James B. Jackson
1854.
On the reproduction of bone

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In all the wide domains of Physiology, there are few subjects more interesting, or inviting to closer investigation than that of the reproduction of the tissues of the Human Body after injuries — alike from the diversity of the phenomena which are present, as from the beautiful arrangement which is everywhere apparent. The subject is much too extensive for the limits of such a short paper as the following, and I therefore confine myself to the consideration of that branch which treats more particularly of the reproduction of bone — so a tissue, which as it is of all the textures of the Human body, which are capable of restoration, is the most highly organized, so also presents in the process of reproduction the most complex phenomena, and affords peculiar for a clear insight into that mechanism by which our frames are regulated in health and built up in disease.

It is little wonder that in a process in which the different steps are so numerous, and so apt to be varied or altered according to circumstances that great differences of opinion should have
existed for so long a time between the various distinguished physiologists, who have paid some particular attention to the subject. At the present time physiologists are well agreed as to the phenomena and their sequence, but there still seems to be some diversity of opinion as to the origin of these phenomena, or to the particular parts played in the process by the various portions concerned in it.

It may not be uninteresting to give a slight glance at the opinions entertained on this subject by a few of the older writers, although there is such a mass of history accumulated, each writer considering himself bound to recapitulate the views of those who have gone before him, and to add another stone to the ‘chain’ which had been heaped on their exploded theories—that I must content myself with giving but a very brief sketch on the subject.

The most ancient theory with regard to the reproduction of life after a solution of continuity was that the two ends were united by an exudation of a poisonous fluid, which being
Jammed out between the ends, became concreted, and joined them together in much the same way as glue unites two pieces of wood.

Towards the middle of last century, Duhamel du Monceau advocated the doctrine that bone was reproduced by ossification of the periosteum in consecutive layers, and thus he attempted to prove by forming an analogy between the formation of wood from the inner layer of the bark and the periosteum.

In 1758 Müller instituted a series of experiments on the lower animals in conjunction with his pupil Delisle, and came to the conclusion that ossification was effected by the transformation of a fluid exuded by the fractured ends, which was transformed into cartilage, and from that into bone, the ossification proceeding in the same manner as in foetal cartilage.

Bordenave was the first who drew an analogy between the process of bone and that which obtains in the soft parts. He held that it was the result of the ossification of granulating which spring from the ends of bone.
Mr. Boyer, while allowing an analogy between the cicatrization of the soft parts and the reunion of fractured bones, denied that that ossification necessarily took place through the medium of granulations—indeed that these granulations were alone seen where there was an external opening communicating with the bone, or where that bone was denuded. He affirmed that in bones as well as in soft parts there was a union by first and second intention.

John Hunter and more recently, Mr. Henry, have advocated the view that reunion was accomplished by means of successive organization and ossification of the extravasated blood.

But of all who have written on the subject none have given a clearer or more accurate account of the process and its various stages than that learned physician and surgeon, Baron Dupuytren. He held that the periosteum was not the only peculiar agent in the repair process; but that it along with all the surrounding tissues, ligaments and...
muscular were agglutinated into a mass which surrounded the fractured ends; that this mass, along with the lining membrane of the medullary cavity, became ophosed, and thus enclosing the ends of bone rendered them immovable until a more permanent bond of union should be completed between them. This, which he termed Provisional Callos, from the fact of its being only temporary in its nature, by a beautiful process, undergoes a petrifying movement, and becomes absorbed as soon as the Definitive Callos, or that permanent bond of union, which is interposed between the fragments, is fairly established. Besides those whom I have mentioned, there were many who held intermediate views, neither allowing the entire reproductive power to peristeen, or to the bone itself, but that each acted an equally important part in the process. Such were Virji, Roger and many others.

Indeed, the great discrepancies which appear to exist among the statements of the various men, who have given attention to this subject
Both in their account of the phenomena, and their mode of dealing with them, seem to arise partly from want of repeated observation, and from making these observations at different times about various periods of the year, and partly from falling into the grand error of men enquiring into the cause of certain phenomena, viz., starting with a preconceived notion, and then finding only perceiving the existence of those phenomena which tend to favour their views. Thus views have been handed down from age to age, and accepted as true, which by subsequent investigation have been proved to be erroneous. Dr. Huxley's doctrine of Provisional and Definise Cutis, which was long, and even still is, to a great extent believed to be a correct one, has lately received a severe shock from the investigations of Professor Page. This eminent man, while allowing to the full extent, the accuracy of Dr. Huxley's observations on the lower animals, argues that the great fault which has been committed by all
The writers on the subject as of taking it for granted that the spine is exactly similar to the one which obtains in man. He argues that the higher in the scale of organization a being is, the more complicated are the means which nature employs for the development of tissues, and for their re-development when lost, and that in man who stands highest on the scale many circumstances are present in the spine, which are not necessary in the lower animals. In the case of bone, two, in man a degree of rest and adaptation of the injured portions is obtained, which cannot exist in the lower animals; that the circumstances therefore, under which union takes place are different in the two; and indeed that the presence of proximal Callus, in the former, is the rule, an exception and not the rule.

I shall now, therefore, in commencing the true subject of my paper, in the first place give an accurate account, as I am able, of the phenomena which occur in the spine of man, after fracture of a bone.
In fracture of the shaft of one of the long bones, the first result of the injury is displacement, and consequently pain or deep laceration of the soft parts surrounding the seat of injury. Blood is extravasated to a considerable extent both between the bone and its periosteum, and into the substance of the contiguous soft parts, causing a certain amount of swelling and ecchymosis. This however in some cases is very inconsiderable in the first place; but after the period of incubation has ended inflammation with its accompanying phenomena generally supervenes, so that after a few hours the limb may be enormously swollen from extensive inflammatory exudation. The muscles and surrounding soft parts are involved in this exudation, and are formed into a hard and compact mass, which, by their firm and unyielding nature, resist the first grand step towards the completion of the process viz: keeping the ends of bone in a state of immobility. This mass in a short time becomes very pruritic and when viewed under the microscope is seen stuffed with irregular intervals with patches of radiating
screeds, presenting altogether a very beautiful ap - 9 pearance. Immediately surrounded by the margin, a tumour there exists a space, in circumstances pec - 0 riformed by the peritoneum enclosing the fractured ends of bone, in which is contained at first the originally extravasated blood... This fluid very soon after the injury is coagulated and forms a clot which is firmly adherent to the bone, and which undergoes the following change.

It gradually loses its characteristic dark colour and acquiring lighter and lighter shades at last becomes almost entirely decoloured and at least is only of a slightly pinkish hue. The clot also undergoes a sensible diminution in size, and this coupled with the loss of colour has induced observers to suppose that it is completely absorbed into the circulation, and its place occupied by new and effused organi - 1 zable lymph. But it is much more reasonable to suppose that that view is correct, first prop - 2 osed forward by John Hunter and now advocated by Mr. Paget— that these changes in the clot - 3 are merely steps in the course of its perfect - 4 organization; for this change in its colour,
is not the same as that produced in a disintegrating clot. The gradual decolorization of the former being different from the mottled, purplish look of the latter, and the time requisite for the disappearance of a conglutinum being far longer than what we know as necessary for the above mentioned changes.

Thus the transparent gelatinous looking clot found in the heart of those who have not been dead long appears to be nothing other than the first step towards organization; whereas months and months will elapse before an apoplectic clot becomes absorbed. The consistency of the clot is also quite different in the two cases; in the one it is soft, friable, or nearly fluid, presenting a mottled appearance and evidently in the process of disintegration; while in the other it is tough, firm, and elastic, resembling gelatine and thus a distinct filamentous substance.

But although this clot, where it does occur, becomes organised, and forms part of that substance in which impression subsequently takes place, yet according to Mr. Paget, it is by no means essential to the proper union of fractures, and in some cases indeed is entirely wanting. The swelling which
has been mistaken for blood being oozing in a great measure to evagination into, and desensation of the soft parts, subsequent to the injury. It seems to me, however, hard to believe that such an amount of injury as is necessary for the production of a fracture could take place without extravasation and that to some extent from the torn bloodvessels, and in proportion to the amount of injury inflicted. The less the amount of extravasation, the sooner, ceteris paribus, will the clot as well as the effused lymph become organized, and the subsequent changes be effected; with the same laws regulating the regeneration of bone, as is seen in operation in the reproduction of the lost parts after injury.

But whether the clot of blood is disintegrated and absorbed, or whether it becomes organized, it is certain that at a certain time after the receipt of the injury, a time corresponding to the period of incubation in inflammations, and varying greatly according to circumstances, a new and powerful auxiliary is supplied by the bloodvessels of the bone and periosteum, an effused and organic fluid, which has
which has been denominated exudable lymph, and which as poured forth around and between the fractured ends of bone.

The time when this exudation takes place, or the interval of incubation between its effusion and the receipt of injury is not as the compounded water which elapses before the exudation poured into the surrounding muscular tissue makes its appearance. A few hours only are necessary for the introduction of the swelling and ecchymosis of the test points; but in man some days of inactivity would seem to elapse before the proper organic fluid destined for the formation of callus is effused immediately at the site of injury. In this respect as in many others the process seems to differ materially from that observed in the lower animals, the effusion appearing in them in a most incredibly short period of time.

It seems to be pretty clearly ascertained, as far as our means of chemical and microscopical observation will carry us that the fluid exuded by ecchymosis from the walls of the blood-capsels is identical with that plastic material
which is proven out under all other circumstances for the repair of lost tissue. It first appears as a colorless or slightly dim, granular substance, the granules having a tendency to assume a streaked, stippled appearance, exactly as in recent times, but in a very short time becoming more, firmer, resistant, and elastic, interposed with a slightly reddish tinge. Some analysts have averred that they detected a larger amount of earthy part than in other preparations; but it is more probable that owing to the excessive rapidity with which in the lower animals, from whom the substance subjected to analysis was obtained, the process of calcification occurs, their presence might be owing to that process having already partially

denied.

While these changes are going on immediately round the injured part, and while the exudation is being forced out by a low-inflammatory state of the vessels of the part, the neighboring tissues are also undergoing a remarkable change. The lymph, landed into the muscles and peritoneum, has gradually acquired a filamentous structure, and from that has passed into a true and
compact mass, and from its condensation has greatly increased upon the dimensions of the face. The periosteum now can hardly be separated from the other textures, the whole being interwoven into a strong fibrous reticulum — gradually, however, as the contraction goes on, the muscles and tendons resume their frontal appearance and functions, and may even in some cases be seen to have channeled for themselves grooves in the tumour wherein they work. The medullary cavity also participates in the change; the medulla at first red and particular, later its colour and is gradually absorbed, while its place is occupied by the spongy vascular and spongy medullary membrane. Its substance is much increased by the formation of lymph, and it assumes a gelatinous appearance. Although the medullary cavity is thus dilated on each side of the fractured ends of bone yet the formation of internal callus does not extend to such an extent as the external.

A short time before the tumour is thus thoroughly condensed and perfected, or shortly before it com
ences to undergo the changes which are about to be described, the thistles inspire blood, while in the bones themselves begin to exude a secretion of a viscid, tenacious nature, which adheres firmly to the opposed surfaces of the fractured ends, and especially to any minute projecting points which may exist there. If the bones are at some little distance these points present a dotted vascular appearance, giving one the idea of their being granulations; but they seem rather to be mere collections of the plasma, become rather more vascular than at other parts, from their proximity to the projecting surface of the opposed surfaces. But if the bones are in tolerable opposition as such points are apparent, and instead, there exists a transparent secretion in no whit differing from other exudations.

This intermediate substance is firmly incorporated with the medullary membrane of the inner side, and that part of the callus external to the fractured ends on the outer; but differs from the rest of the exudations in the relation which it bears to the fibrous joints, for while the changes which go on in the tumoral
surrounding the fractured ends, ending at last in osification, are merely temporary, and for a purpose, the osification which in the pencil of the transformation of the intermediate substance is permanent.

Having traced the process of the repair of repair, thus far, we have now to consider the various steps in the process of organization, which comes in the perfect osification of the contents of the tumour and the formation of that to which Dupuytren gave the name of 'Proximal Callus.'

Most authors who have written upon this subject have described the substance of the tumour as gradually acquiring a greater degree of consistence and at last becoming transformed into cartilage or hyaena-cartilage. The perfect formation of callus through the medium of true cartilage, such as is seen in the foetus, has never been detected in man; those who held this view, having fallen into error, from conducting their observations on the lower animals, and comparing the results with the process of osification as it goes on in the foetus. In the lower animals we know that the repair of injuries is much more
perfectly and easily accomplished than in man; as also in the human foetus we perceive that the process of development approaches more and more that of the lower animals, and as life goes on, it becomes more and more difficult and tedious. In fracture of the long bones, especially in the ribs and the clavicles, bones, which from their natural condition it is difficult to keep in a state of perfect rest, and which thus in the process of resorption, more nearly resemble the process as it obtains in the lower animals, in whom their constant state of restlessness presents a well-marked feature of distinction (feature of distinction) of ossification generally takes place through the medium of fibro-cartilage, a form of it in which the fibrous tissue greatly predominates over the cartilaginous. But although the ossification of callus, fibro-cartilage transitional is the most common structure, yet it is by no means to be considered as the only one. Mr. Paget, in his admirable work on Surgical Pathology, has described three other modes through which he has seen ossification proceed.

First, it may be accomplished through perfect fibrous tissue, the same changes occurring in this
structure as are seen in the imperfect attempt at
rabiesation after a portion of the skull has been re-
formed, or in the infiltration of intertrigunal
membrane near the site of injury. This method of repair, he
considers to be much more common than is gener-
ally believed, where especially but little injury has
been received, and the parts have been kept as
nearly complete rest.

Secondly, and this the simplest of all forms of oph-
usion, by means of nucleated plasma, there being
an intermediate organic structure, the calcareous
particles being deposited in the granular matrix
between the nuclei, which in their turn become
the subsequent capsules and lumen of the bone.

This he has observed where the circumstances were
the most favorable to reproduction, where the
amount of injury was very small, and where a state
of perfect rest of the fractured parts had been attained.

Thirdly, through the intervention of nucleated
cells. This is seen where the injury has been greater,
where the fracture is compound, and granulations
exist; or where in simple fractures, from the extent
of violence inflammatory exudations have been
formed out, and the cells united.
Whatever the medium in which the transformation into bone takes place, ossification having been once established proceeds with great rapidity. Calcareous matter is deposited in abundance, and the bone corpuscles or lacunae, from being at first round or oval, gradually lose their form and become pushed in a serrated at their edge, and as last assume the peculiar spider-like appearance of those cavities as they exist in true bone, being connected to one another by the minute canaliculars which perforate the substance of the newly matter. As the new bone begins to assume its true laminated texture it becomes tunnelled into canals, for the reception of the bloodvessels. The osseous callus is at first light porous and of a character resembling cancellated tissue. It is soft, exudes a viscid fluid when compressed, and is quite flexible. But soon it becomes more compact, firmer, and the laminae of bone are seen arranged in concentric circles around the newly formed Haversian canals. In fact perfect bone is formed.

The manner in which ossification proceeds is as a general rule from the circumference to the centre,
and from that part of the tumour where the periosteum and bone are in contact towards a point corresponding to the plane of the fracture. But it often springs as if from separate centres of ossification in the substance of the tumour, but none especially from the points of bone which the reparative material is in contact with. There may generally be perceived running thru the thickest part of the callus, an irregular undulating line of a different colour from the rest of the substance and marking the degree of displacement of the fractured ends of bone. The periosteum which was long since incorporated with the tumour, and in whose substance the process of ossification has gone on, is just reproduced for some time after the callus, and seems to be formed in thin layer on the outside of the callus at length per-

When the proximal callus has acquired a certain degree of consistency, but long before it has come to its ultimate state of perfection, the ossification of the intermediate substance has been steadily advancing — much the same changes
being observable at it, as have been described as occurring in the provisional callus; although from the little pores, which are interspersed, and which adhere intimately to the little suprasympathetic spots on the surface of the opposed bones, it has made the appearance of union by the adhesion of granulations. It differs from provisional callus only in the permanency of its structure after being transformed.

The callus being now perfectly opaque, and having performed the functions imposed on it; viz., the firm cleaving together of the ends of bone until a more perfect ossification has taken place between them, and being of no more service in the process of regeneration, gradually diminishes in size. This retrograde movement first becomes apparent in the callus within the medullary cavity; indeed it totally disappears, and its contents are completely restored, long before any sensible diminution of the exterior callus is appreciable. This is produced by intratubular absorption by means of small cells, which appear in the substance of the callus. These cells
gradually about the intervening osseous substance— they increase in size, their walls become thinner and thinner, the whole having a reticulated appearance. These cells are remarkable for the bright red color of their walls, and for a red gelatinous substance which they contain. In proportion as their walls are absorbed, they themselves degenerate and are broken up, their substance being again occupied by a substance resembling in its minute structure that medulla, and separated from the bone by an investing membrane. The same changes at a later period are observable in the external Callus, the whole ultimately disappearing: the continuity of the parts of bone is ultimately restored, and a slight thickening and increase in size at the point of fracture alone remains to indicate the spot where such a remarkable instance of the mis-sustaining nature had been so lately displayed.
Having now described the normal process of repair as it occurs in a fractured long bone, the parts of which have been placed in nearly exact apposition, it now remains for me briefly to state a few of the deviations which are observable in the process when all the circumstances attending it are not so favourable. In following out these deviations we shall see how beautifully, and with what perfect exactitude nature adapts the various means at her disposal, to the ends which she has to accomplish.

1st. If the fragments slightly overlap each other or do not exactly correspond, the permanent callus completely fills up the angles formed by the overlapping portions of bone, in addition to its being intermediate, in the sense in which we have used this term, viz., interposed between the fragments where their artificed surfaces are in contact.

The reproductive material is placed in that situation where by its mechanical advantages it may afford most support to the injured part and restore the bone as nearly as possible to its former functions.
But still further, if the bones completely overlap one another in such a way that the continuity of the medullary canal is completely destroyed, the reparative material is not forced out from the fractured ends, but appears in the interval, and in quantity, according to their greater or less proximity, between the opposed sides of the bones. The orifices of the everted medullary cavities, are also the site of changes by which they are permanently closed by means of thin opem plates, resembling those which surround the cancellous tissue of joints. A membrane which is continuous with the periosteum at first appears, and becomes subsequently transformed into a firm tissue. The same thing is seen in the closure of the medullary cavity of a stump after amputation. But besides this closure it is necessary for the perfection of the process that the cavity should be continuous and this is accomplished through the softening of those parts of the shaft, and of the intermediate substance which are opposed to this end, by their gradually assuming the character of cancellous tissue, containing a myx-cellular...
substance and by their subsequent transformation. Thus, however crushed and deformed, the continuity of the external and internal walls of the bone and of the medullary texture is completed to the minutest particular. But not contented with affording support anywhere where support is most required, we contented with restoring the perfect functions of that bone, nature removes such portions as may be subsequently the cause of irritation or at the least precepts. All angles and projecting portions of bone are gradually rounded off and absorbed; at first getting after from disappearance of their calcareous matter; the animal matter disappearing last.

2. Where the fracture is complicated with an external aperture, admitting the entrance of air, the hope of union more nearly resembles that as seen in the soft tissues in the granulating process. Mr. Hyndin indeed denies that there mammillated and vascular bodies are ought but minute portions of detached bone surrounded with a deposit of lymph in a rapid state of
transformation; be it so, nevertheless, the process in this and in other points bears a strong resemblance to the union by the second intention.

In attempting to fix any precise dates for the occurrence of the various stages, which have been described, a great many modifying circumstances must be taken into consideration. 1st. The age of the individual. The younger the patient, the more rapidly certain favorable, while the healing process goes on. 2. Constitution. A debilitated and weakened frame, but especially a suspicious cachexia, are all circumstances unfavorable to the speedy termination of the process. 3rd. The direction of the fracture. An oblique fracture is always much longer of uniting than a transverse one, and this from the circumstance of the greater displacement which takes place, and the greater difficulty with which the contraction of the opposing muscles is occasioned, and the bones kept in apposition. 4th. As was noticed by Mr. Dupuy-Thenon, the impaction of portions of bone of the neighboring tibiae, as well as muscle, between the fractured ends.
These circumstances being taken into consideration the following dates, as given by Baron Dupuytren, than whom no Physiologist has paid greater attention to the subject, may be considered as tolerably accurate—

1st. From the date of the injury.

To the eighth or tenth day comprises the changes thought at first as the first effects of the injury—swelling, ecchymosis, etc. with a gradual subsidence of the inflammation or a period of incubation until

2nd. From the tenth to the twenty-fifth day.

During this period the exudation of the true formative material occurs with its transformation into the intermediate tissue; whether fibrous or fibro-cartilaginous, and the transformation of this in its turn into bone.

3rd. From twenty-fifth to sixty or ninety days, comprises more entire consolidation of the provisional callus, although the bone remains in a cancellated, loose form until the 2d. Period which ranges from the first up to the fifth or sixth month, and by which time the intermediate or permanent
callus has become united.

The last period embraces all the time between the last and the eighteenth or twentieth month; by which time the provisional callus has disappeared and the perfect continuity of the bone been restored.

As to the relative amount of the constituents, animal and earthy of callus, there seem to be great discrepancies in the statements of those who have made analyses; but when we consider the variations which arise in the constitution of healthy bone under the influence of disease and of age, we can somewhat account for them. There seems to be no doubt that in provisional callus the amount of the earthy constituents bears a much larger proportion to that of the animal than in healthy bone, and this is well shown by the two following analyses.

Taking the proportion in ordinary bone to be

Animal substances 58
Phosphates of lime & other parts 42

According to Mander, analysis of provisional
Lagrange gives an almost equal proportion between them; but all seem agreed that the partly matters greatly preponderate.

Sometimes from no very apparent cause bone fails to be reproduced after fracture. In these cases, an attempt may be made to restore the portion of continuity by means of strong albums tigre, or complete failure occurs, a false joint being formed. Where a fracture unites as the result of fracture, it would seem to be owing either to a lack of vital energy, nature carrying the process of regeneration up to this point, and no further, an arrest of development being the consequence; or, as in the case of fibrous union after fracture, within the capsule of the hip joint, or the neck of the femur, from preexisting, for purely nature knows too well that the presence of such an enormous mass of matter, as would be necessary to ensure the perfect union through bone, could not fail to create such an amount of irritation in such a delicate.
structure as the post parts of a joint, as would instantly result in total disorganization and destruction. (This reason of inconstancy may also I think be made to account in a great measure for the circumstances of non-rotation after loss of substance of the bones of the cranium) perspective or otherwise. The existence and close contiguity of the subjacent delicate central substance precludes the possibility of the apposition of such a mass of callus, the existence of which would cause most serious derangement of the functions of that organ.)

But failure of the process may occur even before there are any traces of development, as seen in the cases of false joints. But this is owing to a low state of the nutrition of the parts seems to be proved by the fact that certain mechanical agencies causing a certain degree of inflammatory action, a consequent increase in the flow of blood to the part, and of nutrition, often change the lachrymal state of the parts, and promote union. This want of nutrition is the more curious when we see the complicated apparatus of lining membrane, epithelium, and lubricating fluid.
which is found in false joints, every whit as perfect as in true joints.
Having now described the various steps of the process, by which perfect reunion is accomplished after a solution of continuity of the osseous texture, and having seen the various modifying circumstances which influence that process, it now remains for me, partly to consider the part which is played by the various structures concerned — in other words, the source of the osseous power.

The property of forming new bone has been attributed to two principal sources — one party holding that it resides in the periosteum alone; another that the periosteum is perfectly neutral as far as regards the ultimate end of the process, and that the bone is alone the source of the new reparative material — Dubanet, as I formerly stated was the first to advocate the theory that bone was regenerated by means of the periosteum; he was opposed in this by Haller, Bethly, and others — and even in this school such view has been warmly supported at various times by different physiologists.
It would neither be a profitable nor a wise task, nor yet does place or time permit that I should here enlarge on the various arguments brought forward on one or other side of the question. I shall content myself, therefore, merely by advertence shortly to the arguments lately brought to the notice of the profession by Mr. Lyne, and supported by his ingenious and well known experiments — experiments which would seem to be almost conclusive evidence on the point. There were instituted in opposition to the theories held by those who stated that in necrosis of the long bones, the new shell was not produced by ossification of the periosteum, independently of any assistance from the old bone, but that it proceeded from the contiguous sound bone, and not so much in the substance of the periosteum itself, as in the spinous capable lymph diffused in consequence of the inflammation. To prove in the first place that ossification could take place in the substance of the periosteum without the necessary intervention of courage.
able lymph, Mr. Lyne narrated the case of a girl, who had acute necrosis of the shaft of the tibia, and in whom a shell of new bone formed around the dead portion, and evidently in the substance of the periosteum, there being no thickening or any lymph effused.

Having thus satisfactorily made out that ossification in necrosis may occur in the substance of the periosteum and if it alone, and in order to demonstrate that the power of ossification resided in that membrane, independently of the contiguous living bone, he made the following experiments. Having exposed the patellae of a dog, and carefully dissected back the periosteum, he panned out about an inch of the bone; he then exposed the patellae of the other leg of the same animal, and having removed both periosteum and bone, he carefully placed in apposition the soft parts in each case. In six weeks, the dog was killed; in the former instance the continuity was preserved and the substance of the bone even increased in thickness; in the latter scarcely any new bone was formed.
This experiment along with some others seemed satisfactory to prove that some may be regenerated in the periosteum without any appurtenance from the adjacent bone.

But Mr. Goodric notes (Pathological Observations) that in no case does it occur that the periosteum is separated from the bone without at the same time there being detached along with it minute flakes or portions of bone from its surface, which may be detected with the aid of the microscope, and that these are the true sources or nuclei of the osseous process. The thus explains in psoriar the existence of the separate centres from which the new bone may be seen spreading and ultimately ending in the formation of a shell—this process commencing in points altogether removed from the portions of sound shaft at either extremity of the diseased part. In psoriasis, he says, the first changes perceptible are in the cellular tissue which lines the Hansemann canals, it separates their bloodvessels from the osseous wall; it becomes altered, its cells enlarged, and it takes on an absorptive power; by which
the bone separating the mouths of the Haversian canals at the surface is dissipated and absorbed and thus several canals are thrown into one, the whole assuming a honey-combed appearance. Gradually the periosteum is separated from the dying bone by means of pus secreted by the above-mentioned altered cells; but having attached to it minute shreds of healthy bone, which have some of the secreting cells adherent to them. These shreds show a reddish appearance, and resemble granulations, in the centre of each of which is a small portion of bone, which is just as was supposed the result of the ossification of the granulations; that depends on the presence of the dead segment of living bone originally detached. Dr. Fothergill never observed a new shell forming at the same time these existing opposite each other in a corresponding elevation of the bone, the periosteum being firmly separated by the intervention of pus, and dragging with it small portions of living bone. But if the inflammation has been so acute as to cast in complete pieces of a portion of the shaft without any elevation
In an instance mentioned by Mr. Gulliver in the Edinb. Med. Surgical Journal, that gentleman states, that in a case of fracture of the femur, in which the ends of bone met at an acute angle, and `accidental callus' was thrown out between the angles of the bone, at that position which would be of the greatest mechanical advantage, osification commenced in the callus at a point midway between the fractured ends, and was proceeding towards the bone when the man died, and thus afforded him an opportunity of proving that osification of callus does sometimes proceed from a separate centre as in spiral cartilage.
of ossification does not commence in any part corresponding to the necrosed tissues; but the first attempts towards ossification are seen spreading from the healthy parts of the bone near the epiphyses into the substance of the periosteum, and gradually forming an enclosing sheath.

In the same manner, according to Mr. Godwin in fracture of the long bones, when the periosteum is separated for some distance above and below the fractured ends by the liquefied lymph, small detached fragments of bone become the subsequent centers of ossification. This view is held by those who state that no organic structure can be formed without the contact of small living portions, or of germinal centers, of an analogous texture. But we know that this exclusive theory is contradicted by the fact of the existence of what are called analogous growths, in which no similar texture is in contact with them, e.g. the existence of adventitious cartilaginous tumours, and their transformation into bone &c. &c. &c.
Texture is not essential for the production of an organic structure similar to that in which the loss of substance or renin has taken place, it exerts a most marked influence in causing the foreign substance whether in health or disease, to assume characters if not exactly similar, at least approximating as much as possible to the neighbouring structures.

But all this we must therefore conclude that in lesions of continuity of the organic tissue, whether produced mechanically by direct violence or by the agency of disease, as in necrosis, destruction of old and healthy bone, where they occur, do exert a peculiar and marked influence upon the process of organization, or in other words become centers of ossification, yet I think that that thickening and those abnormal changes in the periosteum are not to be considered as merely accompanying as far as their mechanical assistance is extended, the periosteum has, in my opinion, a far higher duty (so to speak) to perform than that laid down for it by some in conjunction with the surrounding parts, viz: to exact the part of a
split in keeping the bones in correct apposition and at rest; or by its firm and unyielding nature to prevent to a certain extent the separals of the joint from being ruptured. It doubtless possesses these qualities; but I also think that its own fibrous texture after becoming greatly altered and enlarged, itself - firm power inherent in itself - and independently of a species of fibre, becomes in some cases and under certain circumstances converted into true fibrous tissue. In such depurification of the substance of the periosteum, and in that which sometimes is seen in interosseal membranes in the neighborhood of fractured bones, it may be that, through knowledge, as it were, of their proximity to the reach of continuity, they may be endowed by nature with the power of extracting the organic matters necessary for their transformation into an organic substance which is destined to be of service in the acts of reproduction. Be this as it may, I think that the periosteum possesses a power, perhaps, of being transformed into bone - and that this is a power inherent in the investing membrane,
in picture of it, being a fibrous membrane, and
in common with other fibrous membranes, I think
is satisfactorily made out by analogy with
the curious transformations of these structures in
other parts of the body. It is a curious fact that
fibrous membranes, and cartilages of a distinct
fibrous character are almost the only tissues
of the body in which abnormal or adventitious
deposits of tarry material occur. In these cases
the first changes are, I am inclined to think, the
same as those which are seen in certain forms
of atrophy of fibrous tissues, the very fibres them-
selves becoming altered, softened, disorganized,
and their very substance be occupied by foreign
matter, which, in the transformations which
I am alluding to, consists of a phosphatic and
calcaceous deposits. We know that this trans-
formation of fibres is the very method in which
the normal process of calcification takes place in
the membranes of the foetal head, and in those
of the flat bones, and I apprehend that the very-
same phenomena obtain in the so-called
Calcification of arteries. This is a term which
has lately been applied by certain physiologists,
Valentine
(who as far as momentaneous is concerned, seem to be attached to them) to that state which was formerly called calcification of the arteries.

They deny that these adventitious products are composed of true bones' texture, but that they consist of an organised calcareous texture, deposited as round, annular, or circular, compact bodies, with prolongations radiating in all directions — within a peculiar, more or less lamellated and finely granular texture.

The distinction here drawn between the structure of these deposits and true bone, even allowing that the parts held with regard to their intimate composition were correct, did not seem to me to be sufficiently pronounced to warrant the withdrawal of them from the category of bone, which they so much resemble to the naked senses. There appeared, however, a few months ago a paper by Mr. Trench, in which that learned physiological states that he has distinctly seen these products to consist of the peculiar structure of bone, to profuse its lamellated texture, its corporeality (at one time the nuclei of the fine cells)
transformed into calcaneum—in fact all the characters of true opaque tissue. The fact of the presence of atheroma does not militate against this view; but that substance is to be considered as simply a deposit of embolic matter from the passing stream of blood into the substance of the fibres of the middle coat of the artery, constituting one of the steps in the transformation of the fibres peculiar to this species of ossification. It is also worthy of remark that small patches of fibro-cartilaginous substance—though, elastic, and in all respects resembling those substances as found in the first stage of transformation of callus, are often found intimately connected with these fibrous patches, and in some cases evidently in parts of a bony structure. Some eminent men, however, declare that in these instances the cartilage is formed subsequently to the bony plates, and is by no means in the course of transformation; but their opinion must be taken with reservation, as it is hard to believe that nature should here, for no evident purpose, break through those laws which are known to obtain in other parts of the body.
I have no doubt that in the case of a great many fibrous membranes as well as in that of the arteries,what has been hitherto believed to be calcification, will be found upon accurate examination to be true calcification. I may briefly mention two or three cases that I have met with and which are to the point.

In the American Journal of Med. Science for Jan., there appears an extract from the transactions of the Boston Society for Medical Improvement.

Two specimens of bone from the inner surfaces of the dura mater were shown by Dr. DeBakey, which upon being examined under the microscope was declared by the members to present the most perfect and the minutest characters of bone. This must of necessity have been formed independently of old bone and either in the substance of the fibrous membrane, or by the transformation of cartilaginous substance analogous to the first stage of callus. Is it at all likely that nature who knows so well how to employ these means least likely to be of danger, should have furnished out a large quantity of foreign matter, exactly in that situation where we know that the slightest abnormal
I presume it is productive of the most serious results. This I consider as an incontrovertible case of true ossification of a fibrous membrane, independently of the contact of a peculiar structure.

The pleura is very liable to osseous deposits, and these seemingly of two kinds, one in which by some change in nutrition thin lamelleas of bone and fibro-cartilaginous and osseous tumors are found interlaced in the substance of the pleura, and quite distinct from any inflammatory deposit, the other a transformation of strongly organised fibrous bands, adhering the result of inflammation, into distinctly laminated plates of bone.

There is a case mentioned in Virchow's Archives for 1853 p. 580 in which the fibrous matter of the posterior part of the vitreous humor of the eye was found ossified, the ossification extending by means of incrustations into the anterior part of the body.

It would be needless on any part to multiply further examples of these analogous growths — it is sufficient that it be established as a general rule that true ossification of fibrous membranes may take place without the contact of living bone.
I have thus entered so minutely into their structure and formation, as I think that if it can be proved that these analogous growths consist of true bone, and as they exist and are formed independently of old bone, an additional and strong argument is gained in favour of the opinion that germium may, and that under certain circumstances it does, become ossified, by an inherent, independent power. Where there is an intermediate fibro-cartilagineous matrix or callus, and where the ossification has commenced in the germium and is proceeding onwards to meet that supplied by the old bone, I think that it is much more reasonable to suppose that each little separate centre of ossification originated without any (maternal) germ, than that in every centre there must be a separate speculum of living bone. But often the only matrix in the spicule power deposit is the germium itself, these never having been any callus—any effusion of compatible lymph. Indeed that a great proportion of the callus which
which has been ascribed as the normal product to the process of regeneration as it goes on in man, is hypothetical and derived from forming too close an analogy between the process of regeneration as it proceeds respectively in man and the lower animals, has been proved by Mr. Paget by the examination of a great number of specimens. In these very few exhibit provisional callus (using the term as applied to the temporary deposit around the fractured end, the only ossification which has proceeded external to the fractured ends, existing in the substance of the periosteum itself. In fact the limits the occurrence of a fibro-cartilaginous matrix to those cases in which through carelessness or otherwise great motion had been allowed between the two ends of the fractured bone, as generally occurs after fracture of the ribs in their perimor, and clavicles, which, preserved as rigidly immovable as surgical aid is capable of effecting, resemble in one point at least the conditions under which union takes place after solution of continuity of the bones in the lower animals.
Seeing then that ossification may take place in the periosteum by direct transformation of its fibres, and quite independently of any rudimentary callus, or other intermediate matrix exuded by surrounding parts — seeing that the same transformation of fibres exists continually in other parts of the body, and that without the slightest aid from old bone — I see no reason why ossification of the periosteum may not be allowed to exist by virtue of a power independent of the old bone, or that there is necessarily a germ of living bone present in such centres, from which the ossification springs as a tree from a single seed.

The old bone truly exercises a marked influence on the result of this reproductive process but I hold that it is merely by its poising that it does so, nature itself insinuating itself into the intermediate structure, whatever that may be, such a vital force (for want of a better name) as ends into its transformation into a perfectly organised and analogous fibre. And I cannot allow that in the vicinity of foci of ossification alone advances from
Portions of old bone.

These conclusions I course only refer to external, or provisional callus, in the term in which that is applied to such of the scanous tibias as exist external to the definitive callus of Dupuytren. In necrosis also, I think, that it is more reasonable to suppose that, where the peristea is epipied, that epipetation is subject to the same laws as are found in operation in the epipetation of other fibrous membranes, such as I have formerly described, than that in every separate little centre of epipetation, there must be present a minute germ of living bone from which it springs.

In permanent or definitive callus the epipetation of course springs directly from the entypic surfaces of bone; but I can no more allow that the bone in these cases reproduces bone, than I can admit that it has the power of forming fibrous tissue. Granting the former, I should be compelled to admit that, in those cases in which from a want of nutrition, the solution of continuity has been alone restored by fibrous tissue, that fibrous tissue was
produced by the bone itself.

To conclude, I may summarize the above scattered remarks by the following conclusions.

1. That reproduction of bone after fracture takes place by the transformation of certain inter-
   mediate tissues or structures into osseous sub-
   stance.

2. That this matrix, which is the pith of the
   osseous deposit, may consist of
   
   a. The cartilage, as is commonly seen in
      the lower animals, and most perfectly and
      almost exclusively, in man, in the ribs
      and clavicles.
   
   b. Fibrous membrane, as where periosteum
      is transformed into bone, and in the
      almost abortive attempt at regeneration which
      is seen after fractures and lysis of substance
      of the bones of the cranial vault.
   
   c. Nucleated plasma, as was observed
      by Dr. Paget in cases where there had been
      the least amount of injury, and the most
      perfect rest, and want of motion after
      wounds.
   
   d. Nucleated cells, as in formation of
granulations in compound fractures &c.

3. That, where this exudation is present, it differs not at first from that effused under any other circumstances in other parts of the body.

4. That as to the origin of the new bone, undoubtedly where old living bone is present, the ossification proceeds in preference from these portions, whether they consist of the fractured ends alone, or small detached spicules adhering to the periosteum.

5. That next to purely ossification may commence from a spontaneous centre; that is, at a portion of the periosteum, or from a point in the substance of the callus, which is in immediate connexion with any portion of old living bone.

6. That we are not to consider that the new reparative bone owes its origin to the old bone, in virtue of any reparative power existing in the bone corpuscles of the old bone, even where the ossification is proceeding free in a part of the matrix in contact with the living osseous tissue.

7. That we are not to consider that passage
On account of the proximity of the living bone—that bone being placed under certain circum-
stances wise, in a state requiring regeneration—
sets up such a series of changes in an im-
mediately neighboring texture, as ends
in its ultimate transformation into bone.

James R. Jackson
March 28th, 1854