitis following gunshot wounds where the periosteum has been freely reflected during the operation. The flakes of necrotic bone which separate from the surface in such cases result from the mechanical destruction of the circulation produced by the operation. One should, therefore, make it a rule never to interfere with the periosteum more than can possibly be helped during any operation on bones, and even the attachment of the soft tissues to the periosteum should be preserved. The practice of freely separating the muscles from the whole circumference of a fractured bone, and roughly stripping the periosteum, cannot be too strongly condemned. The same rule applies to operations on simple fractures, to operations on septic stumps, and to operations for the cure of septic osteomyelitis. While it is necessary to remove all the dead bone in the two latter conditions, the periosteum should not be reflected further than the point of application of the saw or chisel.

3. The third question, which relates to subperiosteal resection, is of importance because of the persistence with which this operation is recommended for such conditions as tuberculosis of the diaphysis, acute osteomyelitis, and myeloma. Before undertaking such operations it is necessary to have some definite idea of how freely the bone can be removed with a good prospect of restoration of the normal structure. Undoubtedly it is possible sometimes to do a subperiosteal resection of three to four inches of a rib and obtain the ultimate restoration of its continuity. We have followed the after-results of such operations in children with *x* rays taken at intervals of one week, until complete restoration of the bone had occurred. We have also studied the results of subperiosteal resection of two inches of rib in young dogs and found that bony union took place. It must be observed, however, that the formation of new bone first becomes apparent at the ends of the divided rib, and that it is completed in this area while the central portion is still very slender. This observation suggests that the restoration of the shaft has resulted from the migration of osteoblasts from the ends of the fragments, and not from the activity of cells clinging to the periosteum. This idea is amply supported by the experiments already referred to, in which living tissues were placed beneath the reflected membrane both in adults and in the young, without any evidence of subperiosteal bone formation. It is also supported by further experiments which more clearly resemble the actual operation of subperiosteal resection. In the first of these an inch of rib was removed from a young dog, the ends of the bone covered with tinfoil, and the periosteal tube closed. (*Exp. 8.*) When the specimen was recovered eight weeks later, it was found that the ends of the bone were now only half an inch apart, owing possibly to collapse of the rib or to outgrowths from the divided ends. The space between the coverings of foil was occupied by fibrous tissue in which a few nodules of new bone had formed. This experiment was repeated without using the foil, a ligature of catgut being tied around the periosteal tube at each end of the gap, thus sealing off the ends of the severed bone. (*Exp. 11.*) Ten weeks later the specimen was recovered, and no restoration of the rib had occurred. Similar experiments were performed

on the radius in puppies, and it was found that only short distances could be expected to bridge over with new bone. For example, if an inch and a half of radius were removed, non-union invariably resulted, and the space became filled with fibrous tissue. Experiments were also performed in which an inch and a half of bone was removed from the radii of puppies and the space filled with the same piece of bone after it had been boiled for five minutes. No subperiosteal new bone appeared except over the area close to the saw-cut. (*Exps.* 50, 51, 52.) These observations go to show that while restoration of the normal structure may sometimes occur after subperiosteal resection in the young, if does not result from any osteogenetic quality in the periosteum, and it can only be expected to occur in very cellular bones such as the rib, from the ends of which masses of osteoblasts can migrate. Such a conclusion appears to be at direct variance with the observations of those writers who have found a small amount of bone formation to occur after experiments and operations similar to those described. It is even in partial disagreement with our own experiment in which tinfoil was used to cover the cut ends of the rib, for here a few small nodules of bone developed in the fibrous tissue. This is readily explained, however, when one remembers that in the young the subperiosteal osteoblasts are very numerous, and that in the reflection of the membrane some of these cells may sometimes cling to it and so form a nucleus for the formation of small nodules of bone. The evidence is strong, however, that even in the young this does not frequently occur, certainly never so frequently as to lead one to believe that the periosteum can be relied on to restore the normal structure.

In adults the evidence that repair of bone takes place from the reflected periosteum is even more scanty. After subperiosteal resections of ribs one rarely finds restoration of continuity. In none of our experiments on adult animals has there been any sign of new bone growing from periosteum, and, when more than half an inch has been resected from the shaft of one of the long bones, non-union has been the invariable result. Clinical experience fully corroborates these experiments. The large number of patients who were admitted to military hospitals with ununited fractures during that period of the war when extensive periosteal resections for comminuted and infected fractures were a common procedure show conclusively the fallacy of depending on the periosteum for restoration of the bone.

There still remain to be answered the arguments of those surgeons who have shown restoration of the shaft following subperiosteal resection for tuberculosis of the diaphysis of the long bones. Undoubtedly cases are on record in which a considerable length of the diaphysis has been removed and in which restoration of the shaft has occurred. The explanation, however, is simple when one remembers that the bone in such cases is in a state of chronic inflammation, and that the superficial osteoblasts have undergone marked proliferation previous to operation. When the periosteum is reflected in these cases, particularly if the operation is performed with a sharp instrument and if the surface of the bone is thoroughly scraped, it is quite reasonable to expect the formation of new bone to result from the activity of osteoblasts which are reflected with the membrane. The restoration of the shaft which sometimes occurs under such circumstances must be attributed to the subperiosteal osteoblasts as well as to those which migrate from the ends of the mildly inflamed fragments. But even in circumstances such as these, clinical experience has shown that failures to obtain union are frequent. While the method is of undoubted value in removing the focus of disease, it must be undertaken with a full appreciation of the danger that union will not result.

It is evident, therefore, that, when subperiosteal resection is contemplated, the surgeon must abandon the idea that by preserving the periosteum he is providing a certain means of securing restoration of the normal structure. If it appears wise to resect a portion of the shaft of a bone, the operation must be done with the full realization that non-union will very probably result unless the severed ends of the fragments are brought together, or unless some other procedure is introduced to assist in bridging the gap. Such a conclusion will naturally cause the surgeon to hesitate before undertaking early subperiosteal resection for such conditions as infected comminuted compound fractures, early acute

osteomyelitis, and benign tumours of bone. Before such an operation is undertaken it must be clearly shown that the benefits to be gained are sufficiently great to outbalance the serious effects of the operation. In the cases of the pathological conditions enumerated there is no doubt in our minds that the disadvantages in many cases outweigh the advantages. In compound fractures the only advantages are the possible improvement in drainage and lessening of the severity of the infection, with the hope of earlier healing of the wound. The disadvantages are the almost complete certainty of non-union, or of great shortening if a whole-hearted attempt is made to encourage the fragments to unite. In acute osteomyelitis the extensive removal of supposed necrotic bone, before involucrum formation has commenced, has little to recommend it over the ordinary drainage operation, and it almost invariably results in deformity owing to the absence of bone regeneration. In the case of benign tumours it is better, if possible, to remove the tumour sufficiently widely, without doing a complete resection, or, if this is impossible, to complete the operation by an immediate transplantation of bone to bridge the gap and so prevent the collapse of the fragments.

4. The fourth question, relating to the manner of dealing with the periosteum in amputations, is of great practical interest at a time when amputations and re-amputations are frequent. When the operation can be performed without danger of septic infection, the method of dealing with the periosteum is of very small importance. With a view to preventing the formation of spurs from the end of the bone, some writers have recommended the complete removal of the periosteum from the terminal inch or more of the stump. This idea was based on the faulty premise that, by so doing, one would remove the osteogenetic cells. In reality, the removal of the periosteum is an actual stimulant to osteogenesis, as the damage so produced always results in a mild inflammatory reaction which leads to the laying down of a moderate amount of new bone on the surface. Other writers have advocated that the periosteum be dissected back in the form of a cuff, and, after the section of the bone, that it be closed over the end so as to prevent the outpouring of osteoblasts. Theoretically this would appear to be a rational procedure if there were any real danger of spur formation. In our clinical experience, however, the formation of spurs is only to be feared when sepsis is present, so that such a precaution is unnecessary. The method has this in its favour, that by covering the cut end of the bone with normal periosteum the possibility of adhesion of a terminal scar is prevented. It is sometimes useful in amputations of the leg and forearm. In the majority of cases, however, the simple method of cutting through the periosteum and bone at the same level is quite satisfactory, and while the addition of the modifications described will do no harm, they must be considered as superfluous.

When the amputation is done in the presence of sepsis, or when there is any possibility that sepsis will ensue, as is always the case in re-amputations for the closing of unhealed wounds, the rules for the treatment of the periosteum can be more clearly defined. Here the problem is the same as in operations for osteomyelitis. If the periosteum is stripped from the bone in the presence of sepsis, necrosis and sequestration are sure to follow. The aperiosteal method should, therefore, never be employed. An objection can also be raised to the cuff operation in that, by closing the reflected periosteum over the end of the bone, drainage is interfered with. All things considered, the safest procedure in these cases consists of the simple sectioning of the bone and periosteum at the same level.

#### THE TRANSPLANTATION OF BONE.

To observe the changes in a bone graft which must be attributed solely to the cells of the graft itself, it is necessary to place it in such a position that none of the changes can be attributed to cells derived from neighbouring living bone. A series of experiments on dogs was accordingly performed, in which small grafts were removed from the radius and implanted in the muscles of the back. (*Exps.* 13, 16, 20, 24, 26, 27.) These grafts were made by removing a section of half the thickness of the radius, about three-quarters of an inch in length, including the periosteum. The specimens were recovered after the

lapse of one, two, three, and five weeks respectively, and were then sectioned longitudinally with a sharp osteotome, and preserved in formalin. After decalcification the sections were cut from the surface exposed by the osteotome, thus showing distinctly the changes on the periosteal and medullary surfaces and in the body of the bone.

In the specimens recovered one week after implantation in muscle, the appearances are as follows :—

1. The periosteum appears to have changed very little, apart from a moderate proliferation of the cells nearest the surface of the bone.
2. The subperiosteal osteoblasts have undergone moderate proliferation.
3. On the medullary side of the graft there has been a marked proliferation of cells and capillaries which has resulted in the formation of typical granulation tissue.
4. The bone itself has the usual appearance of necrosis. The blood-vessels and cellular tissues throughout are coagulated, except in the mouths of the Haversian canals where these form wide openings on the surfaces. Here new blood-vessels are in evidence, and many connective-tissue cells are undergoing proliferation. In the lacunæ the cells are shrunken and stain dimly, resembling the necrotic cells in neighbouring Haversian canals. These bone-cells are evidently dead, and although it is impossible to say, from the examination of a histological section, that every bone-cell dies when the circulation is cut off, nevertheless the change in the appearance of these cells is general throughout the section. Even cells in lacunæ which are separated by the minutest wall of bone from the surfaces are in the same necrotic condition.

It would therefore appear that, when a piece of bone is completely separated from its circulation and implanted in such a position in the same animal that a good supply of lymph is available, those cells which are in contact with this lymph are capable of continuing to live, and of proliferating; but those cells which are encased in the lacunæ of the bone, being beyond the reach of a proper supply of lymph, undergo necrosis. It is interesting to note that the periosteum is not a sufficient barrier to the passage of lymph to prevent the proper nutrition of subperiosteal osteoblasts.

Examination of the specimen recovered two weeks after implantation shows the following appearances :—

1. The periosteum is changed very little except that it is thicker and more cellular than the normal, indicating cell proliferation.
2. The subperiosteal osteoblasts have multiplied considerably, forming a loose granulation tissue. The cells are sometimes round, sometimes fusiform, and sometimes polygonal, with long protoplasmic processes, resembling ordinary fibroblasts. Occasionally multinucleated cells occupy cavities on the surface of the bone. In a few places the osteoblasts have commenced to produce new bone in the form of fine trabeculae which extend out under the periosteum or form a thin layer laid down on the necrotic graft.
3. The endosteal surface closely resembles the periosteal, with the difference that the former is extremely irregular, owing to the cancellous character of the bone. Over the whole of this irregular surface is a network of capillaries and osteoblasts, quite similar to that under the periosteum.
4. The cut ends of the graft also show some cellular activity, but much less than the two surfaces. In fact, in sections in which no Haversian canals open at the ends, no osteoblastic proliferation is to be seen. In cases, however, where canals do open at the ends, the same newly-formed connective tissue is in evidence, and some new bone is being laid down.
5. The bone itself shows many important changes. The cells in some places have disappeared, and in all others stain very dimly and are evidently undergoing autolysis. The circulation is being re-established rapidly by the ingrowth of new vessels along the open Haversian canals. With these blood-vessels are to be seen many connective-tissue cells, evidently osteoblasts, which surround the vessel and form a loose meshwork about it. These changes can be recognized most distinctly close to the surfaces of the graft. On passing to the deeper portions the evidence of cellular activity gradually lessens until in the centre it has completely disappeared. The most interesting phenomenon to make



its appearance at this time, however, is the commencing absorption of bone. The presence of giant cells or osteoblasts, located in small excavations on the surface of the graft, has been mentioned above, but in addition to this, extensive absorption of bone appears to be taking place in the open Haversian canals and irregular indentations of the surface, and even in canals cut transversely at some distance from the surface; wherever, in fact, there are considerable collections of proliferating osteoblasts. The typical appearance is that of a bay or excavation, at the border of which is arranged a row of osteoblasts, each resting in a small pocket which it has evidently produced by absorption. The central portion of the cavity is loosely filled with osteoblasts and blood-capillaries. In specimens recovered a day or so later new bone has begun to appear in these cavities, and by the beginning of the third week the mouths of the bay are often completely filled with new bone, while absorption is still actively going on in the blind extremity (*Fig. 240*). These processes of absorption and replacement are at first in evidence only along the surfaces of the graft; but as time goes on they extend deeper and deeper until they ultimately reach every portion of it. The evident explanation of these changes is that, as the blood-vessels grow into the old Haversian canals, the osteoblasts which have survived and are proliferating on the surface either migrate into the bone or grow along the capillaries. They do not spread quite so rapidly as the blood-vessels, for the most advanced zone of the invading living cellular tissue can be seen to be composed solely of blood-capillaries, but within twenty-four to forty-eight hours the osteoblasts have reached this zone and commenced the process of absorption. Rapid cellular proliferation then occurs, and within a few days the canals and spaces of this whole area are filled with cells which are actively engaged in producing excavations in every direction. This process of absorption is almost solely dependent on the activity of the osteoblasts, as it does not occur when these cells are absent. This may be demonstrated by boiling the bone before implanting it in muscle. Such an implant will remain practically unchanged for many months, only showing the result of the extremely slow solvent action of the body fluids and of the activity of a few giant cells which appear along the edges. Although the circulation becomes re-established as in the unboiled grafts, and connective-tissue cells appear along the Haversian canals, nothing resembling the appearances produced by the masses of osteoblasts occurs. It can further be demonstrated that the boiling has not produced such a change in the bone that it cannot be absorbed. Evidence will be produced later to show that boiled bone, when brought in contact with living osteoblasts, is attacked in practically the same way as is the unboiled.

Examination of the grafts recovered at the end of three, four, and five weeks confirms the observations and deductions already outlined. The number of osteoblasts on the surface continues to increase. The absorption of the old and the laying down of new bone become more pronounced. The circulation soon becomes re-established throughout the whole graft. The old cells in the lacunæ become less and less distinct, until after four or five weeks not a vestige of a bone-cell is to be seen. It has been observed that in the second and third weeks the invading osteoblasts produce marked evidences of absorption on the surfaces and along the Haversian canals, and that, after a few days, many of these cells return to their adult function of bone formation, with the result that new bone



FIG. 240.—High-power photomicrograph of the same specimen as shown in *Fig. 238*. It shows the invasion of the graft by osteoblasts from the surface from which the periosteum had been removed. It also shows the laying down of new bone on the walls of the cavities produced by absorption. (*Exp. 21.*)

appears on the surfaces and on the walls of the recently produced excavations. Absorption, however, continues to be the more prominent of the two processes until the old bone has mostly disappeared (*Fig. 241*). This has usually occurred by the end of the third month, and by this time the graft is represented by a very irregular mass of cancellous living bone which is considerably smaller than the original implant, and which contains not more than a half or a third of the original weight of osseous tissue. It will be pointed out in later experiments that, if the bone had some function to perform, this process of absorption would cease and give place to a building-up process in obedience to the law of Wolff. But in bone implanted in muscle, where it has no function to perform, absorption continues to be the more active process, until, after the lapse of five or six



FIG. 241.—Low-power photomicrograph of autogenous graft, five weeks after implantation in muscle. It shows the lacunæ of the dead bone empty, the re-establishment of the circulation, the extensive absorption of the graft by invasion of osteoblasts, and the laying down of new bone on the walls of the cavities and on the irregularities of the surfaces. (*Exp. 24*.)

months, depending on the original size and density of the graft, the bone has completely disappeared and its place is occupied by a simple fibrous-tissue scar. (*Exps. 29, 30, 31*.)

Up to the present our remarks have applied solely to the changes occurring in grafts made from the hard compact bone of the middle of the shaft of the radius. It is quite evident from what has been said that the rapidity and the extent of the changes depend on the number of osteoblasts that survive the disturbance of the circulation. It would, therefore, appear reasonable that the larger the area of surface exposed to lymph, the greater the number of osteoblasts that would survive, and thus the greater would be the value of the graft. In an investigation of this point a series of experiments was performed, similar to the first series, except that the grafts were obtained from the cancellous extremities of the radius. (*Exps. 26, 27, 33.*) Sections of such grafts are evidently porous when viewed with the naked eye. The specimens were recovered,

as in the former experiments, at intervals of one week. In brief, the changes observed resemble those already described, except that they have occurred much earlier and much more extensively. The bone-cells in the lacunæ all die and disappear, as described before, but the circulation is fairly well re-established in one week. Not only do the surface osteoblasts survive, but the osteoblasts in the open Haversian canals, for a considerable distance inward from the surface, continue to live and functionate, so that at the end of three weeks absorption is taking place in all directions through the graft, and new bone not only surrounds the graft on its external surfaces, but extends throughout its whole length and thickness. The picture is in marked contrast to that of the compact graft of similar age. Not only is this increased rapidity of absorption and replacement due to the increased number of active cells present, but it is also due to the greater ease with which the new blood-vessels and osteoblasts can advance from the periphery to the centre.

#### TRANSPLANTATION OF HETEROGENOUS BONE INTO MUSCLE.

To arrive at an estimate of the comparative value of grafts removed from other animals, a series of experiments similar to the above was performed in which cats' bone was removed from the living animals and transplanted into muscles of dogs. (*Exps. 15, 18, 22, 49.*) The specimens were recovered at the end of one week, two weeks, and eight weeks. The results of the experiments were, briefly, as follows :—

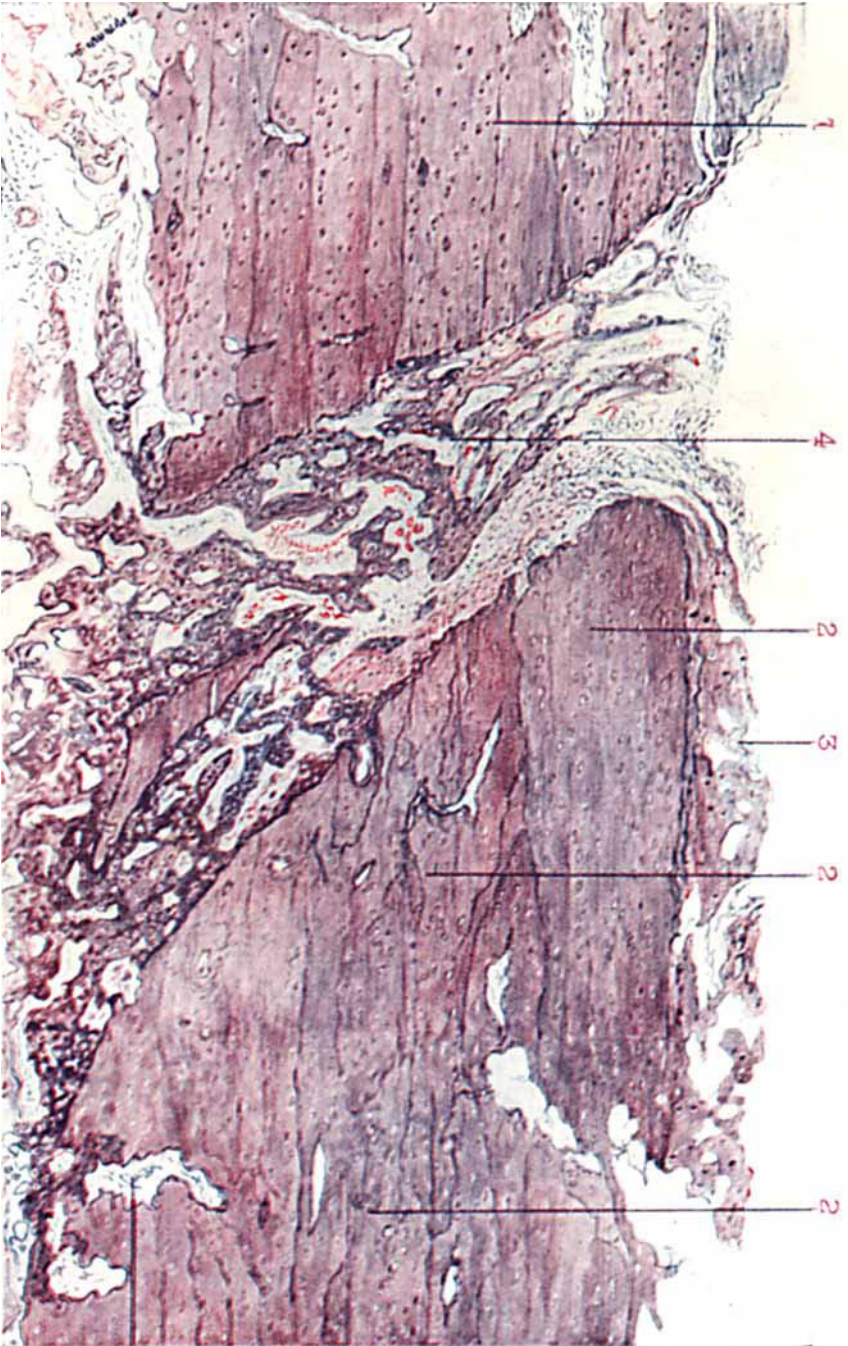


FIG. 212.—Drawing of junction of normal bone with autogenous graft, three weeks after implantation. (Low power. *Ezp.* 36.) 1. Normal bone of bed. 2. Graft: showing the disappearance of the cells from the lacunae. 3. New cancellous bone laid down on the surface by subperiosteal osteoblasts which have survived the transplantation. 4. Saw-cut, filled with new cancellous bone which has united the graft to its bed. 5. This area illustrates the method of absorption of the dead graft by osteoclasts, the re-establishment of the circulation, and the replacement of the dead by living bone.

1. At the end of one week the blood-vessels and cells in the Haversian canals are coagulated, and the cells in the lacunæ are shrunken and stain poorly.

2. At the end of two weeks the circulation is being re-established, as in the case of autogenous grafts, although a little more slowly. There is no evidence of new bone formation, the bone being surrounded by newly-formed fibrous connective tissue. The cells in the lacunæ are disappearing.

3. At the end of three weeks the above changes are more pronounced. If the bone is very compact, the circulation is re-established slowly; if cancellous, rapidly.

4. At the end of eight weeks the circulation is well established and the cells have completely disappeared. The bone is surrounded by fibrous tissue, with, here and there, giant cells resting in lacunæ on the surface, indicating some slight degree of absorption. No osteoblasts are anywhere in evidence, and no formation of new bone. In fact, the graft is practically unchanged. Some writers have stated that, if such grafts are left a long time in the tissues, osteoblasts do appear on the surface, and absorption and new bone formation develop, due to metaplasia of the surrounding connective-tissue cells, but we have never observed this phenomenon. It is clear, therefore, that heterogenous bone is useless for transplantation where it is desired to utilize the osteoblasts on the surfaces of the graft. These osteoblasts are evidently destroyed by the fluids of the other animal (*see Fig. 237*).

#### BOILED BONE TRANSPLANTED INTO MUSCLE.

In addition to the above, several experiments were performed in which autogenous bone was implanted in muscle, after it had been boiled for fifteen minutes. The changes observed resemble closely those following transplantations of heterogenous bone. One difference observed is that at the end of the first and second weeks the bone-cells stain quite well in the boiled graft, autolysis being slowed by the heat. At the end of several weeks, however, the circulation is re-established and all the cells have disappeared. No osteoblasts are to be seen about the bone. After eight weeks very little change can be noted in the specimen as a result of its transplantation.

An important difference between the early reaction of the tissues to autogenous and to heterogenous or boiled bone should be noted. In the former the granulations which form about the graft unite to it rapidly and firmly, so that within three weeks the adhesion of the surrounding tissues to the bone is quite strong. In the latter the adhesion of the granulations is delayed and, when it does occur, is feeble until four or five weeks have gone by. This can be seen well in the gross specimens and is corroborated by microscopical examination. Further, the ingrowth of new blood-vessels and the re-establishment of the circulation occur more quickly in the autogenous graft than in the others. These differences are quite possibly due to the fact that all or many of the exposed cells on the surface of the autogenous graft live. They may, therefore, assist in forming the adhesion to the surrounding tissues and in the production of new capillaries.

#### TRANSPLANTATION OF BONE INTO SKELETAL GAPS.

With this preliminary knowledge of the changes occurring in the various types of bone grafts, when separated from contact with living bony tissue, we are in a position to study the transplantation of bone into gaps occurring in the skeleton. A series of experiments was performed in which sections of half of the thickness of the shaft of the radius, about one inch in length, were removed, both with and without periosteum, and immediately replaced in their beds. These specimens were recovered at weekly intervals up to ten weeks. (*Exps. 32 to 45.*)

The changes observed resemble, in a general way, those already described in grafts of a similar age implanted in muscles. Soon after the operation, coagulation of all the cellular elements in the substance of the bone occurs, both in the Haversian canals and in the lacunæ. On the exposed surfaces, however, many cells live, and by their proliferation form a granulation tissue about the graft. During the second week new bone begins

to develop on these surfaces, but particularly on the medullary side. On the periosteal side the formation of new bone is decidedly less, being practically the same as occurs in this side in grafts which have been implanted in muscle. But in the medullary cavity the production of new bone in the form of trabeculae is enormous, and so firm is the union at the end of two weeks that the gross specimen can sometimes be sectioned longitudinally with a saw without disturbing the graft. On the cut ends there is usually very little evidence of cellular proliferation or of the laying down of new bone, but, pouring out through the saw-cut, can be seen myriads of osteoblasts, in the midst of which much new bone is developing. It is quite evident that most of these osteoblasts have resulted from the proliferation of the cells of the living bone, and not from those of the graft. A general view of such transplants recovered at about the end of the second week, when compared with autogenous bone implanted in muscle, must lead to the conclusion that by far the greater proportion of the osteoblasts about the transplant come from the neighbouring living bone. These grafts also resemble, in a general way, those implanted in muscle, in the manner of the restoration of the circulation and of the invasion by living osteoblasts.



FIG. 243.—Low-power photomicrograph of medullary edge of autogenous graft, three weeks after the operation. It shows strong union of the graft to its bed, restoration of the circulation, invasion by osteoblasts, and replacement of the old by new living bone. (*Exp.* 36.)



FIG. 244.—High-power photomicrograph of the edge of an autogenous graft, three weeks after implantation. It shows the lacuna empty or containing only the shrunken remains of the nuclei of the cells. It also shows the process of invasion of the dead bone of the graft by osteoblasts from the surface, and the laying down of new bone on the walls of the cavities so produced. (*Exp.* 36.)

These processes, however, proceed more rapidly when the graft is in contact with living bone, apparently owing to the greater supply of living cells. In specimens recovered at the end of three weeks, the circulation is well on the way to completion, and the canals are everywhere filled with proliferating osteoblasts. Absorption and replacement have made very decided progress, particularly on the medullary surface, where the graft is covered with adherent newly-formed trabeculae, and is being attacked by masses of osteoblasts which are producing deep excavations and laying down new bone. These processes have also made marked progress in the Haversian canals, particularly on the medullary side. Elsewhere the graft is in much the same condition as in the specimens transplanted into muscles. In the succeeding weeks the replacement of the dead bone continues, until, after the lapse of three or four months, only occasional traces of the original graft can be found. It has been replaced by living cancellous tissue. Gradually the trabeculae thicken and the spaces disappear, and ultimately the area returns to the lamellated structure of normal compact bone. (*Figs.* 242, 243, and 244).

If the suggestion made above is true, that autogenous bone grafts depend for their



absorption and replacement largely on osteoblasts derived from neighbouring living bone, similar changes should occur in grafts in which we know that no cellular life exists. To investigate this point a series of experiments was performed in which a section of half the thickness of the radius of a dog, and about one inch in length, was removed, and the gap filled with a similar piece of bone obtained from a living cat. (*Exps. 46 to 49.*) In another

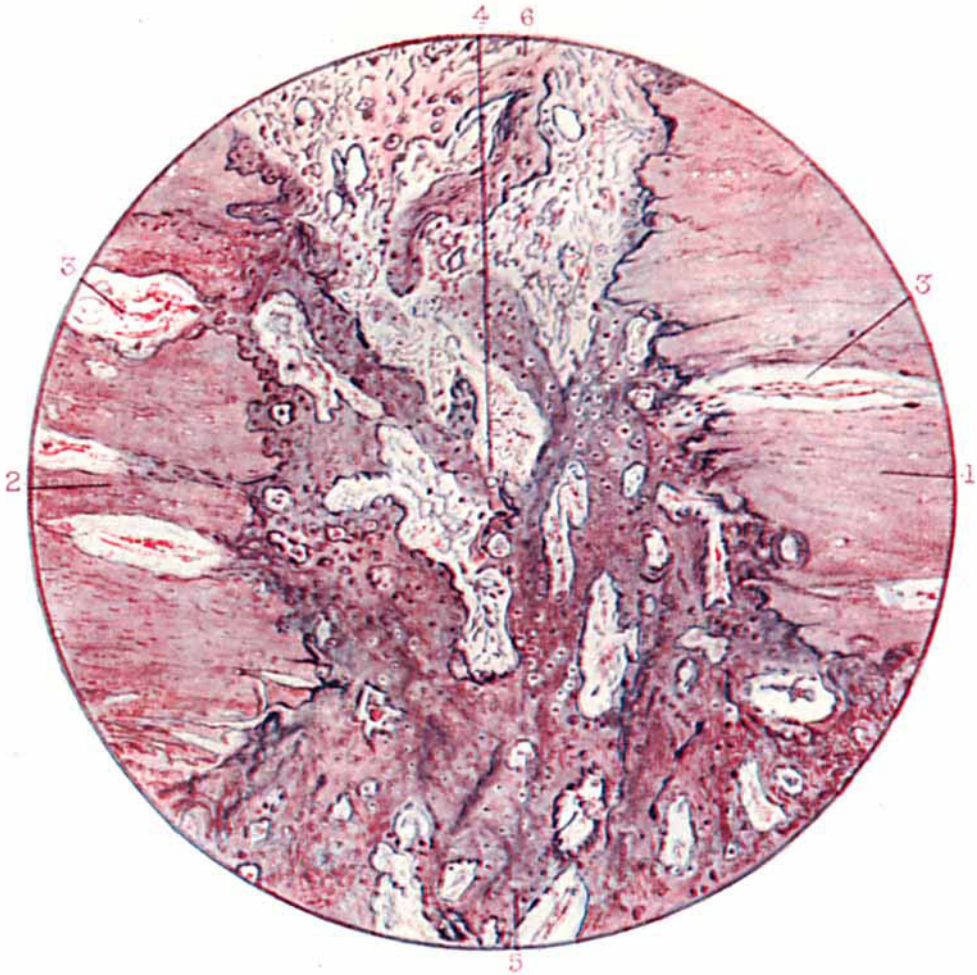


FIG 215.—Drawing of low-power magnification of junction of boiled and autogenous grafts, recovered three weeks after implantation. (*Exp. 55.*) 1. Autogenous graft, showing disappearance of cells from the lacunae. 2. Boiled graft, showing changes identical with those in the unboiled graft. 3 and 5. These areas show the re-establishment of the circulation and the processes of absorption and replacement. 4. Saw-cut, filled with proliferating osteoblasts and cancellous new bone. The new bone is firmly united to the grafts, and has produced a solid fixation of each to its bed. 5. Medullary cavity, filled with cancellous new bone. 6. Subperiosteal region in saw-cut. A comparison of areas 5 and 6 shows that by far the greater osteoblastic activity takes place in the endosteal region.

series the section of bone removed from the dog was boiled for fifteen minutes and then replaced in its bed. (*Exps. 50 to 53.*) As usual the specimens were recovered at intervals of one week. As far as we are able to judge, the heterogenous and the boiled grafts behaved in quite a similar manner. When such grafts are compared with similar grafts implanted in muscles, it is seen that the coagulation of the cells and blood-vessels, the

re-establishment of the circulation, and the absorption of the cells in the lacunæ, occur in exactly the same way. On the periosteal side there is the same absence of embryonic cellular activity, and of the active absorption and replacement which characterize so-called autogenous grafts. But when the medullary surface is examined, it is seen that there is no longer any resemblance to the grafts implanted in muscles. Here the appearances are very similar to those already described in autogenous transplants. At the end of the first week the bone is imbedded in a soft granulation tissue. At the end of the second,



FIG. 246.—Drawing of high-power magnification of an area on the endosteal side of the autogenous graft shown in Fig. 245. (*Exp.* 55.) 1. Old bone of graft. The cells have disappeared from the lacunæ. 2. Area showing re-establishment of the circulation and absorption and replacement of the old bone by osteoblasts which invade it from the medullary surface. 3. Medullary cavity filled with new cancellous bone which unites the graft to its bed.

new cancellous bone has begun to appear in this granulation tissue and on the surface of the graft. At the end of the third, the processes of absorption and replacement are well established, and the osteoblasts are spreading throughout the Haversian canals along with the newly-formed blood-vessels. In the saw-cuts, also, the same activity is to be seen. At the end of the first week, the new granulation tissue is pouring out towards the periosteal surface. At the end of the second, new bone is appearing on the cut surfaces and



irregularly through the granulation tissue. At the end of the third, the space is filled with trabeculae of cancellous tissue which forms a bony union between the graft and its bed.

In order to demonstrate accurately the similarities and differences between autogenous grafts and those in which all cellular life is known to be extinct, a series of experiments was performed in which an attempt was made to obtain specimens of autogenous and boiled grafts which had been placed for varying periods of time under exactly similar

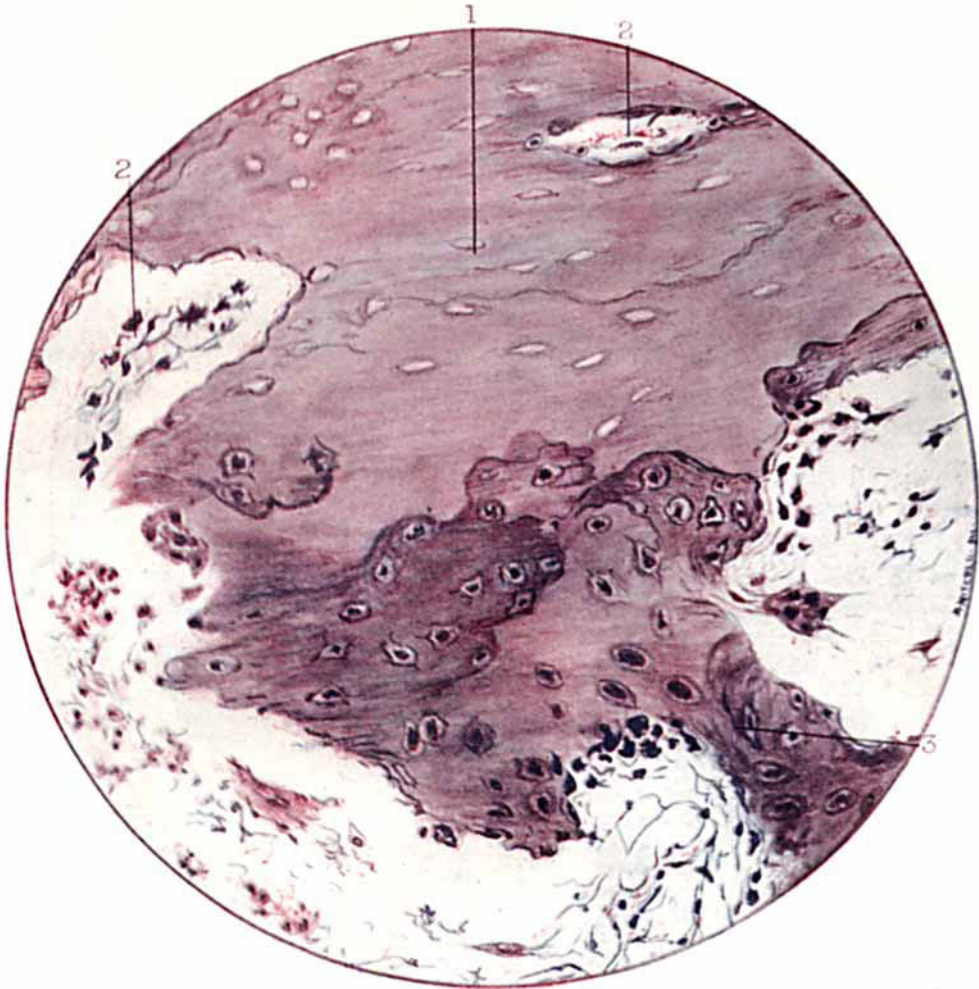


FIG. 217.—Drawing of high-power magnification of an area on the endosteal side of the boiled graft shown in Fig. 215. (*Brp.* 55.) 1. Old bone of graft with cells absent from lacunae. 2. Areas showing re-establishment of the circulation and absorption and replacement of the old bone by osteoblasts which invade it from the medullary surface. 3. Medullary cavity filled with new cancellous bone which unites the graft to its bed.

conditions. In these experiments a section of bone, two inches long and a quarter of an inch wide, was removed, with its periosteum, from the radius of a dog. It was then cut into two equal parts and one part boiled for ten minutes. The two grafts were then replaced in their bed and the ends marked with silk threads laid in the transverse saw-cuts. The specimens were recovered as usual at intervals of one week. When the histological sections were prepared they were so arranged that each section would show a



portion of each graft, with the space marked by the thread in the middle of the slide. In this way we have made certain that the autogenous and boiled graft in each of the specimens was composed originally of bone of the same size and density, and that each was subjected to exactly similar conditions after implantation. (*Exps. 54 to 58.*)

From the study of such specimens the changes occurring in boiled and autogenous grafts which are in contact with living bone can be readily compared. When the gross specimens are examined it is seen that bony union of the grafts to the bed takes place with remarkable rapidity. The autogenous graft is solidly united in from two to three weeks, and the boiled in from three to four weeks. After the specimen has been split longitudinally with a thin circular saw, new cancellous bone can be seen to be laid down on the medullary surfaces of each and to fill the saw-cut between them. Examination of the specimens recovered after three weeks shows that the circulation has been partially re-established in each, but that greater progress has been made in the autogenous transplants. The grafts which have been recovered five and six weeks after the operation show decided rarefaction, but again the greater degree of change is to be seen in the autogenous bone. Histological examination corroborates these observations. During the first two weeks a very cellular granulation tissue develops in relation to the medullary surface, but this granulation tissue is more adherent to the autogenous than to the boiled bone. In these granulations new cancellous bone develops very early, but it is laid down on the autogenous graft nearly a week earlier than on the boiled. This accounts for the more rapid union of the former. The circulation is re-established in the two types of grafts in quite the same way, by the ingrowth of blood-vessels into the Haversian canals, but the process commences earlier and makes more rapid progress in the autogenous bone. Similarly, absorption and replacement proceed in the same manner in each, but these processes are at least a week in advance in the autogenous graft. The old cells in the lacunæ behave quite similarly in each, except that they disappear more slowly in the boiled bone, probably owing to the fixing effect of the heat. Up to the present our examination has involved only the medullary surfaces and the deeper portions of the grafts. If the periosteal surfaces be now examined, very marked differences can be observed. These differences are first noted during the second week, when marked proliferation of osteoblasts appears on the surface of the autogenous graft. During the third week new bone appears on this surface, and absorption and replacement commence as already described. On the surfaces of the boiled bone no such cellular activity appears, and this surface and the bone subjacent to it remain for a long time in the condition of similar specimens implanted in muscle. The boiled periosteum is simply replaced by a new fibrous membrane from which blood-vessels pass into the open Haversian canals. (*Figs. 245, 246, and 247.*)

As the weeks go by, the differences between the two types of grafts become more and more indistinguishable. The union becomes more solid, the blood-vessels and osteoblasts spread in all directions, and absorption and replacement go on in much the same way in each. At the end of eight weeks it is difficult to tell which graft was boiled and which unboiled. Careful examination, however, even at this stage, shows that absorption and replacement are slower in the boiled specimen. Examination of the periosteal side no longer shows the marked difference observed in the earlier specimens, as the boiled graft is now covered with osteoblasts, giant cells, and new bone. The cells which have produced this change have spread through the graft from the medullary side, and their progress can be traced week by week until they have reached the periosteal surface. The same phenomenon occurs both in experiments in which the graft had been removed subperiosteally and the periosteum stitched over the bones after it had been boiled, and in those in which the periosteum was boiled with the bone. No osteoblasts appear on the surface until sufficient time has elapsed for them to have spread from the medullary side.

The results of these experiments very strongly support the theory already advanced to explain the changes in bone after transplantation. There are many who believe that, when autogenous bone is severed from its circulation and implanted in a bony gap where a good supply of lymph is available, the whole graft will live and functionate. These

experiments must show the fallacy of such a theory. Such an idea is based on the clinical observation that, following the implantation of an autogenous graft, primary union of the wound occurs, and the gap into which the graft was implanted has remained permanently closed. The fact that grafts known to be dead, either owing to incompatibility of the cells with the lymph, as in heterogenous transplants, or to complete destruction of the cells by boiling, act in a manner so similar to autogenous transplants, adds to the observations already made on the autogenous transplants themselves, further proof that, following the destruction of the circulation, all the bone of the graft dies, and any changes or signs of life that may appear later result from the growth into it of osteoblasts from neighbouring living bone or from its own exposed surfaces.

#### THE BRIDGING OF SKELETAL GAPS.

In order that we might understand more definitely the changes which occur when bone is transplanted for the purpose of bridging gaps, a series of experiments was performed in which complete sections of the bone were removed from the radii of dogs and the space bridged by various kinds of grafts. (*Exps.* 59, 60, 61, 62, 64, 65, 66.) In these experiments the grafts were well embedded in the ends of the fragments, sometimes by the ordinary sliding method and sometimes by the bone-wedging method previously described by one of the writers.\* In making the sliding graft the motor-saw was applied to the radius, and a strip of bone, two and a half inches long, composed of about one-third the circumference of the shaft and including periosteal and medullary surfaces, was removed. The shaft was then sectioned transversely in two places, and about three-quarters of an inch of bone removed. The graft was then replaced in its bed and fastened in place with kangaroo tendon. In the bone-wedging method the graft and saw-cuts were tapered so that when a graft was imbedded it could be driven home in a longitudinal direction and thus ensure more perfect fixation of the fragments.

Except in those instances in which bones were knocked out of place by the movements of the animal, the grafts united rapidly to the fragments and a circulation was soon established as in the experiments described above. The part of the graft which formed the bridge showed the same restoration of circulation and absorption and replacement of the dead bone as described in the implantations into muscles. When the part of the graft which formed the bridge, and the part implanted in the fragment, are compared at the end of three weeks, it is seen that these processes have advanced much more rapidly in the latter, owing probably to the assistance of the osteoblasts of the neighbouring living bone. At the end of four weeks, however, the changes are general throughout the whole graft.

A point of the utmost clinical importance was observed at this stage. The process of absorption of the graft goes on much more rapidly than the process of replacement. The result is that after the lapse of five weeks the graft is exceedingly porous and fragile, and it remains in this condition until the irritation produced by the presence of dead bone disappears, that is, until from eight to nine weeks have elapsed. This pathological change must be remembered in operations for non-union with loss of bone substance. We have seen several such operations fail because of the apparent complete absorption of the graft at one point, or because of a fracture occurring in it. We have also seen several cases of Albee's spinal operation, which appeared quite successful at first, ultimately result in failure because of fracture or absorption of the graft at a point between two of the spines. When one is dealing, therefore, with a gap in a long bone, the graft must be sufficiently thick to retain considerable strength during the stage of osteoporosis, and the longer the gap the thicker the graft should be. Although a graft composed of porous bone retains more cellular activity than compact bone, it also has a much greater tendency to rapid absorption, and hence must be used with care. We have seen several failures when attempts were made to bridge gaps with sections of rib, because of this rapid absorption.

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\* *Canadian Medical Association Journal*, 1915, February.

From these experimental and clinical observations it is evident that the bone to be used as a transplant must be chosen for each individual case. Theoretically, the best bone to use would be cancellous bone such as a rib, because of its greater cellular activity. But, unfortunately, this activity is directed primarily chiefly in the direction of absorption, so that rib must not be used if any great strain is likely to be placed on it during the commencement of active movements. Where the gap to be filled is long, or the strain likely to be appreciable during the early stages of return to normal functions, it is better to use a strong tibial graft and to surround it with several thin strips of bone for the purpose of providing an increased number of living osteoblasts. (*Exps.* 28, 29, 30, 31.)

Returning to the examination of the transplants made to bridge gaps in the bones of animals, the following changes were observed. Between three and four weeks after the operation the graft is noticed to become thickened at its point of junction with the fragments. At the exact point of junction the thickening is the full diameter of the dog's radius, and as one proceeds along the graft it rapidly thins out, until at a distance of a quarter of an inch from the fragment it disappears. This thickening is evidently the result of the formation of new bone from the ends of the fragments. No gross thickening occurs at this time in the central portions of the graft.

Similar changes have been observed, by means of the *x* ray, in patients on whom this operation has been performed. The graft gradually becomes less dense throughout, and a new shadow appears at the points of junction of the graft and the fragments, indicating new bone formation in this area. This can be demonstrated well after Albee's operation. At first the graft is seen to meet the split spines at an angle depending on their obliquity, but gradually, during the lapse of some six weeks to two months, the angles disappear and the graft and spines form a series of Gothic arches, due to the spreading of new bone from the spines along the under surface of the transplant.

After the lapse of about six weeks the microscopical examination of the transplants in dogs shows the gradual cessation of the process of rarefaction, and when two months have gone by it is quite evident that bone production is in advance of rarefaction, and that an increase in density is occurring. This change is coincident with the disappearance of the dead bone, which by this time has been very largely absorbed. At the same time the central portion of the graft begins to thicken, and from this time forward the thickening process advances, until, after five or six months, the bone is restored to practically its former anatomical outline. It must be noted that during the lapse of the first two months the animal has been using the limb more or less constantly. For the first two weeks he hops about on three legs, but after that period he begins to carry weight on the fourth paw, in spite of the presence of splints and bandages. Notwithstanding this partial use of the limb, no thickening occurs in the central portion of the graft until the process of absorption is well on the way to completion. This is readily explained when one realizes that the graft is dead. The influence of function on the architecture of the transplant could not be made evident until the transplant is actually composed of living bone, and until the irritative influence of the dead bone has disappeared.

The same sequence of events occurs in patients who have had operations similar to the above, except that in them the commencement of increase in the thickness and density of the graft is delayed several weeks. This is probably due to the fact that these patients are kept absolutely at rest in splints for from two to three months. More rapid increase in density and thickness occurs when a certain amount of strain is brought to bear on the graft at an earlier date. Thus, in several cases of gunshot wounds of the mandible in which gaps of an inch and a half have been bridged with autogenous rib, moderate movement of the jaw was allowed after two months, fracture being guarded against by a dental splint fastened securely to the lower teeth. In these cases the hardening and thickening of the graft corresponded with that observed in the experiments on animals.

The inference to be drawn from these observations would be that absolute fixation of the parts should not be continued longer than two months, and that a mild degree of muscular contraction and joint movement should be commenced at that time.

**IMPLANTATION OF BOILED BONE FOR THE PURPOSE OF BRIDGING GAPS.**

So interested were we in the histological changes occurring after the implantation of boiled bone, that a series of experiments, similar to the above, was performed, in which gaps were bridged with strips of bone which had been boiled for ten minutes. The specimens were recovered at intervals of a week, as in the case of the autogenous grafts. (*Exps.* 68, 69.) Up to a certain point the results were strikingly similar. In those cases in which good fixation of the parts was maintained, the dead bone united to the fragments, a circulation was re-established, although more slowly than in the autogenous bone, and absorption and replacement were apparent in the vicinity of the point of union of the bridge and the fragments. The same thickening of the graft over the area within a quarter of an inch of the ends of the fragments, produced by the activity of the osteoblasts pouring out of the open ends of the bones, occurred, and at the end of five weeks the gross appearances were practically indistinguishable from those in the preceding experiments. Examined microscopically, that part of the implant which was in contact with the living osteoblasts of the fragments acted exactly as did the boiled bone which was laid in a bed of living bone. (*Exps.* 50 to 58.) As the implant was examined, however, further and further from the point of junction of the fragment and implant, the evidences of osteoblastic activity grew less and less until, at a distance of a quarter of an inch from the end of the fragment, the cellular activity ceased altogether and the implant remained practically as it was at the time of operation. The only changes observable after five weeks were the re-establishment of circulation and the appearance of giant cells, apparently engaged in absorption, lying in small cavities on the surfaces. As the weeks went on, the osteoblasts growing in from the ends of the fragments spread somewhat further into the implant, but never more than half an inch. In the meantime the part of the implant invaded by osteoblasts became more and more porous, until the point of union of the regenerating and the dead bone was apparent even to the naked eye, the dead bone remaining white and compact as at the time of the operation. At this stage *x* rays show the central portions of the implant to be dense bone, and the ends, close to the fragments and in the fragments, much rarefied. These experiments were not followed sufficiently long to determine the ultimate fate of the middle portion of the implant, as a year or more would elapse before its complete absorption could occur. The experiments have gone sufficiently far, however, to demonstrate that such a procedure would have no clinical value. One would expect the implant to fracture ultimately, and a portion of it to separate as a sequestrum and to undergo gradual absorption. An ununited fracture would be the result. In those cases, however, in which the gap to be bridged was not greater than three-quarters of an inch, the invading osteoblasts met in the middle of the implant and thus established conditions practically the same as when autogenous bone is used. A successful bridging of the gap occurred, the dead bone being absorbed and replaced, and the area ultimately filled up to normal thickness of the shaft of the bone.

We were so impressed by the success of these experiments in bridging short gaps, where the cut ends of the fragments consisted of perfectly healthy living bone, that it was determined to try the experiment clinically in the bridging of the spines of the vertebræ in cases of Pott's disease. The operation was first done on a dog, the exact technique of Albee being employed, with the exception that the bone to be implanted in the spines was prepared beforehand and was boiled with the instruments before insertion. (*Exp.* 69.) When it was demonstrated that successful union of the spines could be obtained by this method, five patients were operated upon, boiled human bone, beef bone, dog bone, and in one case a piece cut from an old skeleton, being used. It is now three years since these operations were performed, and four of the patients are alive and as well as if they had been treated by any other method. One patient died at the end of the first year, of meningitis, and we were unable to obtain an autopsy. The others have been followed carefully by physical examination, by *x* ray, and in one case by histological examination of the implant after the lapse of six months and two years. The implants were prepared beforehand, of the correct size and shape, as estimated from the lateral

*x*-ray photographs, and were made wedge-shaped in cross-section, to make them fit more closely into the split spines. They were cut with an ordinary saw, and shaped up on a grindstone. Two of the cases had an extreme degree of kyphosis, so that the implants had to be very much curved longitudinally. The operation consisted of exposing six or seven spines in the region of the deformity, splitting them with a sharp osteotome, and fastening the implant in place between the lateral halves with kangaroo tendon. The deep fascia of the back was then sutured together over the implant, and the skin and superficial fascia closed. All the cases healed by primary union, and have done as well as after the ordinary bone-graft operation. One died of meningitis a year after operation; one developed a psoas abscess two years after operation, and this is still discharging; one is still wearing a spinal corset, but is quite well; and the other two are running about quite as normal children, without any restraining apparatus. The *x* rays, at intervals of three months since the operations, show the same changes as after the autogenous graft operation, with some exceptions. The union of the implant to the spines is apparently slower, but after two months definite rarefaction can be seen in the dead bone at its point of contact with the spine. New bone is being laid down by the spine, so that the sharp angle of contact of spine and implant has been converted into a gentle arch. At the end of six months the spine and this part of the implant are of the same density, and are evidently solidly fused, but the quarter of an inch of the implant midway between two spines stands out quite distinctly as compact bone, throwing a deep shadow as compared with that of the bone in the immediate neighbourhood of the spines. At the end of one year these areas of compact bone have also undergone marked rarefaction, and by the end of eighteen months the whole of the implant has evidently been absorbed and replaced, and the six or seven spines are united by arches of new bone of the same density as the spines. (Fig. 248.)



FIG. 248.—X-ray photograph of spinal column of patient described in text, two and a half years after the implantation of a boiled graft in the spines.

These *x*-ray findings have been corroborated by histological examination in the second case operated upon. Owing to a miscalculation, the implant was not made sufficiently curved to fit the shape of the kyphosis, and one end did not fit snugly down into its bed. After five months it looked as if this might cause a perforation of the skin, and it became necessary to cut down on this portion of the implant and remove it. During the operation the solidity of the union of the implant was tested and found to be very strong, and the presence of a free circulation in the dead bone was demonstrated when the projecting end was removed, bleeding occurring from many minute openings in the cut surface. When decalcified and sectioned, this piece of bone showed the condition described in the experiments in which gaps were bridged with boiled bone. The circulation had been re-established, the area close to a spine had been converted into living bone by absorption and replacement, but the middle portion furthest from the spines still contained considerable dead compact bone. Two years after the original operation this same patient returned with a psoas abscess which required operation, and while the patient was under the anæsthetic a portion of two of the spines and the intervening bony bridge was removed. The bridge was seen to be covered with normal periosteum, and to consist of two outside layers of compact bone with intervening cancellous tissue. Histological examination showed all the structures to be exactly as found in ordinary living bone. (Fig. 249.)

The apparent success of these cases does not lead us to recommend this treatment for Pott's disease very strongly. In the first place, it is not certain that any form of spinal-graft operation is of real value in the treatment of the disease, although it certainly splints

the area involved better than any form of external apparatus, and it looks as if it should retard the tendency to increase in deformity. Its actual value can only be judged by a review of large numbers of cases over long periods of time. In the second place, our experience with the boiled bone has been so limited that it is not possible to say that it will always unite to the spines or that it will always be replaced with living bone. In

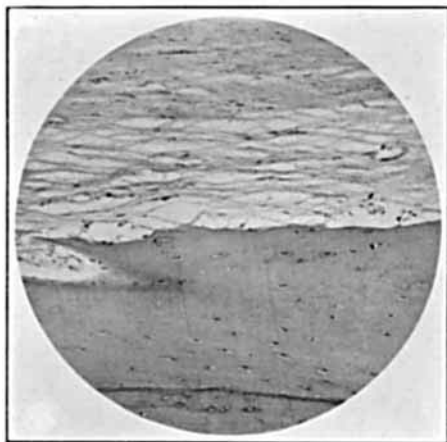


FIG. 249.—Low-power photomicrograph of section removed from the area of the graft shown in *Fig. 248* two years after the original operation. Note that there has developed a perfectly natural periosteum with normal subperiosteal osteoblasts, and that the boiled graft has been completely replaced by living bone.

favour of its use are the advantages that no second incision is necessary to obtain the graft, and that the implant can be made the correct shape previous to operation, which is of considerable importance in marked degrees of angulation. Against it are the disadvantages that solid union of the implant to the living bone is slower than when autogenous bone is used, and that the greatest care must be taken to see that perfect contact of the dead and the living bone is obtained, otherwise union cannot occur.

The above experiments, in which boiled bone was used for the purpose of bridging gaps, explains the failures which have followed operations where a similar procedure was employed, which at first appeared successful, but later proved unsatisfactory. For example: one case has been recorded in which the lower third of the tibia was replaced by a tibia obtained at autopsy and boiled before insertion. For some months the result appeared excellent, bony union occurring as described. But ultimately the greater part

of the implant was absorbed and the deformity recurred. This was due to the inability of the osteoblasts from the living bone to completely permeate the implant. The experiments also explain the failures and successes which have followed the implantation of bone from other animals.

#### EXPERIMENTAL STUDY OF METHODS OF INSERTING BONE GRAFTS FOR NON-UNION.

In order that we might arrive at some conclusion as to what method of operation would be most likely to prove successful in bridging gaps or overcoming ordinary non-union in fractures, other experiments were performed in which gaps were produced in the radii and ribs of dogs and the space filled in various ways. (*Exps. 59 to 66.*) In one series, after reflecting the periosteum, sections of bone were removed from the radius or rib, and immediately replaced in their beds, and the periosteum stitched over them. In the case of the rib, union occurred rapidly, with marked bony thickening at the point of junction of the graft and fragment. This is as one would expect, as one is accustomed to see small gaps in ribs bridge over rapidly without any transplantation of bone, and is due to the great outpouring of osteoblasts from the open ends of the fragments. In the case of the radius, however, unstable union occurred in all cases which were observed up to three months, and sections of the specimens showed that the area of junction of the graft and the fragments was filled with a mass of proliferating cells in which was a considerable quantity of cartilage and fibrous tissue. In another series the segments of bone which were removed from the rib and radius were split longitudinally or chopped up into small fragments and laid back in the periosteal tube. (*Exps. 12, 28, 29, 30, 31.*) In the case of the rib, union occurred rapidly and solidly, but in the case of the radius delayed or fibrous union resulted. While the strips or small pieces of bone often

united solidly to one another by new cancellous tissue, unstable union occurred at the point of junction with the fragments.

The explanation of the failure of such transplants to bridge gaps in the long bones successfully is not difficult to find when the causes of non-union in ordinary simple fractures are considered. One of the most potent factors in causing non-union is failure to secure immobilization of the fragments. This is common clinical experience, and it has been demonstrated experimentally on animals by Hey Groves and ourselves that, unless perfect fixation is secured, non-union is almost the invariable result. When gaps in the bones of animals are filled with transplants placed in end-to-end apposition with the fragments, it is impossible to maintain complete immobilization, and the result is that any callus that does form fails to solidify. (*Exps.* 59, 60, 61, 44, and 45.) Another cause of non-union is failure on the part of the osteoblasts in the ends of the broken bone to respond sufficiently to the irritation of the injury. When a simple transverse section is performed in the middle of the shaft of a long bone in a child, or through the cancellous bone near the extremities in an adult, we are accustomed to see a rapid and firm union, if the fragments are in good contact. This is not the case, however, in a transverse osteotomy in the middle of the shaft of such a bone as the tibia or ulna in an adult. We have seen several cases of delayed union, and in one case complete non-union, result from such operations on soldiers, in spite of perfect apposition and fixation of the fragments, and in spite of the perfect general health of the patient. On the other hand, such results are rare in oblique or fissured or more ragged fractures in the same region, when good apposition is maintained. This is readily understood when the histology of such bones is reviewed. In a child the osteoblastic activity is at a maximum, and, when a transverse fracture occurs, there is rapid proliferation of osteoblasts beneath the periosteum, in the medullary cavity, and in the open mouths of the Haversian canals. The comparatively open texture of the bone in such patients assists this materially. Similarly, in transverse fractures or osteotomy sections of the more cancellous bone near the extremities in adults, a great outpouring of osteoblasts occurs and rapid union results. Contrast with this the condition in the middle of the shaft of a long bone in an adult, where there are very few osteoblasts under the periosteum or in the medullary cavity, and where the compact bone is so dense that the open Haversian canals are very minute and contain but few bone-forming cells. Here is the reason for slow union in perfectly transverse sections, and for rapid union when the fracture is irregular or fissured. In the former the irritation of the injury is mild, and the opportunity for the pouring out of proliferating cells is slight. In the latter the injury is more severe, and the cells in the neighbourhood have much freer access to the line of fracture.

These observations are quite corroborated by an examination of the experiments in which sections of the junction of the autogenous grafts with the fragments were made at weekly intervals after the operation. (*Exps.* 32 to 43.) It was observed, both in the case of the graft and of the living fragment, that the greatest cellular activity and formation of new bone occurred on the periosteal and medullary surfaces, and that practically no new bone was laid down on the cut ends until quite late. Even then the cells seemed to flow in over the ends from the deep and superficial surfaces. In many cases no osseous union had occurred between the cut ends of the bones as late as two months after the operation.

From these considerations it may be concluded that in operations designed to bridge gaps in the long bones, two details are essential to success. First, provision must be made for perfect fixation of the parts until union is sufficiently firm to stand the strain of moderate motion; and second, the graft and fragments must be placed in contact through a sufficient distance to make use of the bone-forming qualities of the periosteal and endosteal surfaces of both graft and fragment. This means that the graft must extend well into the fragments. Wherever possible, we cut the graft so that it extends at least two inches beyond the extremity of the fragments. If the graft is made to fit fairly well into a slot prepared for it, good fixation is secured which is easily made perfect by external splinting. The clinical results following the various methods of bone-grafting for gaps,

which aim at extensive contact of the graft and the fragments, are all infinitely better than those methods which simply fill in the space between the severed ends of the bones. From our experience in military surgery we have no doubt that, excluding sepsis, the commonest cause of failure to obtain union after a bone-graft operation is the neglect of this important essential. The most striking demonstration of the error of this method of operation came under the observation of the writers in a series of five cases of ununited fractures of the bones of the forearm with gaps varying from one to three inches, all operated upon in one hospital within a period of three months. The ends of the fragments were freshened and segments of autogenous tibia laid in the gap, closely abutting the ends of the fragments. In all the cases non-union of one or both ends of the graft persisted after the lapse of four months, and the operator was inclined to condemn bone grafting as a useless method of treatment in such cases. Similar failures have been observed in the jaw, femur, humerus, and tibia. If it is impossible to be sure of the union of the end of a graft to the fragment, it is certainly impossible to be sure of the ultimate union of the fracture. (*Exp.* 63.) For similar reasons failure to secure union may be expected if the graft does not come in close contact with healthy bone beyond the sclerosed ends of the fragments. If the end of a graft is simply placed in contact with, or even buried in, the sclerosed bone, only fibrous union will occur, and ultimately the graft will be absorbed. The osteogenetic power of the graft is not sufficient to produce union with sclerosed bone, and, having no physiological function to perform, it acts as do the grafts imbedded in muscle, and slowly disappears. As demonstrated repeatedly in these experiments, the strongest factor in producing union of bone-grafts to their beds is the osteogenetic power of the bed. If this is below normal or absent at the extremities of the fragments, the graft must be sufficiently long to secure contact over a considerable distance with healthy bone beyond the sclerosed extremities. These observations are based on failures noted in several clinical cases, and on the pathological findings recorded in *Exps.* 63, 64, and 65.

#### EXPERIMENTAL STUDY OF METHODS OF IMPLANTING GRAFTS IN THE FRAGMENTS.

To arrive at a decision as to which is the best method of implanting a graft in the fragments, several experiments were performed and many clinical observations recorded. Four methods are in use: in one the graft is inserted into the medullary cavity; in another it is applied as an external plate; in a third it is introduced as an inlay; and in the last the fragments are split longitudinally and the graft driven into them in much the same way as a gardener grafts a tree.

The medullary-graft method succeeds very well in those cases in which it can be applied; but its application is limited, as it is impossible to insert such a graft unless the gap in the bone is considerable. Some method of inlay must be used in one of the fragments where the bones are in contact or the gap is short. When it has been carefully inserted, however, the graft unites to the fragments, and absorption and replacement, with the ultimate strong union of the fracture, occur. In the cases in which we have used this method, the graft has been cut from the tibia subperiosteally, and includes both periosteal and endosteal surfaces. No effort was made to shape it into the form of a peg or dowel, as by this means most of the osteoblasts would be removed, and its value from the standpoint of osteogenesis lessened.

The external autogenous plate has also been used successfully, and in some cases has special advantages. It is common experience, in operating for non-union, that one sometimes finds difficulty in holding the fragments in apposition, there being a strong tendency to lateral displacement. In these cases one cannot depend on the ordinary absorbable ligatures to hold the graft and fragments in position, even when some method of inlaying is employed. This difficulty has been overcome by using a plate of autogenous bone which is fastened to the fragments by wire, screws, or pegs. In our first experiments we used shoemaker's tacks, and, in operations on patients, ordinary steel screws, but since the histological changes occurring in boiled implants have been more clearly understood, we



have substituted screws made from boiled beef-bone, with satisfactory results. In some instances the autogenous plates were made from sections of rib, and in others from the medial surface of the tibia. Both types of plate proved successful in the experiments on animals, but clinically it was soon found that the rib is not sufficiently trustworthy to be used when strength is an essential. A rib is so porous that it is apt to become completely absorbed before sufficient progress has been made in the formation of new bone. Lateral displacement then recurs, and a persistent non-union is the result. (*Exp.* 66). To prepare a plate from the tibia, the periosteum is reflected, the exact outline of the plate marked with a chisel, the screw-holes drilled, and finally the plate is cut free with a motor-saw. A trench, roughly an eighth of an inch deep, is then cut in the fragments with a chisel, the plate and fragments are fastened in place with a special clamp, holes drilled in the fragments and tapped out with a steel tap, and the bone-screws driven home. The fate of these screws will be described later.

While the external autogenous plate may be useful in cases in which there is a strong tendency to lateral displacement, the disadvantages of the method are so important that without modification it can never be considered suitable for general use. In an ununited fracture the ends of the fragments are so sclerosed, and the tendency to osteogenesis is so reduced, that any method of treatment that fails to overcome these pathological conditions in the most effective manner must result in a high percentage of failures. When the external plate is used, no use whatever is made of the endosteal osteoblasts of the fragments, upon which, it has been shown, the principal hope of union must be based. The plate is merely placed in contact with the chiselled cortex and must, therefore, depend almost entirely on the osteoblasts of its own endosteal surface for union with the fragments. We have seen a sufficiently high percentage of failures following the method to know that it should not be generally employed. When the fragments are difficult to hold in position, however, the plate is of decided value, and its disadvantages can be largely overcome by combining with it a medullary graft or some form of inlay.

In our experience the best general method of inserting the graft is the inlay method described by Albee. The bed for the graft is prepared by cutting a trench in the fragments with the twin saws, the trench extending two to three inches into each fragment, if possible, and certainly well into healthy bone. The graft is then cut from the tibia with the same saws and fitted into the slot prepared. It is fastened in position with kangaroo tendon passed over the graft and through drill-holes in the fragments. The advantages of the method are many. As a general rule it is the easiest operation to perform; it brings the graft into very intimate relationship with the fragments over a long distance, and brings those surfaces of the graft and fragments together which are most energetic in the formation of new bone; it freely cuts open the fragments, thus stimulating osteogenesis and allowing the outpouring of the cells from the interior; and, finally, it assists materially in the immobilization of the parts. Clinically we have had more general satisfaction from this method than from any other.

There are certain cases, however, in which the ordinary inlay method cannot be employed. Thus, in fractures of the mandible, the fragments are apt to be so thin that a slot of sufficient depth to receive a graft cannot be made. Similarly, in fractures of the ulna or radius in which the ends of the fragments have become attenuated, it is impossible to cut a slot of sufficient width to receive a graft without further increasing the gap between the fragments. These difficulties have been overcome by a method which resembles somewhat the procedure of the gardener in grafting a tree. This consists of making a single saw-cut in the thinned-out fragments and driving in a graft in the form of a wedge.\*

The following technique is employed for filling gaps in fractures of the mandible. The fragments are exposed by an incision along the lower border of the jaw. The motor-saw is then applied to the fragments, and a saw-cut made along the inferior border, extending an inch to an inch and a half back from the end of the fragments and about half

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\* Gallie and Robertson, *Jour. Amer. Med. Assoc.*, 1918, April; and Albee, *Bone-Graft Surgery*.

an inch deep. Great care must be taken to avoid opening into the cavity of the mouth or into the sockets of the teeth. An osteotome is then driven into the saw-cut and a wedge-shaped slot produced in the lower border of the mandible for the reception of the graft. An interdental splint which has been previously cemented to the teeth of both jaws is now locked, with the teeth of the two jaws in exactly the correct relations to one another. The graft is made by resecting three inches of a rib subperiosteally. This piece of rib is then split on the flat, in order that the endosteal surface may be bathed in lymph. Half of the graft is then driven into the slots in the fragments, the smoother concave side of the rib facing towards the mouth-cavity. This leaves the rough cancellous surface of the graft facing outward and sunk somewhat below the outer surface of the jaw. This depressed area is then filled out by laying a piece of the outer half of the rib in the gap, with the smoother side out. The fragments and graft are now fastened solidly in place with kangaroo tendon passed through drill-holes. This adds additional security, although it is really unnecessary, as the principal graft is self-retaining.

The operations on the jaws have been most satisfactory. Several soldiers have been operated on in our clinic, who have been able to masticate ordinary food five months after the implantation of a graft which has bridged gaps of from one to two inches.

Similarly, in gaps in the ulna and radius in which the ends of the bones are attenuated, a single longitudinal saw-cut can be made through the whole thickness of the fragments, extending back from the extremities for two or three inches. A graft is then cut from the tibia, tapering to a point at either end, and this is driven into each of the saw-cuts. Excellent fixation and very intimate apposition of the graft and the fragments are thus secured. The clinical results have been excellent. This would really be an ideal method of bone transplantation, but, unfortunately, it is only applicable to those cases in which the fragments are thin enough to yield to the driving home of the wedge.

While the above remarks on methods of inserting grafts into the fragments apply particularly to those cases in which gaps are to be bridged, they apply equally well, except in those cases where mechanical difficulties interfere, to ordinary non-union in which the ends of the bones can be brought into contact. In the treatment of ordinary non-union, however, older methods should not be discarded. Thus, in addition to inserting the graft, the ends of the fragments should be thoroughly freshened and brought into good contact. The additional precaution of drilling numerous holes into the sclerosed ends of the bones will provide for the outpouring of osteoblasts, and give additional stimulus to cell-proliferation. The perfect fixation of the parts is essential.

#### THE TRANSPLANTATION OF BONE FROM ONE ANIMAL TO ANOTHER OF THE SAME SPECIES.

To determine the histological changes occurring in bone grafts transplanted from one animal to another of the same species, two experiments were performed, but, unfortunately, at the time this work was being done, the clinical importance of the information to be gained had not presented itself, and it must be admitted that the experiments were not carried sufficiently far to be of real value. In these experiments a segment of a rib was removed subperiosteally from each dog. This piece of rib was then divided into two portions, and one portion implanted in a muscle in each animal. Thus, with each homotransplant was placed an autotransplant which acted as a control experiment. All the specimens were recovered at the end of three and a half weeks. (*Exp.* 70). They showed firm adhesion of the bone to the surrounding tissue, the re-establishment of the circulation, the absorption of the cells in the lacunæ, and some evidence of osteoblastic activity and the formation of new bone. As far as we could see, there was no difference between the changes occurring in the homogenous and autogenous bone.

From these results there can at least be deduced the conclusion that bone from one animal can sometimes be transplanted to another animal of the same species with retention of vitality in the exposed osteoblasts. A recently published paper by Masson on skin grafting from one patient to another is interesting in this relationship. He states that

in his experience skin grafts do not 'take' when the blood of one agglutinates that of the other, whereas, if the bloods are compatible for transfusion, grafts take readily. A similar guide as to the probability of success in the transplantation of bone might be obtained by blood-examination. It is quite clear, at any rate, that more information must be obtained on the subject before the transplantation of bone from one patient to another can be recommended. Unfortunately, experimental work on dogs cannot clear up this question, as practically all dogs belong to the same blood-group. If occasion arises, however, to do a bone transplantation on a patient from whom it is impossible to obtain the graft, we shall not hesitate to use bone from a donor whose blood is compatible with that of the recipient.

#### THE CLINICAL USE OF BOILED BONE.

The appreciation of the gross and histological changes occurring in boiled bone when implanted into living tissues led to the immediate application of the information gained to clinical problems. The surgical practice of the writers includes a large number of fractures of the long bones, many of which require open operations for the correct alinement and fixation of the fragments. The technique described by Lane has proved quite satisfactory in our hands; but the frequency with which patients have presented themselves in ordinary hospital practice who have had metal plates applied apparently successfully but who have late trouble from the presence of the plate, such as sinus-formation, pain and tenderness, and loosening of the plate or screws, made us anxious to substitute some absorbable material for the metal. Boiled bone has proved to be a satisfactory substitute.



FIG. 250.—Photograph of gross specimen of dog's radius eight weeks after the shaft had been divided transversely and a plate of boiled bone applied and fastened in position with pegs of the same material. The specimen has been sectioned longitudinally with a saw through the plane of two of the pegs. It shows the solid union of the plate and pegs to the living bone. (*Exp. 68.*)



FIG. 251.—Very low-power photograph of section of specimen shown in *Fig. 250*. It shows the intimate union of the boiled plate and pin to the living dog-bone. (*Exp. 68.*)



FIG. 252.—Low-power photomicrograph of the area of the drill-hole in the plate (*Fig. 250*), showing a portion of the pin (to the right) and a portion of the plate (to the left), and between the two a mass of new bone firmly united to each growing up from the underlying radius. (*Exp. 68.*)

The first experiments were performed on dogs, and consisted of the production of fractures, and the immediate application of plates of boiled beef-bone, fastened in position with screws of the same material (*Exps.* 67, 68). *Fig.* 250 shows the gross appearance of the first animal so operated upon, two months after the operation. The specimen has been sectioned with a saw throughout half its length, the saw passing longitudinally through two of the screws. At the end of two months the fracture is united, the plate



FIG. 253.—X-ray photograph of a fracture of the humerus, taken through plaster-of-Paris, immediately after operation in which a plate of beef-bone was applied and fastened in place with screws of the same material.

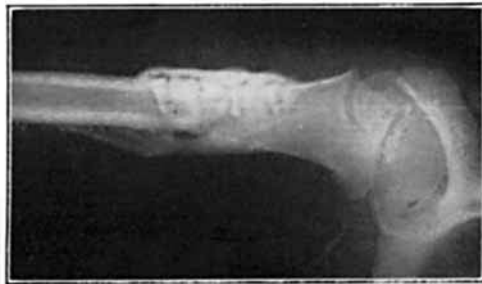


FIG. 254.—X-ray photograph of the same patient, taken two months after the operation. It shows the union of the fracture and the commencing absorption of the beef-bone.

is solidly united to the fragments, a circulation is established in the plate and screws, and the absorption and replacement described above is well started. At the end of eight months these plates can be recognized in the gross only as simple fusiform swellings, and the microscopic examination shows no dead bone present. After a year the bone is completely restored to its normal outline. (*Figs.* 251 to 255.)



FIG. 255.—X-ray photograph of the same patient, taken one year after the operation. It shows the complete absorption of the plate and screws, and the return of the whole area to a normal condition.

disappears and never causes late trouble. In the series of one hundred operations performed in our clinics, no plates have ever had to be removed, no suppuration has occurred, and in only one case did the plate break. In this case, fortunately, no displacement took place.

In *oblique fractures* requiring open operation the plate has been eliminated altogether,

For the past six years this technique has been used in all fractures requiring open operations, and has proved satisfactory. It must be admitted that the operation is a little more difficult than the Lane operation, as the bone-plate is not so strong as the steel, and the limb must be handled more gently. With reasonable care, however, this is not an objection. The operation also takes about five minutes longer than the Lane operation, because of the necessity for using the tap to make the thread in the cortex of the fragments after the holes have been drilled. Further, it is necessary to use a splint after the operation, owing to the comparative weakness of the bone-plates. The writers use plaster-of-Paris. The advantages of the method, however, outweigh these objections, as the foreign material introduced

and long bone screws which pass through both fragments are used. These long screws are useful also in fractures of the patella. They fasten the fragments securely together for a sufficient length of time to ensure bony union, and yet do not introduce the disadvantages of non-absorbable materials.

The technique of the operation on the long bones is simple. After the exposure of the fragments, the bones are brought together with forceps and fastened solidly in position with a special clamp, described in the *Canadian Journal of Medicine and Surgery*, May, 1916. This instrument has the advantages that it holds the fragments perfectly without requiring the separation of the soft tissues on the deep side of the bones, and it allows freedom in drilling the holes and cutting the thread. The periosteum is then reflected over the area to which the plate is to be applied, the plate is adjusted, and the pin in the clamp screwed down to prevent lateral movement of the plate during the further manipulation. The holes are then drilled, and an ordinary steel tap, seventeen threads to the inch, is used to cut the thread in the cortex. The screws are rapidly driven home and the heads cut off flush with the plate. If a screw should break, it is simply cut off flush, the hole drilled and tapped again, and a second screw inserted. The procedure is similar when long screws are used.

The plates and screws are made from ordinary beef-bone. The plates are cut out with a saw and shaped up on a grindstone, so that they are thick at the centre and taper down at the ends. They are made curved in cross-sections to fit the surface of the fractured bone. The screws are turned on a lathe, the thread being cut free-hand by a tool called a chaser. The thread on the screws corresponds with that cut by the tap.

#### SEPSIS AND BONE TRANSPLANTATION.

Failure to obtain a successful result following the transplantation of bone for gaps or ordinary non-union is, unfortunately, very common. The most frequent cause is sepsis. If the wound becomes septic, no cases in which gaps are present are ever improved by the operation, and very few unions occur even when the bones are in apposition. The reason is that, following the healing of the septic wounds which produced the fractures, the ends of the bones gradually become sclerosed and the osteogenetic activity is reduced to a minimum. If sepsis occurs following the operation for the repair of the fracture, the cells on the surfaces of the graft are killed and the graft becomes an ordinary sequestrum which must be removed before healing can occur. Some writers have cited cases in which the graft has been left in place even after sepsis has developed, with the ultimate union of the fracture; but such cases must be very rare, for we have seen a considerable number in which no sign of union developed, and the histological examination of the graft when removed showed it to be completely necrotic. This refers to those cases in which the whole area of the fracture has been infected, and not to those in which slight sepsis has occurred at one end of the wound, or to those cases which develop a small sinus with a slight serous discharge. These latter sometimes do result successfully after discharging serum from a small sinus for several weeks; but in those which suppurate profusely it is very rare for union to occur, whether the graft is removed or not. The most rational treatment, under such circumstances, is to remove the dead bone as soon as possible, and to allow the wound to heal preparatory to another operation.

With ordinary careful technique, the danger of introducing infection into the wounds appears to be no greater in bone transplantation than in any other extensive operation. This is evidenced by the uniformity of the primary healing following the operative treatment of simple fractures. But, unfortunately, the non-union of fractures in soldiers is practically always secondary to septic gunshot wounds, and infection will often remain latent in the area of the ends of the fragments for many months. In one case of complete severance of the musculospiral nerve complicated by osteomyelitis of the humerus, we operated to suture the nerve seven months after the wound had finally healed. When the incision reached the level of the nerve, a small pocket of pus, about the size of a bean, was opened, and in it was found a small sequestrum. The bacteriological examination

of the pus showed staphylococci. In another case of non-union following a septic compound fracture, the patient was warned for operation six months after all signs of infection had disappeared. A few days before the operation was to take place the limb became inflamed, and a day or so later a pocket of pus was evacuated and two small sequestra were removed. On the other hand, successful bone transplantation has been done within two months of the final healing of the wound. It would therefore appear that no definite time can be laid down as a safe interval to intervene between the healing of the wound and the grafting operation. Each case must be decided upon individually. Much assistance can be obtained from *x*-ray examination. If the ends of the fragments are clear, with no spots of rarefaction and no suggestion of sequestration, and if they are closed in by a terminal plate of thin compact bone, one can confidently proceed with the operation even if no longer than three months has elapsed. But if there is any suggestion of osteoporosis about particles of bone of only slightly decreased density, or if the ends of the fragments are surrounded by masses of callus, and the shadow gradually fades away at the extremities, indicating marked rarefaction without closure of the ends of the bones, an operation must be considered more or less dangerous, no matter how long a time has elapsed. From bitter experience we have learned to leave such cases alone. It is a general rule in our services to have the ununited fractures of small or superficial bones, such as the ulna, radius, and mandible, come up for consideration four months after the first healing of the wound, and the fractures of the humerus, tibia, and femur after the lapse of six months. If there are no signs whatever of inflammation, and if the *x*-ray photographs are satisfactory, the operation is proceeded with, but otherwise it is postponed.

Another reason for delaying operation in these cases, particularly when they are complicated by extensive formation of scar-tissue, is the great vascularity of the area for many months after the final healing of the wound. It is quite impossible in some of the ununited fractures of the femur to secure adequate hæmostasis if the operation is done within the first six months after healing. The result is that the healing is complicated by the formation of hæmatomata, which are exceedingly dangerous where attenuated living bacteria may be lurking. The insertion of a drain is also an element of danger. It would therefore seem safer to allow a longer time to pass before operating on these badly-scarred cases. We now delay operation for a year in all severely comminuted fractures of the femur, or those which show evidence of extensive inflammation in the bone, or which are complicated by extensive scar formation in the soft tissues.

Other causes of failure to obtain union after the transplantation of bone have been referred to in the course of the paper, and require no further discussion.

### CONCLUSIONS.

In conclusion, it may be of value to review the deductions which have been formulated from the research involved in this paper, and to outline the principles derived therefrom which have proved of value in ordinary clinical practice.

1. The periosteum, as viewed by the surgeon, is not osteogenetic, and should not be depended upon under any circumstances to assist in the production of new bone.

2. The presence or absence of the periosteum in autogenous bone transplants has no decided influence on the activity of the subperiosteal osteoblasts, and is of no practical clinical importance.

3. The periosteum is of great importance, however, from a clinical standpoint, because of its control of the circulation throughout living bone. Extensive stripping of the periosteum at operation will result in necrosis, which may cause delay in the union of aseptic fractures, and which will result in sequestration where sepsis is present. Disturbance of the circulation should be reduced to a minimum in all operations on bone.

4. Subperiosteal resections can only be performed with a reasonable certainty of restoration of the continuity of the bone where previous inflammation has caused extensive proliferation of the subperiosteal osteoblasts and commencing new bone formation.

5. When a piece of bone has been cut free from its circulation and transplanted to some other position in the same animal, and if its surfaces are freely bathed in lymph, those cells which are present on the surfaces and in the open mouths of the Haversian canals will live and undergo rapid proliferation. The cells in the lacunæ or deep in the Haversian canals die, and in the course of two or three weeks disappear. The proliferating cells on the surface, whether derived from the graft or from neighbouring living bone, immediately commence the absorption of the graft, and do not cease their activity until every vestige of the old bone has disappeared. In the meantime, however, new bone is being laid down on the surfaces, particularly the periosteal and endosteal, and a circulation is re-established throughout the whole graft by the ingrowth of new blood-vessels. Along with these blood-vessels the osteoblasts also pass into the interior of the bone and rapidly continue the process of absorption. As the old bone disappears, its place is taken by fine trabeculæ of new bone. During the first two months the process of absorption goes on much more rapidly than that of replacement, so that at the end of this period the dense bone of the graft has become more rarefied. If the graft is not subjected to any strain and has no definite part to play in the function of the area in which it was implanted, the absorptive process continues in advance of replacement, and gradually the new bone disappears and its place is taken by an ordinary scar. If the graft, on the other hand, is implanted in such a position that it is subjected to strain and has some definite function to perform, the process of rarefaction is gradually outstripped, after the lapse of two months, by the process of new bone formation, and the new bone steadily thickens and hardens until it assumes the form and density required by the work it is called upon to do.

6. Bone transplanted from one species into another retains no viable elements.

7. Bone transplanted from one animal to another of the same species may act similarly to autogenous transplants. It probably always does so in dogs and cats, but in man there is reasonable doubt as to whether the cells from all donors will live in the fluids of all recipients. Until this is cleared up experimentally, it appears wiser to avoid using any but autogenous bone, and if this is impossible, to use bone only from a donor whose blood is compatible with that of the recipient.

8. When heterogenous or boiled bone is placed in close contact with living bone, the resulting gross and histological changes closely resemble those which follow the implantation of autogenous bone. The cells of the living bone respond to the stimulus provided by the dead bone, rapid proliferation occurs, and the dead bone becomes securely united to the living by trabeculæ of new bone laid down on its surfaces. Active absorption by osteoblasts commences on the surfaces and, as the circulation is re-established, the osteoblasts spread throughout the implant and continue the work of absorption as in the cases of autogenous bone. At the same time new bone is laid down on the walls of the excavated cavities, so that, by the time the dead bone is completely absorbed, its place has been taken by a mesh of new cancellous tissue which is gradually changed to the density that the physiological function of the area requires.

9. In transplanting bone for the purpose of bridging gaps in ununited fractures, autogenous grafts only should be used, unless some certain method is discovered of foretelling whether the cells on the surfaces of bone obtained from a donor will survive in the lymph of the recipient. The importance of using autogenous bone depends on the fact that cells survive on its surfaces which are capable of absorbing and replacing it and, later, restoring the area to the required density and anatomical outline. Heterogenous and boiled bone fail because the invasion of the implant by osteoblasts from the ends of the fragments is only able to advance short distances, and the central portion of the implant slowly absorbs and disappears. Further, autogenous bone is preferable in ununited fractures because of the assistance given by the cells of the graft in producing union of the graft to the fragments.

10. When it is desired to bridge short gaps between perfectly healthy bones, such as the spines of the vertebræ, boiled bone may be used with the expectation that the gap will be ultimately bridged with living bone.

11. When operations are performed for the bridging of gaps or for ordinary non-union, two points in technique must be observed. First, complete immobilization of the parts must be secured until solid union of the graft to the fragments has taken place. Second, the transplants must be embedded in the fragments for a considerable distance in order that the bone-forming qualities of the periosteal and endosteal surfaces of both transplants and fragments may be enlisted to make certain of solid bony union.

12. The best general method of implanting the transplant in the fragments is the so-called inlay method, although the methods in which the medullary graft and the external autogenous plate are employed, and also the method in which the graft is wedged into the fragments, may be used successfully and have advantages in special cases.

13. In open operations on fractures, fixation of the fragments can be readily obtained by using plates and screws made of boiled bone, or in special cases by screws alone. The advantage in using this material rests in the fact that the boiled bone unites to the fragments and is ultimately absorbed and replaced by living bone.

14. Asepsis is essential to success in bone implantation. The utmost care must be taken in the selection, for bone transplantations, of cases of non-union following septic gunshot wounds. Cases in which there is any probability of the presence of latent infection should not be operated upon.

#### APPENDIX.—DETAILS OF EXPERIMENTS.

##### EXPERIMENTAL STUDY OF THE PERIOSTEUM.

*Experiment 1, May 16, 1912.*—Adult terrier. Middle third of radius exposed. Incision made in periosteum,  $2\frac{1}{2}$  in. long, and the periosteum reflected and removed from the area. Bone wrapped in strip of tin-foil,  $\frac{1}{2}$  in. wide, and the muscles and skin closed over it with catgut.

Oct. 19.—Specimen recovered. Over the foil was a thin fibrous membrane, resembling ordinary reflected periosteum. It was continuous with the periosteum attached to the bone on either side of the foil. The bone under the foil was not thickened and was normal in every way. Histological examination confirmed the gross appearances, there being no bone between the periosteum and foil.

*Exp. 2, June 5, 1912.*—Adult fox terrier. Middle third of radius exposed. Periosteum incised and reflected over an area  $2\frac{1}{2}$  in. long, without disturbing the attachment of the muscles to the membrane. A strip of tin-foil,  $\frac{3}{4}$  in. wide, was then wrapped about the bone in the middle of the denuded area. The periosteum was sewn over the foil with fine catgut, and the muscles and skin closed.

Oct. 19.—Specimen recovered. The periosteum is now lying as originally placed upon the tin-foil. There is nothing between periosteum and foil. At the edges of the foil the periosteum is lying in normal relation to the bone. Histological examination showed the bone under the foil, and the periosteum over it, to be normal. No new bone had developed between the foil and periosteum.

*Exp. 3, Nov. 2, 1912.*—Adult fox terrier. Incision down to radius, and periosteum reflected over an area  $1\frac{1}{2}$  in. long, and half the circumference of the bone. A wedge-shaped piece of bone,  $\frac{3}{4}$  in. long, was then cut from the bone, the saw penetrating to the medullary cavity at the base. Tin-foil was wrapped around the thin end of the wedge of bone, which was then replaced in its bed and the periosteum sewn over it.

Dec. 30.—Specimen recovered. Graft solidly united to its bed throughout the half which was not covered with foil. Marked thickening of the specimen in the region of the saw-cuts due to the laying down of new bone. No new bone between the periosteum and the foil. When the periosteum and the foil were split longitudinally and reflected from the graft, the area covered by the foil was marble white, and the uncovered portion pink. Further, the covered portion was as hard as when imbedded, and apparently the same size, while the uncovered area was soft and had thinned considerably, there being a distinct drop as one passed from the covered to the uncovered bone.

The specimen was sectioned longitudinally, and, after decalcification, the sections for microscopical examination were cut from the exposed surfaces. The histological findings in the uncovered portion will be described in *Exp. 40*. The covered portion is apparently dead at its tip, except that a circulation has been re-established throughout. The distal half of this portion contains no living cells except those of the blood-vessels. Moving along the section towards its middle, the Haversian canals are seen to become larger and more numerous and to be filled with osteoblasts, which are absorbing the dead bone in places and in others laying down new bone on the walls of the cavities. As one moves along the section to the uncovered portion, the evidence of dead bone



disappears, and the graft is seen to consist nearly entirely of new cancellous bone. The invasion of the dead covered portion of the graft has advanced about a quarter of an inch beyond the edge of the foil.

*Exp. 4, Nov. 3, 1912.*—Adult hound. Periosteum of radius reflected as in former experiments, the muscles remaining attached, and a section of bone,  $\frac{1}{2}$  in. long and  $\frac{1}{4}$  in. deep, removed. The space was filled with warm paraffin, which quickly solidified, and the periosteum was sewn over it.  
Jan. 23.—Specimen recovered. No new bone found between periosteum and paraffin.

*Exp. 5, Nov. 28, 1912.*—Terrier puppy, five months old. Radius exposed and periosteum reflected as above. Several holes were drilled through the middle of the shaft of the bone, and these were connected with a fine saw, so that a slot,  $\frac{1}{2}$  in. long and  $\frac{1}{4}$  in. wide, was made. This slot was completely filled with soft paraffin wax, which was smoothed down perfectly level with the cut edges of the bone, and the periosteum stitched over it.

Feb. 21, 1913.—Specimen recovered. No new bone between periosteum and paraffin. The slot in the bone is plugged with wax. The surrounding bone has thickened appreciably with the growth of the puppy, and the result has been a rounding off of the cut edges of the slot and a tendency for the bone to close over the edges of the paraffin. No irregularity or callus, such as occurs when saw-cuts are made in bone without being plugged with wax, was evident. Specimen was split longitudinally. The wax is enclosed in a complete bony cavity, except where the periosteum closes over the ends of the slot. A wall of new cancellous bone shuts out the medullary cavity.

Thus in a growing puppy no bone developed from the reflected periosteum over the wax, while the remainder of the bone thickened. The suggestion that the paraffin prevented the periosteum from producing bone must be considered, but it is interesting to note that the paraffin does not prevent the endosteum from producing bone on its surface.

*Exp. 6, Dec. 14, 1912.*—Bull puppy, age two months. Weight  $2\frac{1}{2}$  kilos. Radius exposed and periosteum raised from the circumference of the middle of the shaft over an area 1 in. long. A silver wire was passed around the bone in the denuded area and drawn tight, and the ends twisted. A quarter of an inch away from the wire a sheet of tin-foil,  $\frac{1}{2}$  in. wide, was wrapped around the bone, and the periosteum was sewn over wire and foil.

April 2, 1913.—Specimen recovered. Animal's weight, 5 kilos. No new bone between periosteum and foil or between the periosteum and wire. The wire lies in a distinct groove in the bone, almost as deep as the thickness of the wire. The wire is no longer tight, but is slightly loose. The shaft of the radius has thickened about twice the diameter of the wire, and it has thickened as much in the area covered by tin-foil as it has elsewhere.

The findings corroborate Macewen's modification of Duhamel's experiment, and show the fallacy of the deduction that the increase in thickness of growing bones is due to the periosteum.

*Exp. 7, Feb. 20, 1913.*—Fox terrier puppy, four months old. Sixth rib exposed, periosteum reflected, and 1 cm. of the bone removed. Periosteal tube closed with catgut.

April 14.—Specimen recovered. Union of the cut ends of the rib solid, with much bony thickening in the area. Periosteum very adherent to the new bone.

Microscopical examination shows the space between the ends of the rib to have been reduced to about half a centimetre. The ends of the fragments are much rarefied, and the space is filled with spongy new bone, covered with normal periosteum, under which are many free osteoblasts.

*Exp. 8, Feb. 20, 1913.*—Same animal. Seventh rib exposed and one inch of rib removed subperiosteally. The ends of the cut rib were then covered with tin-foil, which was tied in place with a silk ligature. The periosteal tube was then closed with fine catgut.

April 14.—Specimen recovered. Ends of ribs have closed together until only half an inch intervenes. The space is filled with white fibrous tissue in which are several small nodules of new bone. The tips of the rib under the foil are quite white and hard and evidently dead. No union.

Histological examination shows the tips of the rib to be dead, but with restored circulation. The dead bone is being absorbed and replaced, as described in *Exps. 37, 38, 39, and 40*. The nodules in the periosteal tube are composed of new bone. The remainder of the space between the tips of the rib is filled with scar-tissue.

*Exp. 9, Feb. 25, 1913.*—Collie puppy, six months old. Radius exposed and sectioned transversely near its middle with a saw. A steel plate was then nailed to the fragments outside the periosteum, cobbler's wire nails being driven into drill-holes. Muscles and skin closed over plate with catgut. Plaster-of-Paris bandage applied.

March 12.—Plaster removed. X-ray shows plate and bones in correct position and union commencing.

May 27.—Specimen recovered. Union firm. Plate and bones in same position as after operation. Over the plate are several layers of loose areolar tissue, which allow the muscles and tendons to slip freely over it. Under the areolar tissue is a dense layer of fibrous tissue completely surrounding the plate. When this was reflected, the plate was found firmly fastened in position, the nails

being slightly looser than when inserted. The periosteum is thickened and adherent to the bone for  $\frac{1}{2}$  in. on either side of the fracture. The bone is slightly thickened in this area.

The specimen was sectioned longitudinally, and microscopical examination showed solid bony union and some new subperiosteal bone for  $\frac{1}{4}$  in. on either side of the fracture.

*Exp. 10, March 17, 1913*.—Adult terrier. Radius exposed; periosteum elevated to allow application of a steel plate. Bone sectioned at about the middle of the shaft with a saw. Plate applied and nails driven into drill-holes. Periosteum sewn over plate. Wound closed and covered with firm bandage without a splint.

June 10.—Specimen recovered. Union solid. Bone considerably thickened about the site of fracture, particularly on either side of the plate. There is no new bone between the periosteum and the plate, except that opposite the saw-cut the new bone has grown up and has spread slightly over the edges of the plate, firmly clamping it down. The nails are still firmly fixed in the holes. Surrounding the plate, and completely separating it from the bone, is a fibrous sheath which has developed since the operation.

*Exp. 11, April 4, 1913*.—Terrier puppy. Weight 6 kilos. A rib exposed and periosteum reflected, and a section of rib  $1\frac{1}{2}$  in. long removed. The periosteum was then sewn up in the form of a tube with No. 0 catgut. The tube was closed over the cut ends of the fragments by purse-string sutures of catgut, catching up the inside of the periosteal tube.

June 17.—Specimen recovered. Weight of animal 7 kilos. The space between the ends of the fragments is now only  $\frac{3}{8}$  in., due to collapse of the rib and growth from the ends. The space is filled with white scar-tissue to which the periosteal tube is very adherent. No new bone in this scar.

Microscopical examination showed no new bone in the closed periosteal tube.

*Exp. 12, April 4, 1913*.—Same animal. A section of rib,  $1\frac{1}{2}$  in. long, removed subperiosteally. The bone removed in *Exp. 11* was cut into a series of sections about  $\frac{1}{4}$  in. long and laid in the periosteal tube, and the tube closed with catgut.

June 17.—Specimen recovered. Rib solid throughout and normal in outline, except that in the region of the multiple grafts it is nodular. The periosteum in this area is densely adherent. The point of union of the ends of the fragments with the grafts is considerably thickened. Histological examination of a longitudinal section of the area of the multiple grafts and the ends of the fragments shows the periosteal tube to be filled with cancellous new bone of very irregular arrangement, with an occasional small piece of bone in which the bone-cells are absent from the lacunæ. The ends of the fragments are thickened by layers of new bone under the periosteum, and have themselves undergone marked osteoporosis. The continuity of the bony trabeculæ is complete throughout the specimen.

#### TRANSPLANTATION OF BONE INTO MUSCLE.

*Exp. 13.—One-week autogenous graft in muscle, with periosteum undisturbed.*

March 20, 1913.—Adult terrier. Radius exposed and a section of bone,  $\frac{1}{4}$  in. long and half the thickness of the radius, removed, with the periosteum undisturbed. This graft was buried in a neighbouring muscle.

March 27.—Specimen recovered. Small block of the muscle containing the bone removed, and the whole divided down the middle with a knife and hammer. Sections cut from the exposed surface for microscopical study.

In the gross the bone appears abnormally white. Surrounding it on all sides is a fibrous-tissue capsule, moderately adherent, particularly so on the periosteal side. Examined microscopically the periosteum appears normal, except that it is slightly thickened and a little more cellular than usual. It is attached to the bone by the normal reticulum. In this reticulum are a few osteoblasts, possibly in slightly greater numbers than are found under the periosteum in adult animals. On the medullary side is an ordinary granulation tissue, adherent to the bone. The whole is covered with the newly-formed capsule mentioned above. At the ends this granulation tissue and fibrous capsule are present also, but not so adherent as on the superficial and deep surfaces. On all sides, wherever an open Haversian canal is cut, this granulation tissue extends a short distance into the bone, and a few large cells which look like osteoblasts are lying along its edges. The bone is evidently necrotic, the blood-vessels and cellular tissues in the Haversian canals being coagulated and staining poorly. The cells in the lacunæ are shrunken and stain poorly also.

*Exp. 14.—One-week autogenous graft in muscle, with periosteum removed.*

March 29, 1913.—Same animal. A section of the radius,  $\frac{1}{4}$  in. long and half the thickness of the bone, removed subperiosteally and buried in a neighbouring muscle.

March 27.—Specimen recovered. Both in the gross and microscopically this specimen resembles that in *Exp. 13*, except that no periosteum is present, and its place is taken by a

*Exp. 15.—One-week heterogenous graft in muscle, with periosteum intact.*

March 25, 1913.—Adult terrier. A cat anaesthetized and a section of tibia removed,  $\frac{1}{2}$  in. long, and consisting of half the thickness of the bone, the periosteum remaining intact. This was buried in the muscles of the dog's back.

April 2.—Specimen recovered. The whole of the bone and periosteum is necrotic. Surrounding the specimen is granulation tissue and a thin fibrous capsule similar to the one described above. This granulation tissue enters the mouths of the open Haversian canals.

*Exp. 16.—Thirteen-days autogenous graft in muscle, with periosteum intact.*

April 6, 1913.—Adult terrier. Section of the middle third of the radius,  $\frac{1}{4}$  in. long, and consisting of half the thickness of the bone, removed, with the periosteum intact, and buried in a neighbouring muscle.

April 19.—Specimen recovered and sectioned as in *Exp. 15*.

In the gross the bone is seen to be surrounded by a fibrous tissue capsule, firmly adherent on all surfaces. The bone is pink.

Histologically the periosteum appears slightly thickened, but otherwise normal. Underneath the periosteum there is marked proliferation of osteoblasts. The whole reticulum is filled with these cells, and here and there they can be seen to be laying down new bone on the graft and building up trabeculae which extend irregularly outward towards the periosteum. In other places, groups of osteoblasts are seen occupying cavities in the surface of the bone, the cells being arranged in a row against the wall of the cavity, each cell occupying a small cavity slightly larger than itself. Evidently these cells are engaged in absorption of bone. In some of these excavations new bone is being laid down on the surfaces. Numerous blood-vessels are ramifying in the reticulum and entering the old Haversian canals and new-formed cavities. Along with these blood-vessels are large groups of proliferating osteoblasts which are engaged in absorbing the walls of the canals, in the same way as on the surface, and laying down new bone.

On the medullary side of the graft the fibrous-tissue capsule mentioned above closely resembles normal periosteum. Beneath this capsule exactly the same changes are occurring as under the periosteum, namely proliferation of osteoblasts, absorption of the surface of the graft, laying down of new bone on the surface and in the loose connective tissue adjacent to it, ramification of new blood-vessels, and the spreading of these blood-vessels along with masses of osteoblasts into the open Haversian canals.

The ends of the graft are covered with the fibrous capsule, which is loosely adherent as compared with the tissue over the superficial and deep surfaces. Under the capsule the same processes are occurring as on the surfaces, but the osteoblasts are very few in number, and absorption and new bone formation are difficult to find. New blood-vessels are freely entering all openings into the bone.

The bone itself is definitely necrotic. The cells in the lacunae are much shrunken and in places have disappeared. The others stain very dimly. Near the ends and surfaces the circulation has been re-established, and the coagulated tissue has been absorbed. At the most advanced edge of the re-established circulation the canals are occupied by blood-vessels only, but halfway between the advanced edge and the surface, groups of osteoblasts can be seen absorbing the walls and laying down new bone upon them. In the central portions of the graft, necrotic cellular tissues and blood-vessels still occupy the canals.

*Exp. 17.—Thirteen-days autogenous graft in muscle, with periosteum removed.*

April 6, 1913.—Same animal. Section of radius,  $\frac{1}{4}$  in. long and half the thickness of the bone, removed subperiosteally and buried in a neighbouring muscle.

April 19.—Specimen recovered. The gross and histological findings are identical with those of the last experiment, except that on the periosteal side the newly formed fibrous tissue capsule is not so closely attached to the bone as was the periosteum which was transplanted with the graft in *Exp. 16*.

*Exp. 18.—Thirteen-days heterogenous implant in muscle, with periosteum intact.*

April 6, 1913.—Same animal. A piece of the tibia of a cat removed, with periosteum intact, as in *Exp. 15*, and buried in the muscles of the dog's leg.

April 19.—Specimen recovered. Bone found surrounded by a fibrous-tissue capsule, adherent, but not so closely as in *Exps. 16* and *17*. Within this capsule is a mass of proliferating connective-tissue cells and new blood-vessels which are entering the open Haversian canals in the bone. No evidence of osteoblasts or of bone absorption or bone production on any of the surfaces. The bone is quite necrotic, the only evidence of cells in the lacunae being the shrunken nuclei. The circulation has been re-established in the borders of the implant as in the case of *Exps. 16* and *17*. No signs of absorption or new bone formation.

*Exp. 19.—Thirteen-days boiled implant in muscle.*

April 6, 1913.—Same animal. Small piece of bone removed from radius subperiosteally and buried in a neighbouring muscle after being boiled for five minutes.

April 19.—Specimen recovered. The piece of bone is lying in a fibrous-tissue capsule which is slightly adherent. The firmness of the adhesion is much less than in the case of the unboiled autogenous graft.

Examined microscopically, the capsule is similar to that in the preceding experiment, and the circulation is being re-established in the same way. There is no evidence of absorption or new bone formation.

**Exp. 20.—Three-weeks autogenous graft in muscle, with periosteum intact.**

Dec. 21, 1915.—Terrier dog. Middle third of radius exposed and a section of bone,  $\frac{1}{4}$  in. long and about the same width, removed, without disturbing the periosteum, and buried in a muscle.

Jan. 12, 1916. Specimen recovered. The bone is surrounded by a strong fibrous capsule, firmly adherent on all sides. The sectioned bone is pink and decidedly more porous than when imbedded.

Examined histologically, the periosteum appears normal. It is now continuous with the fibrous-tissue capsule covering the ends and the medullary side of the graft. This capsule is more open and irregular in the arrangement of its fibres than the periosteum, and not so closely laid down on the bone. Beneath it is a more open and delicate reticulum, and it is less firmly adherent.

On all the exposed surfaces of the bone, absorption by masses of osteoblasts is very evident. This is more marked on the periosteal and medullary surfaces, but is present at the ends as well. At intervals along these surfaces are irregularly shaped giant cells, each containing from three to six irregularly placed nuclei. These cells each occupy a pocket in the surface of the bone, which they have produced apparently by absorption. On the surfaces, also, new bone is being laid down by the osteoblasts. This appears to be about equal on the periosteal and medullary sides, and less marked at the ends. Under the periosteum it is laid down mostly as flat layers on the surface of the graft, but on the medullary side it is more irregular and extends into the areolar tissue in the form of trabeculae.

Within the graft itself the peripheral eighth of an inch is now decidedly porous and the spaces are filled with blood-vessels, areolar connective tissues, and masses of osteoblasts, which are engaged in enlarging the cavities and laying down new bone. An occasional giant cell occurs here as on the surfaces. The central portion of the graft is of about the same density as when imbedded. The larger canals now have a re-established circulation, and along with the blood-vessels are a few osteoblasts. The cells in the lacunae have largely disappeared, although in places the dim outline of the shrunken nucleus can still be made out.

**Exp. 21.—Three-weeks autogenous graft in muscle, after removal of periosteum.**

Dec. 21, 1915.—Same animal. Section of bone, similar to that in *Exp. 20*, imbedded in muscle after removal of the periosteum.

Jan. 12, 1916.—Specimen recovered. In the gross and histologically the findings resemble those in the preceding experiment, except that the normal fibrous periosteum is absent, and its place is taken by a more irregular newly-formed fibrous-tissue capsule. The same degree of absorption and new bone formation is taking place on the periosteal side as when the periosteum was transplanted with the bone. (*Figs. 238, 239, 240.*)

**Exp. 22.—Three-weeks heterogenous implant in muscle, without periosteum.**

Dec. 21, 1915.—Same animal. A section of a cat's bone removed subperiosteally and imbedded in the dog's muscles.

Jan. 12, 1916.—Specimen recovered. A strong fibrous-tissue capsule surrounds the bone and is adherent to it, although not so firmly as in the two preceding experiments. There is no evidence of absorption or new bone formation anywhere. No cells resembling osteoblasts can be seen. The circulation is re-established through the whole bone, but the canals are not enlarged perceptibly and the bone appears as dense as when inserted.

**Exp. 23.—Three-weeks boiled implant in muscle.**

Dec. 21, 1915.—Same animal. A section of bone similar to that in *Exp. 20* removed subperiosteally, and boiled for five minutes and imbedded in a muscle.

Jan. 12, 1916.—Specimen recovered. Surrounding the implant is a fibrous-tissue capsule which is loosely adherent to the bone. Examined microscopically the capsule is similar to that surrounding the other implants, but is much more loosely adherent. The bone is necrotic throughout, and the cells have mostly disappeared from the lacunae. All evidence of necrotic cellular tissue has disappeared from the larger Haversian canals, but is still visible in the smaller canals. In the larger canals a circulation which enters from the fibrous-tissue capsule has been re-established, and along with the blood-vessels is a cellular connective tissue. There is no evidence of osteoblasts or of bone-cell activity.

**Exp. 24.—Five-weeks autogenous graft in muscle, with periosteum intact.**

March 17, 1915.—Adult terrier. Radius exposed in its middle third and a section of bone removed with its periosteum, about half an inch long and half the thickness of the shaft. This was implanted in a muscle.

April 20.—Specimen recovered. Capsule dense and firmly adherent. Specimen decidedly more porous than when inserted. On all surfaces and in the newly formed spaces in the bone, absorption is far in advance of replacement. The bone-cells have completely disappeared from the lacunæ of the dead bone. The picture is identical with that described in *Exp.* 20, except that the changes are more advanced. (*Fig.* 241.)

***Exp.* 25.—Five weeks autogenous graft in muscle, without periosteum.**

March 17, 1915.—Same animal. A section of bone similar to that described in the previous experiment removed subperiosteally and buried in muscle.

April 20, 1915.—Specimen recovered. In all respects this specimen is similar to that just described.

***Exp.* 26. — Thirteen-days autogenous graft of cancellous bone in muscle, with periosteum intact.**

April 6, 1913.—Adult terrier. Same animal as in *Exp.* 16. Section of bone,  $\frac{1}{4}$  in. long, with the periosteum intact, removed from the radius close to one extremity. Here the bone was cancellous in structure as compared with the graft in *Exp.* 16.

April 19.—Specimen recovered. The gross and histological appearances of this specimen resemble those in *Exp.* 16, with the exception that the circulation is re-established throughout the graft, and proliferating osteoblasts are evident at a much greater distance from the surfaces, particularly in the larger spaces. These osteoblasts have evidently been able to obtain a supply of lymph, owing to the open texture of the bone. Deep in the specimen the same commencing absorption and new bone formation, as described on the surfaces of specimen 16, is resulting from the activity of these cells. The old bone of the graft is necrotic as already described.

***Exp.* 27.—Five-weeks autogenous cancellous graft in muscle, with periosteum intact.**

March 17, 1915.—Adult terrier. Same animal as in *Exp.* 26. Section of bone removed from the radius close to its extremity, with its periosteum, and buried in muscle.

April 20.—Specimen recovered. When compared with the specimen in *Exp.* 24, the gross and microscopical appearances are similar, except that all the changes are more advanced. The old structure of the graft is now no longer apparent, and the dead bone appears as isolated masses completely surrounded by blood-vessels, connective tissue, osteoblasts, and newly-formed cancellous bone. Absorption is much in advance of replacement.

The explanation of the greater progress made by the osteoblasts in this experiment rests on three factors. These are, first, the fact that there is less bone in the graft owing to its cancellous character; second, the open character of the graft made it possible for an early extensive invasion of the bone from the surface by the osteoblasts which accompany the blood-vessels; and, third, the open character of the bone allowed of a sufficient filtration of lymph from the surfaces of the graft to assure the survival of large numbers of osteoblasts already living in the Haversian canals and cancellous spaces of the bone.

The conclusion to be drawn from these last two experiments is that cancellous bone, when used as a graft, shows much earlier and greater activity than dense bone, but it is absorbed much more quickly and, after six or seven weeks, becomes very fragile.

***Exp.* 28.—Seven-weeks autogenous grafts placed in contact in muscle.**

Dec. 14, 1914.—Adult terrier. A section of the radius,  $\frac{1}{4}$  in. long, removed subperiosteally, including both periosteal and endosteal surfaces, and divided into four equal portions. Each piece formed a cube, the sides of which measured about  $\frac{1}{8}$  in. These were buried in contact with each other in a muscle.

Jan. 29, 1915.—Specimens recovered. The mass of bone was surrounded by a dense, adherent fibrous-tissue capsule as already described. The specimen now consisted of a single irregular mass of bone, the fragments being firmly united. Microscopical examination showed a picture similar to that already described in single autogenous grafts of the same age, except that the amount of osteoblastic activity is increased by the fragmentation, and greater progress has been made towards the absorption of the dead bone. The mass consists of a very irregular arrangement of new cancellous bone, surrounding and uniting the necrotic grafts. The dead bone is being attacked on the surfaces and in the interior from the canals, in the usual manner.

The increase of the rapidity of the changes is explained by the greater exposure of surfaces to the bathing lymph, and hence the preservation of larger numbers of living osteoblasts. The grafts being smaller also, the osteoblasts are able to reach all parts of the bone more readily.

***Exp.* 29.—Eleven-weeks fragmented autogenous grafts in muscle.**

April 4, 1913.—Terrier puppy. Same animal as in *Exp.* 11. A rib exposed and the periosteum reflected, and a section of bone  $1\frac{3}{8}$  in. long removed. This was cut into segments about  $\frac{1}{8}$  in. long, and buried in one mass in muscle.

June 17.—Specimen recovered. The bony fragments were found encapsulated in a dense adherent fibrous capsule. The mass is half its original size, and the particles are all solidly united.

Microscopical examination shows the mass to be composed of an irregular arrangement of

trabeculae of new bone, surrounded at the periphery by a thin, more or less continuous, layer of new bone, through which are many openings for blood-vessels from the capsule. The trabeculae and the outside layer of bone are surrounded on all sides by living osteoblasts. At irregular intervals can be found small particles of the original grafts in which the cells are absent from the lacunae, but absorption of the dead bone is very nearly complete.

**Exp. 30.—Nine-weeks fragmented autogenous grafts in muscle.**

April 14, 1913.—Adult bull terrier. Section of rib removed subperiosteally and broken into several fragments. These were buried in muscle and in contact with one another.

June 17.—Specimen recovered. Is now consists of a single, irregular mass of bone, about half the size of the original fragments, surrounded by a fibrous-tissue capsule which is closely adherent. Microscopical examination shows the mass to consist of irregular trabeculae of new cancellous bone, with no signs of the original graft. The latter has evidently been completely absorbed.

**Exp. 31.—Ten-weeks autogenous fragmented grafts in muscle.**

Nov. 13, 1913.—Adult hound. Same animal as in *Exp. 4*. Six small fragments of a segment of the radius removed subperiosteally and buried in muscle. The whole made a mass about the size of a pea.

Jan. 23, 1913.—Specimen recovered. No trace of these fragments of bone could be found, only a small scar marking the place where they had been inserted.

The result of this experiment is in marked contrast to what may be expected when the transplanted bone has a function to perform.

**AUTOGENOUS GRAFTS PLACED IN CONTACT WITH LIVING BONE.**

**Exp. 32.—Six-days autogenous graft.**

March 20, 1913.—Spaniel pup, age 4 months. Radius exposed and periosteum reflected over half the circumference of the middle of the bone for a distance of  $2\frac{1}{2}$  in. A wedge-shaped piece of bone was then cut from the radius,  $3\frac{1}{4}$  in. long, by two saw-cuts, one of which extended transversely half-way through the radius, and the other passed obliquely from the surface to the deep end of the transverse cut. The graft was then replaced in its bed and the periosteum stitched over it.

March 26.—Specimen recovered. Graft in perfect position. Periosteum intact and weakly adherent to both radius and graft. The graft is firmly adherent to its bed, and remained in position while being sectioned longitudinally with a circular saw attached to a lathe. At the edges is a soft material, filling the saw-cuts and projecting slightly from the surface, resembling granulation tissue.

After decalcification the sections were cut from the surface exposed by the circular saw.

Microscopical examination shows conditions as follows:—

1. The periosteum which had been reflected is normal, except that it is slightly thickened.
2. The subperiosteal area is much more cellular than normal, and contains many new blood-vessels, thus forming a granulation tissue. On the surface of the bone, osteoblasts can be seen in normal or slightly increased numbers.
3. Wherever Haversian canals open into the bone, the granulation tissue extends inward for a short distance, and a few osteoblasts can be seen along with the blood-vessels.
4. The medullary surface is covered by typical granulation tissue which is adherent to the bone and enters all large openings. Along the edge of the bone and in the mouth of the Haversian canals a few osteoblasts can be seen.
5. The graft itself is definitely necrotic. The cellular tissue and blood-vessels in the canals are coagulated, and the cells in the lacunae are shrunken and stain dimly.
6. The saw-cuts are filled with granulation tissue, similar to that on the medullary surface, and it is quite evident that this tissue has flowed out from the interior of the bone which surrounds the graft.
7. The ends of the radius adjacent to the saw-cuts are in a condition very similar to that of the graft. The periosteum which had been reflected is thickened, and the subperiosteal osteoblasts are beginning to proliferate. A similar condition is present on the medullary side. The blood-vessels in the canals near the ends are coagulated, and the cells in the lacunae stain poorly and appear shrunken. As the sections are examined further from the saw-cuts, these changes disappear.
8. There is no sign of new bone formation anywhere.

**Exp. 33.—Eight-days autogenous graft of cancellous bone.**

April 30, 1914.—Adult fox terrier. A section of half the thickness of the shaft of the radius,  $\frac{1}{8}$  in. long, removed subperiosteally and immediately replaced in its bed. The periosteum was stitched over it. This graft was composed of cancellous bone from near one extremity of the shaft.

May 8.—Specimen recovered. The graft was in correct position and adherent, but not sufficiently so to stand the application of the saw. The periosteum was loosely attached. The

specimen was placed in 10 per cent formalin for a few days, and then decalcified in phloroglucin and nitric acid. It was then split down the middle with a knife, and the sections cut from the exposed surface.

Histologically these sections exactly resemble those in the preceding experiment, except that there are more osteoblasts on the surfaces and in the mouths of the Haversian canals, and the circulation has advanced further into the graft. On the medullary side in the granulation tissue are many osteoblasts, which in some places are engaged in excavating cavities in the surface of the bone, and in others in building up trabeculae of new cancellous bone. In some places these trabeculae are attached to the graft by their extremities, and in others are laid horizontally on its surface. A general view of the section shows this new bone formation to be much more extensive at a little distance from the graft, and it is evidently resulting largely from the activity of cells derived from the bed in which the graft lies. The saw-cuts are filled with granulation tissue in which are many osteoblasts but no new bone. This tissue is not adherent to the ends of the graft except where there are large openings into it, and it appears to be flowing out from the medullary cavity.

*Exp. 34.—Two-weeks autogenous graft.*

March 22, 1913.—Adult spaniel. A wedge-shaped graft removed subperiosteally from the middle of the shaft, as in *Exp. 32*, and immediately replaced in its bed and covered with periosteum.

April 5.—Specimen recovered. The graft is much more firmly adherent to its bed than in the two previous experiments. The periosteum is also more adherent to both the graft and the surrounding bone, but particularly adherent to the tissue in the saw-cuts.

Microscopical examination shows the periosteum considerably thickened and more cellular than normal. Under the periosteum there is marked proliferation of osteoblasts, with, here and there, small newly-formed excavations in the surface of the bone filled with these cells. In a few places new bone is being laid down by these cells both on the surface and as trabeculae arranged at an angle to the surface. Many new blood-vessels are ramifying in this area and entering the old Haversian canals. On the medullary surface there is an enormous proliferation of osteoblasts and the same commencing formation of excavations at intervals along the bone. On the surface of the graft, and in the granulation tissue beneath it, is a great production of new cancellous bone, and this extends out into the saw-cuts. This new tissue in the saw-cuts is only slightly adherent to the ends of the bone, and is quite evidently produced by migration from the medullary tissue. On the deep surfaces, and at the ends, new blood-vessels are entering all open Haversian canals. Along with these vessels are swarms of osteoblasts, and, for a short distance into the bone, the same commencing absorption of the graft and laying down of new bone can be detected. The new blood-vessels have advanced considerably further into the bone than the osteoblasts, and many Haversian canals close to the surface, which have been cut transversely, show new blood-vessels without any evidence of osteoblasts. Deeper in the bone the Haversian canals are empty or contain faintly-staining necrotic tissue. All the cells in the lacunae are shrunken, and stain dimly or have completely disappeared.

The amount of osteoblastic activity in the form of bone absorption and new bone formation on the medullary side of the graft is much greater than on the periosteal side, and, remembering that in the grafts which are transplanted into muscle the activity of these cells was equal on the two sides, one must conclude that the increased activity arises from the cells from the living bone of the bed.

Compared with the absorption and new bone formation on the periosteal and medullary surfaces, the changes at the ends of the graft are slight.

The condition in the ends of the living bone closely resembles that in the graft. These areas are undergoing a simple rarefying osteitis as in any ordinary fracture. The cells have disappeared from irregular patches of this bone close to the ends and under the reflected periosteum. On the periosteal and medullary surfaces marked absorption is going on, and new bone is being laid down. These processes are considerably in advance of the same processes in the graft.

*Exp. 35.—Eighteen-days autogenous graft.*

April 30, 1914.—Terrier puppy. A section of half the thickness of the middle of the radius,  $\frac{1}{2}$  in. long, removed subperiosteally and immediately replaced in its bed. The periosteum was sewn over it.

May 18.—Specimen recovered. Graft firmly in place and stood sectioning with the circular saw. The periosteum is moderately adherent to the graft and firmly adherent to the material in the saw-cuts.

Microscopical examination shows the same processes more advanced than in the previous experiment. Under the periosteum there is more evidence of cavity formation and more production of new bone. On the medullary side the whole medullary cavity is filled with newly-formed cancellous tissue, which is firmly united to the graft by trabeculae laid flat on the surface and at an angle to it. On this surface are many cavities filled with osteoblasts which are engaged in absorption. The saw-cuts at the ends are filled with osteoblasts and blood-vessels, but there is little evidence of adhesion of this tissue to the graft or of absorption or new bone formation, except in the deepest part. The circulation is re-established in all the larger canals throughout the graft,

but the smaller ones are still empty or contain faintly-staining necrotic tissue. The osteoblasts have advanced considerably further into the bone, and have commenced the same absorption and new bone formation on the walls of the canals as on the surfaces. The cells in the lacunæ are disappearing. In the ends of the radius adjacent to the saw-cuts the rarefying osteitis is advancing.

*Exp. 36.—Three-weeks autogenous graft.*

March 25, 1913.—Adult fox terrier. A wedge-shaped section of bone,  $\frac{1}{2}$  in. long, and reaching to the centre of the shaft, removed subperiosteally from the middle of the radius. The graft was immediately placed in its bed and the periosteum sewn over it.

April 14.—Specimen recovered. This specimen is the most important of the series, as it shows most perfectly all the changes which occur in a bone graft.

Examined in the gross the graft is found to be firmly united to the radius. The periosteum is thickened and about normally adherent to the graft, but more firmly adherent to the callus in the saw-cuts. This callus is now firm, but is easily crushed. It is distinctly calcareous.

The specimen was split longitudinally with the circular saw, and after decalcification the sections were cut from the exposed surface.

Examined histologically the periosteum is thickened and cellular. On the surface of the bone is a layer of new cancellous tissue. In the spaces between the trabeculae and under the periosteum are swarms of osteoblasts engaged in new bone formation. At intervals on the surface of the graft small excavations are being produced by groups of osteoblasts whose function is absorption. In these cavities the cells are arranged in a row against the walls of the cavity, each cell occupying a small cavity slightly larger than itself. Wherever openings occur into the bone, blood-vessels are entering freely, and along with them are crowds of osteoblasts which are engaged in absorbing the walls of the canals.

On the medullary side of the graft the whole medullary cavity is filled with new cancellous bone which is firmly adherent to the graft. Here the same process of absorption is in progress as on the periosteal side, but is much further advanced. Great excavations, four or five times as deep as they are wide, have been made directly into the bone, and the deepest portions of these cavities are lined with the row of osteoblasts described above, with an occasional giant cell. At the neck of the excavation these cells have resumed their adult function of bone production, and the walls of the cavities are covered with layers of new bone. The openings into some of the cavities are completely filled with new cancellous tissue. (*Figs. 242, 243, 244.*)

In the graft itself the circulation has been re-established throughout, even the smallest canals containing blood-vessels. Except in the smaller canals these blood-vessels are accompanied by proliferating osteoblasts which are engaged in absorption, as described on the surfaces. In the large Haversian canals cut transversely near the surfaces, these cells are also engaged in covering the walls with new bone. The cells in the old lacunæ have completely disappeared, except for an occasional shrunken nucleus.

In the saw-cuts the space is filled with proliferating osteoblasts, and the granulation tissue is adherent to the ends of the bones. The same process of absorption is commencing on the cut surface and in the mouths of the canals, and the osteoblasts are laying down new bone on the ends. The deep part of this space is filled with cancellous bone which is continuous with that in the medullary cavity, but the superficial part contains no new bone. This latter area is filled with proliferating osteoblasts and fibrous tissue which is continuous with the periosteum.

The ends of the living bone are now in a decided condition of rarefaction. The old and new canals have become enlarged and irregular, and are filled with osteoblasts engaged principally in absorption, although some formation of new bone is going on. The absorption involves both necrotic and living bone. The living bone of the bed is now much more porous than the graft. (*Figs. 242, 243, and 244.*)

*Exp. 37.—Five-weeks autogenous graft.*

March 17, 1915.—Adult terrier. A section of half the thickness of the middle of the shaft of the radius,  $\frac{1}{2}$  in. long, removed with the periosteum intact, and immediately replaced in its bed and fastened securely with catgut ligatures passed through drill-holes in the shaft. The ends of the graft were marked with a strand of fine silk, laid in the saw-cut.

April 20.—Specimen recovered. The graft is solidly united to its bed, and the saw-cuts are indistinguishable. The periosteum is normally adherent and somewhat thickened. The specimen was sectioned longitudinally with the circular saw, and after decalcification the sections were cut from the exposed surface.

Histological examination shows a more advanced stage of the condition described in the previous experiment. The periosteum is somewhat thickened and a little more cellular than normal. The surface of the graft is covered with new cancellous bone, and in this are crowds of osteoblasts building new bone and absorbing the dead graft. The trabeculae are much thicker than in the three-weeks specimen. The graft is solidly united to its bed, both at the ends and on the medullary side, by strong trabeculae of cancellous new bone. The saw-cuts are completely filled with this cancellous tissue.

The graft itself has become very porous as a result of the predominance of absorption over replacement. The dead bone now appears to be cut into numerous isolated islands by the branch-



ing cavities. Examination of serial sections shows that this is a mistake, however, as the dead bone has simply become spongy from the action of the invading osteoblasts. On the walls of the cavities throughout the graft new bone is being laid down. The quantity of this new bone is small, however, when compared with the amount of the dead bone that has been absorbed.

The ends of the bone of the bed are in the typical condition of rarefying osteitis seen in fractures at this stage.

**Exp. 38.—Six-weeks autogenous graft.**

Dec. 7, 1914.—Adult terrier. Section removed from radius as in previous experiments, with periosteum attached, and immediately replaced in its bed, the ends being marked with silk thread.

Jan. 22, 1915.—Specimen recovered and bone sectioned as usual. The graft can still be distinguished from the remainder of the bone, but it is distinctly porous. It is solidly united to its bed.

Microscopical examination shows progress in the absorption of the graft, with some replacement by new bone, particularly on the surfaces and ends. The central portions of the bone are becoming very porous, although not so markedly as in the previous experiment. The ends of the bone of the bed, on superficial examination, appear practically the same as the graft, that is, they are in a condition of rarefying osteitis, but they can be distinguished by the presence of cells in the lacunae. The saw-cuts are filled with cancellous bone, in which can be detected some cartilage. It has been observed throughout these experiments that when the saw-cut is narrow, and the contact good, union occurs by bony trabeculae only, whereas, if the saw-cut is wide, cartilage is apt to appear.

**Exp. 39.—Seven-weeks autogenous graft.**

Dec. 13, 1914.—Black-and-tan terrier. Operation performed as in previous experiment.

Jan. 30, 1915.—Specimen recovered. All the changes already described are present. The graft is becoming more porous, and the edges are becoming extensively invaded with new bone. This production of new bone is a real replacement, and does not produce a gross thickening of the graft. As a result of the invasion from both sides, the thickness of the dead bone, as compared with the original specimen, is much reduced. Throughout the transplant there is a small amount of new bone formation in the cavities, but the chief change is that of absorption.

**Exp. 40.—Ten-weeks autogenous graft.**

Jan. 13, 1913.—Spaniel puppy. Periosteum reflected from radius and a wedge-shaped graft removed, the saw-cuts extending to the medulla at one end. Ends marked with threads, and periosteum stitched over the graft.

March 26.—Specimen recovered and sectioned with saw. The graft can no longer be distinguished except by the presence of the threads.

Histological examination shows the area originally occupied by the graft still in a condition of rarefying osteitis, but the amount of new bone is increased, and the area is considerably less porous than in the seven-weeks graft. One has to search carefully for dead bone, as its place has been taken largely by irregular trabeculae of new cancellous tissue. The whole picture now suggests bone production rather than absorption, all the spaces being lined with living bone. Over the medullary and periosteal surfaces, and also at the ends, the edges of the graft have been completely replaced, and here the new bone shows a tendency to return to a compact structure with the lacunae compressed laterally and arranged in parallel rows. The rarefying osteitis in the ends of the bed has also subsided, and the bone is assuming the appearance of compact bone.

**Exp. 41.—Three-months autogenous graft.**

Nov. 27, 1914.—Adult bull terrier. Operation performed as above,  $\frac{3}{4}$  in. of bone being removed with the periosteum intact. Silk threads inserted to mark the ends.

Feb. 27, 1915.—Specimen recovered and sectioned with saw. The graft cannot be distinguished except by the threads. Except for an increase in the medullary cancellous tissue, the shaft of the radius appears normal.

Histological examination shows the area of the graft still slightly porous, but much less so than in the ten-weeks graft. The cancellous arrangement of the new bone within and without the graft has largely disappeared, and the bone is now laid down in lamellae as in compact bone. Here and there patches of dead bone can still be distinguished, but the general appearance of the section indicates a return to the normal structure of the shaft of a long bone. The saw-cuts are filled with ordinary lamellated bone, and the ends of the bed have largely lost the appearance of rarefying osteitis. The medullary cavity is still filled with cancellous bone in the region of the graft, but there is indication of re-establishment of the normal cavity near the opposite wall.

**Exp. 42.—Seven-weeks autogenous graft, without periosteum.**

Nov. 20, 1914.—Spines of vertebrae exposed as in Albee's operation, and a graft removed subperiosteally from the radius and inserted into two split spines and secured with kangaroo tendon.

Jan. 7, 1915.—Specimen recovered and sectioned longitudinally with a saw. The graft is

united to the spines, and is covered with an adherent fibrous membrane resembling periosteum. Midway between the spines the graft is about the same thickness as when inserted, but close to the point of contact with the spines it is thickened by the laying down of new bone on its surface. The result is that the graft and the two spines form an arch over the interspinous space.

Histologically examined, the bone is found to be in exactly the same condition as similar specimens of the same age implanted into bone or into muscles. The fibrous membrane covering the bone is indistinguishable from periosteum, and underneath it are osteoblasts and new bone. The same processes of absorption and replacement are going on.

**Exp. 43.—One-year autogenous graft, without periosteum.**

In January of 1914 we operated on a child 6 years of age, doing the spinal-graft operation for Pott's disease. The graft was the usual tibial transplant, removed subperiosteally. Eight weeks later one end of the graft, which had raised up slightly, showed a tendency to ulcerate through the skin. An anæsthetic was given and the projecting tip removed. The cut surface of the bone bled freely. The graft was solidly united to the spines and covered with an adherent fibrous membrane resembling periosteum. The case then progressed uneventfully, and the *x* rays taken at intervals of three months showed the gradual rarefaction of the bone until it ultimately had the same density as the spines, except at its superficial border, where it remained slightly denser than in its deeper area.

Eleven months later the child died of tuberculous meningitis, and the spine was secured at autopsy. The findings were reported in the *Journal of the American Orthopedic Association*, Feb., 1916. The spines were solidly locked together at their tips by a bar of bone which was composed of compact tissue on its superficial surface, and cancellous bone elsewhere. This bar of bone was covered with a fibrous membrane resembling periosteum. When the whole specimen was sectioned sagittally with a saw, it was seen that, for  $\frac{1}{4}$  in. on either side of the junction of the graft with the spines, the graft was much thickened on the deep side, so that the spaces between the spines were thus bridged by a series of Gothic arches. The density of the spines and of the graft was about equal, and the specimen gave the impression of a fusion of the spines, without any suggestion of the presence of a bone graft.

Histological examination of the piece of bone removed from the graft eight weeks after its implantation shows a complete re-establishment of the circulation, but no sign of osteoblastic activity in the area sectioned. The Haversian canals are occupied only by blood-vessels and areolar tissue. The bone is quite necrotic, and the cells have completely disappeared from the lacunæ. Unfortunately, the sections were cut on a horizontal plane, so that the periosteal surface could not be examined.

Examination of the autopsy specimen, recovered thirteen months after the operation, presents an entirely different picture. There is now no evidence of necrotic bone. On the surface is a normal periosteum, and under it the ordinary areolar tissue containing osteoblasts. On the surface of the bone these cells are very numerous, as on the surface of the rib in a young animal. The superficial layers of bone are fairly compact, and the lacunæ show a tendency to arrangement in parallel lines and to be flattened longitudinally, but there is still a good deal of irregularity of arrangement. The deeper areas of the bone form a typical cancellous tissue. The lacunæ contain living cells throughout. The point of junction of the graft and the spine is composed entirely of cancellous bone, and the sides of the Gothic arches are composed of the same tissue.

The study of this case demonstrated the similarity of changes occurring in bone transplanted for clinical purposes to those observed in experiments on animals.

**Exp. 44.—Six-weeks autogenous graft in which good contact was not secured.**

Dec. 14, 1914.—Adult terrier. The usual graft was cut from the middle of the shaft of the radius, with the periosteum intact, and replaced in its bed. It was fastened in place with catgut.

Jan. 29, 1915.—Specimen recovered. The graft has been displaced so that one end is overriding the end of the bed, and the other end is lifted up, so that the whole graft forms a distinct elevation on the surface of the bone. The whole is covered with periosteum, but union is not solid. When sectioned longitudinally the graft is seen to be free from the underlying bone. The medullary cavity is partially filled with cancellous tissue, but immediately under the graft this is deficient, as can be demonstrated by examination with a pin.

Microscopical examination shows the graft to be in exactly the same condition as a similar graft of the same age placed in the muscles. On its medullary surface new bone has been deposited, but the trabeculae are not continuous with those of the medullary cavity. Between the new bone of the graft and the cancellous tissue in the medullary cavity is an area filled with fibrous tissue. The ends of the graft are also covered with fibrous tissue.

The accident which occurred in this experiment demonstrates the importance of close contact between a graft and its bed, if early and solid union is to take place.

**Exp. 45.—Eight-weeks autogenous graft in which motion occurred at the point of junction with the normal bone.**

Nov. 2, 1912.—Adult terrier. Periosteum reflected from radius and a wedge-shaped piece of bone cut out,  $\frac{3}{4}$  in. long, and extending at one end to the centre of the medullary cavity. The

transverse saw-cut nearly severed the shaft. The graft was replaced in its bed, and the periosteum sutured over it.

Dec. 30.—Specimen recovered. A fracture has occurred at the site of the transverse saw-cut, an accident that was noted three weeks after the operation. Only fibrous union has resulted. The graft is firmly united in its bed, being solidly united by its deep surface to the fragment on which it lies. Its base abuts on the line of the non-union.

Histological examination shows that the graft is united on its deep surface to its bed by the usual cancellous bone. But at its base the saw-cut is filled with fibrous tissue and islands of new bone which are not continuous across the gap. The same histological picture which is ordinarily associated with non-union extends across the whole shaft in the line of fracture.

The solid union of the graft to the underlying bone in those areas in which no movement occurs between them is in marked contrast to the condition at the ends of the graft where movement occurred. The accident occurring in this experiment demonstrates the importance of complete immobilization of the graft and the fragments, even where perfect contact is provided, if one desires early and solid union.

#### THE TRANSPLANTATION OF BONE FROM ANIMALS OF A DIFFERENT SPECIES, AND PLACED IN CONTACT WITH LIVING BONE.

##### *Exp. 46.—Eight-days heterogenous graft.*

April 30, 1914.—Terrier puppy. Radius exposed, and a section of half the thickness of shaft,  $\frac{1}{2}$  in. long, removed subperiosteally. A cat was then anesthetized, and a section of bone of similar size removed subperiosteally, and placed in the radius of the dog. The periosteum was then sutured over it.

May 8.—Specimen recovered and placed in formalin for several days, and then in phloroglucin and nitric acid until decalcified. The specimen was then cut longitudinally with a knife, and the sections taken from the cut surface. This is admittedly a poor method of procedure, owing to the difficulty of properly fixing the specimen, but the amount of union of the graft to its bed would not allow of the application of a saw previous to decalcification.

The implant was weakly adherent to its bed, and covered with normal-looking periosteum which stripped very easily.

Histological examination shows the implant to be in a similar condition to bone of the same age buried in the dog's muscles. The bone is necrotic throughout, but the circulation is being re-established. On its outer surface is a normal periosteum under which there is no sign of osteoblasts, which is in contrast to the condition found in autogenous grafts of the same age. On the medullary side and in the saw-cuts the implant is in contact with granulation tissue similar to that described in autogenous grafts. This tissue contains cells resembling osteoblasts. The blood-vessels can be seen entering all openings into the bone.

##### *Exp. 47.—Eighteen-days heterogenous graft.*

April 30, 1914.—Terrier puppy. Same operation as in previous experiment.

May 18.—Specimen recovered. The implant is now firmly united to its bed, and the specimen was sectioned with a saw without disturbing the parts. The periosteum is slightly adherent, and the saw-cuts are filled with calcareous granulation tissue.

Histological examination shows the periosteum normal except for slight thickening. This membrane is laid flatly on the bone without the interposition of subperiosteal osteoblasts, and there is no sign of absorption or new bone formation. (*Fig. 237.*) The medullary surface, however, presents an appearance very similar to that seen in autogenous grafts. The bone is being invaded by crowds of osteoblasts which are producing excavations on the surface, and entering the bone along with the blood-vessels. On this surface trabeculae of new bone are being laid down which are continuous with the cancellous tissue of the medullary cavity. The saw-cuts are filled with granulation tissue, in which new bone is appearing in the deepest parts and is being laid down on the ends of the graft. The sections, in fact, when examined on the medullary surface alone, are exceedingly difficult to distinguish from the same surface of the autogenous graft in the same animal described in *Exp. 35.*

##### *Exp. 48.—Seven-weeks heterogenous graft.*

Jan. 30, 1913.—Spaniel puppy, three months old. Wedge-shaped piece of bone removed subperiosteally from the shaft of the radius, and replaced by a similar wedge removed subperiosteally from the radius of a kitten. The periosteum was then stitched over the implant.

March 18.—Specimen recovered. The implant is solidly united to its bed, and the periosteum firmly adherent over it. The surface of the graft has the same appearance as when inserted, and both this surface and the sectioned surface are much whiter than the surrounding bone. The bone in contact with the implant is decidedly rarefied.

Microscopical examination shows a normal periosteum under which are numerous giant cells lodged in small cavities in the surface of the bone. There is no evidence of new bone or osteoblasts under the periosteum, except at the edges of the implant and near the extremities, where the cells

have migrated from the saw-cuts. On the medullary surface and in the saw-cuts the implant is solidly united to cancellous new bone, as in the case of autogenous transplants. The circulation is re-established throughout the cat-bone. In the portion of the implant closest to the medullary cavity and the saw-cuts, the Haversian canals have been invaded by osteoblasts, and the bone is undergoing absorption. The same laying down of new bone as is seen in autogenous grafts is going on. In fact, it is only at the periosteal surface of the implant that this cat-bone can be distinguished from an autogenous transplant.

*Exp. 49.—Nine-weeks heterogenous graft.*

April 14, 1913.—Adult bull terrier. Two inches of a rib removed subperiosteally, and a piece of human bone, 2 in. long and  $\frac{1}{2}$  in. thick, which had been cut from a child's leg that had been amputated six hours before and kept sterile, laid in the periosteal tube, and the periosteum stitched over it. The periosteum has been removed from the implant.

June 17.—Specimen recovered. One end of the implant has cut through the periosteum, and half of the bone is outside the periosteal tube. The other half is still inside the tube. The continuity of the rib has been restored, so that the implant appears as a spur sticking obliquely out of a rib. This spur is covered with a fibrous membrane loosely adherent to the bone. The hidden portion of the implant is buried in new bone. The specimen was split longitudinally with a saw, and the sections were so cut that a portion of the implant, both inside and outside the periosteal tube, is shown.

In the gross, the solid union of the implant to the rib can be seen, and there is considerable rarefaction in the buried portion.

Microscopical examination shows the buried portion of the implant to be surrounded by cancellous new bone, which is solidly united to it. A complete circulation has been established, and the same invasion of the surfaces and of the Haversian canals by osteoblasts as described in autogenous grafts, has occurred. Throughout this portion of the bone, which was originally very dense compact bone from the crest of the tibia, the Haversian canals are being enlarged and the walls lined with new bone. All cells have disappeared from the lacunæ. Passing along the implant into the portion which is outside the periosteal tube, a marked difference is observed. The bone is covered with a fibrous-tissue sheath, resembling periosteum, from which blood-vessels pass into the old Haversian canals. Under this membrane are a few giant cells lying in cavities in the surface of the bone, but there is no sign of osteoblasts or of new bone formation. The bone is practically in the same condition as when it was inserted, except that a circulation is established. For about  $\frac{1}{4}$  in. beyond the periosteal tube of the rib the Haversian canals contain osteoblasts, and absorption and new bone formation, both in the canals and on the surfaces, can be seen, but beyond this distance there is no evidence of osteoblastic activity.

This experiment is therefore very valuable as showing the complete lack of participation of any living elements in heterogenous bone in the changes which occur when such material is used, as an implant into living bone. It also shows the very large part that is taken by the living bone of the bed, into which the implants are inserted, in bringing about the absorption and replacement of the dead bone of a graft. The only difference that can be observed between the changes in the buried portion of this implant and in an autogenous transplant of similar age is that in the former the process of absorption and replacement is two or three weeks slower.

#### THE IMPLANTATION OF BOILED INTO LIVING BONE.

*Exp. 50.—Eight-days boiled bone implant.*

April 30, 1914.—Terrier puppy. A section of half the thickness of the radius,  $\frac{1}{2}$  in. long, removed subperiosteally, and boiled for five minutes. It was then replaced in its bed and the periosteum closed over it.

May 8.—Specimen recovered. The periosteum was very slightly adherent to the implant, which was only loosely fixed in its bed. It was necessary to decalcify the specimen before sectioning it, for fear of displacing the loose bone.

Histological examination shows a condition practically the same as in *Exp. 33*, in which an unboiled autogenous graft was used. The periosteum is normal or slightly thickened, and a little more cellular than usual. On the medullary side the bone rests on granulation tissue which is entering the large Haversian canals. This granulation tissue is filled with osteoblasts engaged in absorbing cavities in the surface of the bone and in building trabeculae of new bone, which are being laid on the surface of the graft and filling the medullary cavity. Compared with the experiment in which unboiled autogenous bone was used, there is no practical difference in the appearances in this area. This conclusively demonstrates the importance of the cellular activity of the bed in the union of all grafts, whether they be autogenous, heterogenous, or boiled. In the bone itself the canals are occupied by coagulated blood-vessels, and not much progress has been made towards the re-establishment of the circulation, considerably less than in the autogenous graft in *Exp. 33*, but near the edges it is evident that a beginning has been made. The cells in the lacunæ stain quite well, probably owing to the boiling. The saw-cuts are filled with granulation tissue flowing out of the medullary cavity.

*Exp. 51.—Eighteen-days boiled implant.*

April 30, 1914.—Terrier puppy. Operation performed as in the last experiment.

May 18.—Specimen recovered. The implant was composed of very dense compact bone. The union is quite solid, and withstood sectioning with the circular saw. The periosteum is normal in appearance and loosely adherent.

Microscopical examination shows the periosteum normal or slightly thickened. It is loosely attached to the bone, and blood-vessels pass from it into any open canals. There is no sign of osteoblasts or new bone beneath it. On the deep side the medullary cavity is filled with new-formed cancellous bone, which is firmly laid down on the implant. Crowds of osteoblasts are busily engaged in creating excavations in the surface of the bone and in the Haversian canals close to the edge. The saw-cuts are filled with granulation tissue which contains osteoblasts but no new bone. This granulation tissue is not adherent to either the implant or the ends of the living bone, and is evidently streaming out of the medullary cavity. The bone-cells have disappeared from the lacunæ, but the smaller Haversian canals still contain necrotic tissue. In the larger canals a circulation has been re-established, and, close to the deep surface of the graft, these canals are filled with osteoblasts engaged in absorption, with occasionally a tendency to forming new bone.

Compared with the eighteen-days autogenous graft in the same animal (*Exp. 35*), the only difference that can be made out is that the processes of absorption and replacement have not made so much progress in the boiled implant. As far as these changes are concerned, this specimen is about in the condition of the ten-days autogenous graft.

*Exp. 52.—Three-weeks boiled implant.*

Dec. 21, 1915.—Adult terrier. A section of the middle of the shaft of the radius, 1 in. long, and half the thickness of the bone, removed subperiosteally and boiled for five minutes before being replaced in its bed. The periosteum was stitched over it.

Jan. 12, 1916.—Specimen recovered. While the implant is firmly held in position so that it withstood the sectioning with the circular saw, it is evidently not united by bone, as it is slightly movable. When the sections are viewed with the naked eye, the medullary cavity is seen to be filled with cancellous tissue, except in the immediate neighbourhood of the medullary surface of the implant. Here, for an eighth of an inch from the bone, no trabeculae can be seen, except at one end, where the implant is depressed somewhat into the medullary cavity; at this place the cancellous bone is in contact with the implant.

Viewed microscopically, the periosteum is thickened and loosely adherent. Blood-vessels pass from it into the bone. Under the membrane there is no sign of osteoblasts or of new bone. At intervals along the surfaces giant cells can be seen lying in small cavities, which they have produced by absorption. On the medullary side the implant is covered with white fibrous tissue, which is about  $\frac{1}{8}$  in. thick. From this fibrous tissue blood-vessels enter the Haversian canals of the implant. The same arrangement of giant cells can be seen here. At the depressed end of the implant, however, the cancellous new bone which fills the part of the medullary cavity not occupied by the fibrous tissue is in contact with and adherent to the implant, and here the osteoblasts are attacking the surfaces, and the walls of the Haversian canals, and laying down new bone. Throughout the remainder of the bone the circulation is re-established, but there is no sign of osteoblastic activity. The saw-cut at one end is filled with fibrous tissue, and at the other with new cancellous bone, which is attached to both the implant and the end of the bed.

*Failures of Union.*—This specimen, along with several others of a similar type, demonstrates the difference between boiled and unboiled autogenous bone, when used to fill gaps. In these experiments we have never observed a case of non-union in an autogenous transplant, whereas on several occasions boiled implants have failed to unite, except by fibrous tissue. A study of these failures of union shows that in these cases a definite space has existed between the dead and the living bone. Whenever the contact is complete or very close, union always occurs, as in the case of the unboiled grafts, but if a space exists it may not occur. This observation shows the necessity for perfect contact, if boiled bone is to be used for any purpose in operative surgery. It also shows the importance of making the contact with one of the actively osteogenetic surfaces of living bone, that is, the periosteal or medullary surfaces, and not with the cut end of a bone, as here practically no osteogenesis occurs, and fibrous union is the result. The same observation is, of course, true for autogenous unboiled grafts, as failure to place the bones in close contact results in fibrous union in spite of the osteoblastic activity on the surface of the graft. End-to-end apposition also results in fibrous union, owing to the very slight bone-forming properties of the ends of the bones. Closer apposition is imperative in the boiled than in the unboiled implants, owing to the absence of osteogenesis from the implanted bone.

*Exp. 53.—Ten-weeks boiled implant.*

Jan. 13, 1913.—Spaniel puppy. A wedge-shaped section of bone removed from the middle of the shaft of the radius subperiosteally, boiled for five minutes, and replaced in its bed. The periosteum was closed over it.

March 26.—Specimen recovered. The periosteum is now very adherent and union is solid. The sectioned surface shows the bone to be decidedly porous.

Microscopical examination shows the periosteum thickened, and beneath it is extensive formation of new cancellous bone, with crowds of osteoblasts engaged in absorption of the old bone and the building up of new. The medullary cavity and the saw-cuts are filled with new cancellous bone, solidly united to the implant. The necrotic bone has become very porous, and all the canals contain blood-vessels and crowds of osteoblasts engaged in absorption and new bone formation, absorption being much in advance of replacement. In several places wide Haversian canals can be traced from the medullary surface through the bone to the periosteal surface, thus accounting for the presence of osteoblasts and new bone under the periosteum. No difference can now be made out between the boiled implant and an autogenous unboiled graft unless the age of the specimen is known. The amount of change present is about what one would expect in a six-weeks or seven-weeks autogenous graft.

**SERIES OF EXPERIMENTS WITH BOILED AND AUTOGENOUS IMPLANTS CUT SO THAT THEY COULD BE EXAMINED ON ONE SLIDE.**

In order that a more accurate comparison of the changes which occur in autogenous and boiled implants might be made, a series of experiments was performed in which the following general technique was employed. A long section of half the thickness of the shaft was removed from the radii of dogs, and divided into two equal parts. One of these was boiled for five minutes, and then the two pieces were replaced in their bed and fastened in position with catgut. A silk thread was laid in the saw-cut between the ends of the bones, to indicate in the sections the point of junction of the implants. The specimens were recovered at various intervals. When the sections were prepared it was arranged that the medial end of each implant appeared on the slide, with the silk thread, indicating the saw-cut, in the centre. In this way it was made clear that the same conditions obtained for each implant.

*Exp. 54.—Two-weeks autogenous and boiled implants on one slide.*

March 9, 1915.—Operation performed as described above, the periosteum being left intact, and the implants fastened down with catgut passed through drill-holes in the shaft.

March 23.—Specimen recovered. Both implants are firmly united to their beds, and withstood sectioning with the circular saw. Over each is a thin fibrous membrane, easily stripped, and continuous from one to the other. Both implants are imbedded in cancellous bone, which fills the medullary cavity and is firmly adherent to their deep surfaces. The superficial part of the saw-cut is empty, but at a depth of about half the thickness of the implants it is filled with a pink material which can be demonstrated with a pin to be calcareous. Unfortunately, in the decalcification, the implants fell out, and no microscopical study was possible, as we did not care to spoil the other half of the specimen.

*Exp. 55.—Three-weeks autogenous and boiled implants on one slide.*

Feb. 4, 1915.—Adult terrier. Operation performed as described, the periosteum being left intact on each piece of bone.

Feb. 27.—Specimen recovered. The implants are solidly united to their beds and to one another. The medullary cavity and the saw-cut are filled with cancellous bone, firmly united to the implants. When the specimen was sectioned with the circular saw, bleeding points could be seen on the cut surface of each.

Microscopical examination demonstrates the remarkable similarity of the changes in the two types of bone. The medullary cavity and saw-cut are filled with cancellous new bone, which is firmly adherent to the implants. Crowds of osteoblasts are attacking the medullary surfaces and the ends of each implant, and blood-vessels are freely entering all open Haversian canals. In the bone the circulation has been re-established throughout, and the Haversian canals are filled with osteoblasts engaged in absorption and replacement. Absorption is in advance of replacement to the same degree in each case. The cells in the lacunæ have practically disappeared.

When the periosteal side of the specimen is examined, however, definite differences can be made out. Here, in the case of the unboiled graft, the bone is covered with osteoblasts and new cancellous bone, whereas on the boiled bone the new fibrous sheath lies on the surface without any interposition of osteoblasts or new bone. Further, the superficial portion of the bone itself has undergone greater rarefaction in the case of the unboiled than that of the boiled implant, and in this area there are more osteoblasts in the Haversian canals, and more formation of new bone. This is due to the invasion of the unboiled bone from its own periosteal surface, which does not occur in the boiled bone.

These sections, more clearly than any others, demonstrate the similarities and differences between boiled and unboiled bone when placed in contact with healthy osseous tissue. (*Figs. 245, 246, 247.*)

*Exp. 56.—Five-weeks autogenous and boiled implants on one slide.*

March 17, 1915.—Adult Irish terrier. A section of bone removed from the radius, 3 in. long and half its thickness. This piece of bone was then cut into three equal lengths, and the central

piece replaced in its bed, with the periosteum intact. In the space above this was placed a piece of polished beef-bone, which had been boiled for twenty minutes, and in the lower space a piece of human bone, cut from the crest of the tibia of an old human skeleton and boiled for twenty minutes. The implants were held in place with catgut through drill-holes.

April 20.—Specimen recovered and sectioned longitudinally with the circular saw. All the implants are solidly united, but the human implant is raised up from the underlying bone at one end. The saw-cuts are filled with cancellous bone. The specimen was then sectioned transversely with the saw so that four blocks were formed, the first having in it living dog-bone and beef-bone; the second, beef-bone and autogenous graft; the third, autogenous graft and human bone; and the fourth, human bone and living dog-bone. These blocks were decalcified and the sections cut from the longitudinal cut surfaces.

The microscopical appearances of the first and fourth blocks do not call for separate descriptions, as similar specimens have already been described in other experiments. The second block, containing one end of the autogenous graft and the boiled beef-bone, simply shows an advanced stage of the changes described in the previous experiment. Both implants are solidly united to cancellous bone in the medullary cavity and in the saw-cut. A normal periosteum covers each, and absorption and replacement are going on in each, as already described. Considerably more progress has been made in the absorption of the autogenous graft than of the beef-bone, the condition in the latter corresponding with what one would expect in a three-weeks autogenous graft. As in the three-weeks specimen, the only other difference is on the periosteal surface. In the case of the autogenous bone its surface is covered with osteoblasts and new cancellous bone, and much progress in absorption and replacement has been made. In the case of the beef-bone there are now many osteoblasts on the surface and some commencing new bone formation, but nothing to be compared with that on the autogenous graft. These osteoblasts have spread through the implant from the medullary surface, and their course can be traced in several places along newly-formed canals which connect one surface with the other and which contain blood-vessels and crowds of osteoblasts. Many giant cells are now pocketed in the surface of the beef-bone, whereas very few can be found on the autogenous.

*Exp. 57.—Six-and-a-half-weeks autogenous and boiled implants on one slide.*

Dec. 14, 1914.—Adult terrier. Operation performed as in *Exp. 54*. Periosteum intact.

Jan. 28, 1915.—Specimen recovered. Union of both implants solid, and microscopical study simply shows a more advanced stage of the appearances described in block two of the previous experiment. More osteoblastic activity is appearing on the periosteal surface of the boiled implant.

*Exp. 58.—Thirteen-weeks autogenous and boiled implants on one slide.*

Nov. 27, 1914.—Adult bulldog. Operation performed as in preceding experiments, the junction of the boiled and unboiled fragments being marked with a silk thread. The bone was of ivory hardness.

Feb. 27, 1915.—Specimen recovered and sectioned with the saw. In the gross specimen there is now no evidence of interference with the shaft of the bone, except that the area in which the implants were placed, and the surrounding bone also, are more porous than at the time of operations. No signs of the saw-cuts can be seen.

Microscopical examination shows that the two implants are remarkably similar. They are solidly united to their beds and to one another, and it is impossible to say just where the original border of the implant was. If it had not been for the placing of the silk thread, the point of junction could not be determined, as the saw-cut is filled with new bone, which extends into the ends of the implants, and the new bone is changing from cancellous to compact tissue. At the ends and on the medullary sides the dead bone of the implants has disappeared, and its place is taken by new bone which is becoming compact. In the central portions of both there is still some dead bone, and here absorption is still going on, and the structure of the bone is porous. It is only close to the periosteal borders that the real difference can be made out. Here, in the case of the unboiled graft, there is a thick layer of fairly compact new bone, gradually becoming cancellous on approaching the area of dead bone. In the case of the boiled implant the layer of new bone is considerably thinner, which is accounted for by the delay in the commencement of osteogenesis in this region, owing to the absence of osteoblasts until they could migrate through the bone. When compared with other similar experiments, the amount of change in both these implants is relatively small. This is probably due to the intense hardness of the original bone.

This latter series of experiments very clearly shows the close similarity of changes following the implantation of boiled and unboiled autogenous bone. It clearly supports the earlier conclusions that bone grafts merely act as scaffolds, on and through which new bone is able to form. It also shows the folly of trying to bridge long gaps or replace long sections of bone by boiled implants. In addition, it demonstrates the great importance of the osteoblastic activity of the bed in which the implants are inserted, both in accomplishing union and in replacing the dead bone. To ensure success, the greatest care must be exercised in providing a proper healthy bed for a graft, and in securing perfect contact.

**EXPERIMENTS AND CLINICAL STUDIES DEMONSTRATING THE CHANGES FOLLOWING THE  
INSERTION OF AUTOGENOUS GRAFTS, IN THE TREATMENT OF NON-UNION  
AND IN BRIDGING GAPS.**

***Exp. 59.—Three-weeks autogenous graft bridging gaps. Movement allowed.***

Dec. 22, 1914.—Terrier puppy. A section of half the thickness of the shaft of the radius,  $\frac{5}{8}$  in. long, removed, with the periosteum intact. This was again sectioned longitudinally into two equal fragments. An incision was then made near the mid-line of the back, exposing four spines and ribs near the lower costal margin. The dorsal muscles were retracted outward, and from the inner ends of four ribs, close to the transverse processes, sections of half the thickness of the ribs and the width of the tibial grafts were removed. The grafts were then fitted into the mortises thus prepared, the endosteal surface of the graft being applied to the excavated area in the rib. The bones were fastened together with strong catgut. In this way two pairs of ribs were locked together with the tibial grafts.

Jan. 8, 1915.—Specimen recovered. Only fibrous union had occurred between the grafts and the ribs, although the bones were in perfect contact. The specimen was sectioned in the longitudinal direction, and the surface thus exposed showed the absence of bony union. The grafts were in the same condition as the three-weeks grafts in muscles described in *Exp. 20*.

Contrast the result in this experiment with those obtained in experiments in which autogenous grafts are placed in contact with ribs or the shafts of long bones in such a way that movement between the graft and its bed does not occur (see *Exps. 34 to 43*). In these, bony union is always certain at the end of two or three weeks. The failure to unite, in this experiment, indicates the importance of perfect immobilization of the parts, even where actively osteogenetic surfaces are placed in contact with one another.

***Exp. 60.—Seven-weeks autogenous graft bridging gap. Movement allowed.***

Nov. 20, 1914.—Collie puppy. Two vertebral spines exposed and split longitudinally with an osteotome. A graft removed from the tibia with periosteum intact, and inserted into the split spines, the endosteal surface of the graft lying in contact with the cut surface of the spine. Bones secured in position with kangaroo tendon.

Jan. 7, 1915.—Specimen recovered. Only fibrous union has occurred between the graft and the spines, in spite of their being in close apposition. The graft is very porous and considerably diminished in thickness.

Microscopical examination shows the transplant to be in the same condition as autogenous grafts implanted in muscle for a similar period.

Thus is demonstrated the persistence of non-union and the atrophy of the graft where motion between the apposed bones is allowed.

***Exp. 61.—Eighteen-weeks autogenous transplants bridging gap. Motion allowed.***

May 21, 1915.—Adult terrier. The spines of two vertebrae were exposed and split longitudinally with an osteotome. A graft removed from the tibia, with the periosteum intact, was then fitted into the split spines, with the endosteal surface in contact with the exposed bone of the spine, and the parts secured with kangaroo tendon.

Sept. 21.—Specimen recovered. The graft has completely disappeared, and there is no sign of union between the spines. In fact, the spines are normal in appearance.

This experiment shows that, if non-union of a graft designed to bridge a gap occurs, owing to such a cause as motion between the apposed bones, the graft behaves exactly as it does when implanted into muscle where it has no function to perform, and undergoes complete absorption after a period of from three to six months, depending on the size and density of the bone used.

***Exp. 62.—Ten-weeks autogenous graft bridging a gap. No motion allowed.***

Sept. 15, 1914.—Adult collie. Albee's spinal-graft operation performed, five spines being locked together with a long tibial graft, each spine being fastened to the transplant with kangaroo tendon. A plaster jacket applied to lessen motion.

Dec. 11.—Specimen recovered and sectioned longitudinally with the circular saw. The spines are all fastened together with bridges of cancellous bone, and no motion between the fused vertebrae occurs. The bridges no longer resemble the original graft, which was composed of compact bone, but are quite porous. Originally the graft met the spines at an angle, but now the angles have been filled in, so that the spaces between the spines appear to be bridged over by a series of Gothic arches.

The histological examination of the specimen shows solid union of the graft to the spines, as described in autogenous transplants of similar age placed in the radius (*Exp. 40*). Opposite the split spines the dead bone of the graft has practically disappeared, only traces of it being visible, and in this region its place is occupied by strong cancellous new bone. Between the spines, however, particularly in the middle of the space, where the graft is thin, considerable dead bone is still present, and the same appearance of absorption and replacement can be seen as in grafts of a similar age implanted in muscle. As one moves towards a spine the bridge thickens, owing to the



deposit of new cancellous bone on its deep surface. This deposit has evidently come from the activity of osteoblasts which have spread along the graft from the spine. The more closely one approaches the spine, the less evident the original dead bone of the graft becomes, which indicates a greater degree of absorption and replacement resulting from the combination of the cells of both the graft and the bed in which it was placed.

In addition to showing the above interesting facts regarding the changes occurring in graft designed to bridge gaps, this experiment acts as a control for the three preceding experiments, showing that such gaps as occur between spines and ribs in dogs can be bridged if motion between the bones is eliminated. Motion is prevented here by the length of the graft and by the jacket.

*Exp. 63.—Eight-weeks autogenous graft filling gap in radius by end-to-end apposition.*

Nov. 4, 1912.—Adult fox terrier. Radius exposed and a gap of  $\frac{1}{2}$  in. produced by excision of a complete segment of the shaft subperiosteally. This segment was replaced in its bed and the periosteum stitched over it. Limb encased in a plaster bandage.

Dec. 28.—Specimen recovered. The gross specimen shows only fibrous union of the graft to the ends of the fragments.

Microscopical examination shows the space between the ends of the graft and the fragments filled with fibrous tissue, with some areas of cartilage scattered through it. On the outer surface of the fragments, close to the extremity, there is extensive new bone formation, and the medullary cavity at this point is filled with cancellous new bone, but the trabeculae are cut off from contact with the graft by fibrous tissue. The graft is in the condition of autogenous grafts of a similar age which have been transplanted into muscles.

The failure to unite in this case may be due to two causes: first, the small amount of osteogenic activity at the ends of autogenous bone-grafts and of the sectioned living bone, and, second, the motion which must be present in fractures produced in animals. The latter is probably the principal influence in determining non-union, as we have demonstrated a similar non-union in simple fractures and in transverse sections of the radius in dogs, and this tendency to fibrous union is completely eliminated by perfect fixation of the fragments (see *Exps.* 9, 10, 45). Hey Groves has noted the same tendency to non-union in animals, dependent on motion between the fragments. The experiments of Phemister also show the tendency of grafts, similar to that described in this experiment, to unite to the fragments only by fibrous tissue. In all probability such grafts would unite to the fragments if rigid plates were applied to secure immobility, by the spread of new bone from the periosteal and the medullary surfaces of the fragments over the surfaces of the extremity of the graft. But when one remembers that in ordinary ununited fractures osteoblastic activity in the fragments is much reduced, and the chief source of bony callus formation is thus eliminated, the union of the graft to the fragment is very unlikely, even if perfect immobilization is secured. Clinical experience amply upholds this view, and the following cases explain it.

*Exp. 64.—*

A child, J. B., age 4 years, was admitted to the Children's Hospital, Toronto, with congenital non-union of a fracture of the tibia. The *x* ray showed a gap of  $\frac{1}{2}$  in. between the dense attenuated extremities of the fragments about the middle of the shaft.

On July 10, 1913, an operation was performed. The fragments were exposed and freed of fibrous tissue. With the motor saw, a segment of the bone,  $\frac{1}{4}$  in. wide and 2 in. long, extending to the medullary cavity, was removed, and a bone graft from the other tibia, with periosteum and endosteum intact, inserted by the inlay method. The fragments were very sclerotic, and the attenuated extremities of the fragments were composed of solid compact bone, with no medullary cavity. A plaster-of-Paris bandage was applied from the toes to the umbilicus, completely immobilizing the limb. On Sept. 5, ten weeks after operation, the plaster was removed, and no union had occurred. The *x* ray showed the graft in good position, but the outline of the graft and of the slot in the fragments was perfectly distinct, no fusion having occurred. The plaster was re-applied, and on Nov. 15 again removed for *x* ray. Non-union still persisted, and the *x* ray showed marked rarefaction of the graft, with diminution in its thickness. The limb was splinted for another six months, but the *x* rays showed the gradual absorption of the graft, until, after the lapse of one year, it had completely disappeared.

On June 20, 1914, a second operation was performed. The ends of the fragments were now separated by about an inch, and were in much the same condition as at the previous operation. A long tibial graft was then inserted by the inlay method, extending far back into each of the fragments. The graft was thick and strong, and well placed in the slot.

On Aug. 20 the plaster was removed, and the fracture seemed to be united, although no severe test was applied. The *x* ray showed the graft in correct position, and the ends were apparently fused with the fragments, but this fusion appeared to have taken place at the extremities of the gap only. The plaster was re-applied.

On Oct. 20 the splint was removed again, and now complete non-union was found. The *x* ray showed fusion of the graft to the lower fragment, but the part of the graft in the upper fragment had disappeared, and a fracture had occurred at the junction of the graft and fragment.

*X* rays were taken at intervals during the next three months, and showed the steady absorption of that part of the graft extending into the gap, until it became simply a pointed spur extending upward from the lower fragment.

In January, 1915, the leg was amputated at the level of the fracture. The spur extending upward from the lower fragment was found on section to be ordinary cancellous bone, no trace of the dead graft being apparent.

The study of this case shows the very feeble power of repair in the extremities of old ununited fractures, and indicates the importance of placing the graft in contact with bone beyond the sclerosed extremities, if there is to be any hope of union. The graft must not be depended on to secure the union, as its living cells are mostly concerned in the absorption of its own dead bone. The failure after the second operation showed that, although union may occur, the absorptive process may defeat the success of the operation, if the distance between the areas of healthy bone in the fragments is great. The bridging of long gaps, even when the ends of the fragments are healthy, is always attended with considerable risk of failure, owing to absorption of the graft, as is well shown from an analysis of clinical records.

*Exp. 65.—*

A child, F. A., age 12 years, was admitted to the Children's Hospital with congenital non-union of a fracture of the tibia, with 4 in. shortening of the leg and very marked deformity. The fracture was close to the upper end of the tibia, and the extremities of the fragments were very dense, attenuated, and deformed.

On July 10, 1915, an operation was performed, consisting of the implantation of a tibial graft by the inlay method. The graft was strong, and the periosteum and endosteum were intact. The end of the lower fragment was opened back for  $4\frac{1}{2}$  in. into healthy bone. The upper fragment, being only  $2\frac{1}{2}$  in. long, could only be opened back  $1\frac{1}{2}$  in. The bone in this fragment was very dense, and it was only at the upper end of the slot that healthy bone was exposed.

On Oct. 10 the plaster splint was removed and non-union still persisted. The *x* ray showed union of the graft to the lower fragment, but no sign of fusion had occurred in the upper.

The splint was re-applied for three months, and then, as no union had occurred, the leg was amputated at the knee-joint.

The specimen showed solid union of the graft to the lower fragment throughout the length of the slot, but in the upper fragment the graft lay in a groove lined with fibrous tissue, and the graft itself was closely coated with the same tissue, which resembled periosteum. The upper half of the graft was very porous, and thinned to half its original size. Towards the upper end of the lower fragment the graft was considerably thickened, until, at the junction with the fragment, it was equal in cross-section to the tibia into which it was implanted.

Microscopical examination shows the replacement of the graft by new bone throughout, but the upper half is evidently undergoing absorption.

The study of this case shows the necessity for placing the graft in contact with healthy bone over a considerable distance.

*Exp. 66.—*

A soldier was admitted to hospital in Toronto, with ununited fracture of the ulna and a gap of one inch. On July 20, 1916, an operation was performed in which the ends of the fragments were freshened, and a plate, made from a section of one of his ribs, split so as to expose the cancellous interior, was applied to the denuded surface of the ulna and fastened down with bone screws. The other half of the rib was split longitudinally into several strips, which were used as intramedullary splints.

On Sept. 20 the plaster was removed, and movement was still present. The *x* ray showed union of the graft to the fragments, but the portion bridging the gap was much rarefied. The splint was applied for another two months, but at the end of that time the movement was the same as at first. *X* ray showed complete absorption of the middle portion of the graft and of the intramedullary splints.

On Dec. 1 the operation was repeated. When the fragments were exposed the graft was found solidly fused with the fragments, but tapered down to a point in the middle of the gap. The intramedullary strips had disappeared. A tibial graft was then inserted by the inlay method, and solid union of the fracture resulted.

This case indicates the importance of using strong bone to bridge gaps. The chief process during the first two to three months is absorption, and unless the graft is sufficiently thick and strong to withstand absorption until enough new bone is developed to stand the strain of the slight function, the operation will be a failure. We now limit the use of rib, in bridging gaps, to fractures of the mandible, and employ the method already described. Rib may also be successfully used to plate ununited fractures in which the ends are not sclerosed, and can be brought in contact, or for non-union in the patella.

#### THE PLATING OF RECENT FRACTURES, AND THE BRIDGING OF GAPS, WITH BOILED BONE.

*Exp. 67.—Three-and-a-half-weeks plate.*

May 8, 1914.—Adult terrier. Radius exposed and severed about its middle with a transverse saw-cut. A plate of boiled beef-bone, 2 in. long and curved to fit the radius, was then applied to the denuded surface and fastened down with screws made from beef-bone.

June 1.—Specimen recovered. The fracture is firmly united and the plate adherent to the surface of the bone.

The specimen was split longitudinally with the saw, and sections were cut from the exposed surface. The firmness of the union of the plate to the fragments was tested in the other half of the specimen and found to be slight.

Microscopical examination showed the same changes as already described in *Exps.* 52 to 55, in which boiled bone was implanted in the radius. The line of the fracture was filled with new cancellous bone.

*Exp.* 68.—Eight-weeks boiled plate.

April 14, 1913.—Adult terrier. A section,  $\frac{1}{2}$  in. long, was removed from the shaft of the radius, and the fragments were fastened together with a plate of boiled bone applied to the denuded surfaces. The plate was fastened down with screws of boiled bone.

June 17.—Specimen recovered. The fracture is solidly united, and the plate is united to underlying bone. The specimen was split longitudinally with the saw through the line of the screws. The exposed surface shows that the gap in the radius is completely filled with new bone, and that the plate and screws are intimately fused with the living bone. The boiled bone is very hard and white, as compared with the living, but bleeding points on its surfaces can be seen. The plate is covered with a fibrous membrane which is loosely adherent to it.

The sections for microscopical examination were cut from the surface exposed by the saw, and show the plate crossing the gap, and one of the pegs.

Microscopically, the plate and pin are solidly united to the radius by strong trabeculae of new bone. The picture agrees perfectly with those already described in *Exps.* 53 to 57, in which boiled bone was implanted in the radius. The deep surface of the plate and the edges of the pin are undergoing absorption and replacement. A circulation has been re-established throughout, and in the Haversian canals are crowds of osteoblasts and layers of new bone. On the surface of the plate, and over the head of the pin, is a fibrous membrane resembling periosteum, from which blood-vessels pass into the bone. Under this membrane are thin patches of new bone, produced by osteoblasts which have migrated through the plate. The hole in the plate, through which a pin passes, is filled with new bone, and the pin and plate are united by this cancellous tissue. It is quite evident that the plate has not been instrumental in bridging the gap in this case, as the whole space is filled with new bone which has simply formed in the callus poured out of the ends of the fragments, and the plate has merely acted as a splint.

The experiment shows the value, however, of boiled bone as a material for splinting recent fractures. It would be useless in non-union, where the osteoblastic activity of the fragments is low, but in recent fractures it is excellent, combining, as it does, the properties of strength and absorbability. (*Figs.* 250, 251, and 252.)

*Exp.* 69.—Seven-weeks boiled spinal implant.

Nov. 20, 1914.—Adult terrier. Spinal graft operation performed, the bone used for the bridge being boiled before implantation. Several spines were locked together.

Jan. 7, 1915.—Specimen recovered and the graft found united to the spines. Longitudinal section shows that, at the point of junction with the spines, the angles between the spine and the under surface of the implant have been filled out by the deposit of new bone on the surface of the implant. Midway between the spines the implant appears much as it did at the time of the operation, except that it is covered with a fibrous membrane.

Microscopical examination shows union of the implant to the spine, restoration of the circulation in the dead bone, and the laying down of new bone on the surface of the implant near the living spine. The part of the implant which is buried in the spine or covered with new cancellous bone is much rarefied by the advance of osteoblasts into it. The portion of the implant midway between two spines is nearly as compact as at the time of operation, very few osteoblasts having advanced so far into the dead bone. The same absorption and replacement as already described in boiled bone are taking place.

In combination with the complete study of the clinical cases operated upon by this method, the ability of boiled bone to bridge short gaps between healthy bones is well demonstrated.

THE TRANSPLANTATION OF BONE FROM ONE ANIMAL TO ANOTHER OF THE SAME SPECIES.

*Exp.* 70.—Three-weeks grafts.

March 2, 1917.—Two adult terriers. A section of rib, 1 in. long, removed subperiosteally from each animal and divided into equal parts. One part was implanted in a muscle of each dog. Thus with each homogenous graft could be studied an autogenous control.

March 23.—Specimens recovered and sectioned. In the gross they all resemble ordinary autogenous grafts of the same age in muscle.

Microscopically, all specimens resembled the three-weeks grafts in muscles already described (*Exps.* 20 and 21), showing marked osteoblastic activity chiefly in the direction of absorption, but also of new bone formation. The amount of cellular activity in the homogenous grafts was quite equal to that in the autogenous controls.