LECTURES

ON THE

PROCESSES

OF

REPAIR AND REPRODUCTION

AFTER

INJURIES:

Delivered at the Royal College of Surgeons of England,

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&c. &c.

LECTURE I.

The phænomena of repair and reproduction are manifestations of the exercise of the same power as that by which the body was developed from the impregnated germ. Probability that the same power operates in the maintenance of the body by nutrition. Characteristics of the power of the impregnated germ. Evidence of the operation of the same germ-power in common nutrition, and in all normal organization: insufficiency of the accepted explanations of maintenance by assimilation and by succession of germs of tissues. Operation of the same power in repair and reproduction. Phænomena of reproduction of parts in the Hydra, and other Polypi; in species that can propagate by spontaneous fission and gemmation; in those whose development is with less or more apparent metamorphosis. Imperfection of nearly all reparative processes in the highest Vertebrata. Considerations on the purpose and analogies of the various processes for the recovery of lost perfection.

Mr. President and Gentlemen,—Many considerations led me to choose, for the subject of this year's lectures, the processes of repair and reproduction after injuries. The chief of them was in the fact, that the preparations in the pathological museum which illustrate these processes stand next in order after those which suggested the subjects of two former courses. But had I needed another motive for the choice, I might have found one in the advantage which my subject may derive from appearing, in a measure, supplemental to that with which my friend and colleague, Professor Owen, has occupied your attention. The mind, indeed, might gladly rest in the contemplation of such unhindered perfect works of Nature, as those of which he has discoursed; and it may at first seem an ungrateful task to turn from these, and consider the losses of perfection to which such works are liable, especially those losses which, being out of the ordinary course of Nature, abrupt and violent, we might expect would quite spoil the structure and the order of the living body. But, in truth, while studying the means by which living bodies, having suffered injury, regain their perfection, we may find continual manifestations of the same mysterious properties of the germ by which, through development, they first attained it. And in these manifestations we may discern the best evidence that, in developing the body to its perfection, the power of the germ is not lost, or quite exhausted, but rather is diffused through all the parts of the completed being; and that, so diffused, it works in them through all their life, determining, as with continuous design, every natural formative process, in accordance with the specific character of the individual. For I believe that we cannot form a just conception of the scope and nature of even the least of the processes of repair and reproduction after injury, or of the maintenance of the body in ordinary nutrition, or of its natural changes in the course of age, unless we admit that each organism, in its perfect state, retains, diffused through all its parts, some of the specific properties from which the power issued that actuated the impregnated germ in its development. I will therefore first ask for your attention while I endeavour to explain and establish this doctrine.

It is not a new doctrine, for the celebrated theory of the *nisus formativus*, which Blumenbach* maintained, might be expressed in nearly the same terms as I have used; and that which Müller and some others have held of "the organic force," and "the rational creative force," might easily be adapted to them; yet it seems necessary still to argue that such a doctrine should be received as a foundation in physiology. For the general tone of modern physiology is opposed to it, and of late years, especially, the cell-theory of Schleiden and Schwann, and the seeming accuracy which the progress of organic chemistry has given to our notions concerning assimilation, appear to have satisfied most physiologists that we have, in these, sufficiently good hypotheses for the explanation of the maintenance of the perfect organism by nutrition. If it were so, we might need no other hypothesis for the explanation of repair and reproduction; but it will appear, I think, that both in these, and in the processes of common nutrition, a power is in exercise which is not admitted by the cell-theory, or by organic chemistry,—a power continuous with that manifested in the germ, and acting in all essential things like it.

The characteristic property of an impregnated germ is, that when placed in favourable circumstances, all the materials of which it first consists, and all that it appropriates, are developed according to the same method as was observed in the development of its progenitors,—in other words, in conformity with what we may regard as a law of specific character. In all the wonders of development that my colleague has detailed, none, I think, appeared more marvellous than the constancy, the seeming tenacity of purpose, with which the germ is thus developed to the likeness of its parents. However vast its power of multiplication and increase,—however various its metamorphoses,—however far in some of these changes it may deviate from the form in which its parents generated it,—however near in some it may approach the perfect characters of another species,—or, which is stranger still, however much alike all germs may be in their primal structure and earliest developments,—yet, through all these things, each germ moves, with unswerving progress, guided by the same Power as created its first parents, to the formation of a being in which the parental form and properties are reproduced.

Now, the constancy of this result, and its little dependence on external circumstances, justify the expression that every impregnated germ has, in itself, and in the properties with which its Maker has endowed it, the power to develope itself into the perfection of an appropriate specific form. However mysterious the nature of such properties, we cannot deny their existence, or refuse to recognise a law (in the sense in which we generally use that term,) in the regularity with which the power acts that issues from them, when the germ is placed in favourable conditions. And, therefore, if it appear that this power is peculiar in its modes of operation, we may specialize it, whenever acting, as the "power of the germ," or "germ-power," in consideration of its having its apparent origin and intensest action in the germ.

Now, there are certain things observable in the development of a germ, so characteristic of the power exerted in it, that they may be used for determining the differences between this power, and any other supposed to be exerted in the living body, and therefore as tests for determining whether, in any instance after completed development, the same power is in exercise.

First, then, it may be observed, that as surely as the power of the germ tends always to the attainment of the perfection of the specific form, so is it strictly limited to the attainment and maintenance of that

* Blumenbach's theory of the nisus formativus was raised in opposition to that of "pre-existent germs," and derives much of its meaning from its negations. He, mainly, held that generation and reproduction are "absque germinibus sed ex informi materie" (De Nisu formativo, p. x.)

His chief instances in proof are the cases of animal formations, for which there could not have been pre-existent germs, since the formations are the results of accidents or diseases occurring to the individual. Such are false membranes; sacs round foreign bodies; Wormian bones in hydrocephalus; teeth, hair, and bones, in ovarian cysts; various monsters, hereditary malformations, some acquired and then inherited national and other peculiarities,—as flat heads, short tails in horses, and the like. These, he says, prove a *nisus formativus*: these cannot be due to the evolution of pre-existent germs. But he makes so little account of germs, that when he speaks (Specimen . . . inter animantia, p. 31) of nutrition as continued generation, and of reproduction after injury as the same repeated in single parts, he seems rather to have reduced development to the same rank as mere organic formation, than to have shown any relation between nutrition and what we now understand by development.

perfection, and to certain rules of time, and space, and mode of progress. The germ rarely falls short of its designed form, but it never goes beyond it,—no creature is known to attain by development a higher specific form than its parents had; and the differences of size, to which by growth the different individuals of a species may attain, are circumscribed in narrow limits. So, too, are the length of life, and, in narrower limits still, the periods and methods of development. Perfection, whether in the whole body, or in any of its parts or tissues, seems to be attainable only by certain methods appropriate to each species; there are certain fixed transitional forms to which the power of the germ, in its development, seems bound.

Wherever, then, in the full life of any creature, we see organic formation ensuing in conformity with these restricted laws, there, we may suppose, a power is in operation like that which actuated the germ.

But, secondly, it seems to be characteristic of the power of the impregnated germ, that it is diffused through many parts, which, whether they be like or unlike, are all directed to concur, with various time and measure, in the attainment of the design and destiny of the whole.

It is only in few and trivial instances that we can regard the development of one part or system of an embryo as the consequence of the development of another. Rather, the several systems and the parts of each are developed independently, though concurrently and commensurately. Thus, the primordial heart and blood-vessels of the embryo appear together, and are developed with corresponding progress; yet are they independent. Thus, too, there is concurrent development of the blood and the system for circulating and purifying it; yet neither development is, in any strict sense, the consequence of the other. Or, again, in smaller instances, there is a concurrent and commensurate development of each of the several parts of a limb, and of all the several limbs of an animal; yet each limb, and each part of each, is developed independently of all the rest. And, in yet more trivial instances, when even so small a thing as the formation of an arch by two outgrowing blood-vessels is to be effected, it is manifest that there must be concurrent development of both, in order that they may exactly meet and coalesce; but it is as manifest that neither of the vessels is so developed in consequence of the development of the other.

Now, when such development of different things in the same body, though mutually independent, are yet commensurate, and concur to the accomplishment of one design, it is surely because they are all dependent on the operation of one and the same power. Such a power, or, rather, the properties from which it issues, being thus diffused in the first instance through all the embryo-cells of the germ, would seem to be communicated to all their descendants, and to all the materials that they appropriate; so as to actuate them all, in conformity with the same law of tendency towards the attainment of the perfect specific form.

Now this character of being transmitted and diffused through a succession of heterogeneous forms, and of determining them all, by different means, to concur in the achievement of one design,—this seeming capacity of subordinating a multiplicity of processes to an unity of purpose,—this, again, appears to be so characteristic of the power of the germ, that wherever it is manifested, there we may suspect the same power acts.

But, thirdly, it is observable that the germ is not developed according to any model existing in it either before or after impregnation. Herein, more evidently, though not more truly, than in the former characters, the germ-power differs from that supposed to be exercised in the formation effected by mere assimilation of organic matter, as in the maintenance of the perfect organism by nutrition. In this process, all the material that is added to a part is supposed to be fashioned according to the model, and under the influence, of that in which it is inserted. In the germ, the future being and all its parts may be said to exist in power and tendency, but none is there in model or in rudiment. Even when far developed, and when just about to manifest its highest force, the germ appears scarcely more than a mere mass of similar and indifferent cells. But, presently, its cells concur to develope themselves into the several different members of a body, like that of their parent, when that parent was an embryo; and thenceforward all the cells that descend from these, and all the material that is added to the embryo, are developed into the likeness of the same parent at the successive and corresponding stages of its development. But, in no instance, in all the development of the embryo, is a part formed in precise imitation of one already present,—in no instance is there mere assimilation: the only model after which each germ is developed is that type, according to which, from the first, and by the Divine appointment, all the generations of its ancestors have been constructed.

Such are some of the characters that distinguish the operations of the impregnated germ in its development to the perfect form. These are such as few would endeavour to explain by a cell-theory, or by any doctrine of assimilation; for these, I suppose, all would admit that some peculiar power, issuing from the properties of a germ, is necessary.

But with the acquirement of this perfection, the power of the germ seems to be considered as terminated—at least in the higher animals; and the usual expressions of modern physiology would imply that henceforward, the power which acts in the maintenance and repair of the perfected body is not the same in either kind or measure as that which actuated the development of the germ. But let us now see whether we can be content with the explanation that is commonly given of this maintenance of the body.

The accepted doctrine in physiology seems to be, that each structure in the body has the power of taking from the blood, by a kind of elective affinity, certain appropriate materials, and of so influencing them that they assimilate themselves to it; *i. e.* they adopt or receive its form and properties, and incorporate themselves with it; or else it is held that each cell or structural element of a part, while developing itself into some higher form, leaves behind or produces germs, cytoblasts, or off-shoots, which shall pass through the same development as itself, and in due time succeed to its place and office.

Now, without doubt, the existence of such forces is justly assumed, and we may, by the help of these hypotheses, express correctly a part of the processes by which the maintenance of the body in its perfection is accomplished. The power of living parts to incorporate and assimilate to themselves new materials, seems proved by those instances, among many, in which an alteration, being once effected in the properties of a part, is maintained through life, although all the particles on which the alteration was originally effected may have passed away and been succeeded by new ones. Thus, *e. g.* the poison of small-pox or of scarlatina, being once added to the blood, presently affects the composition of the whole: the disease pursues its course, and, if recovery ensue, the blood will seem to have returned to its previous condition: yet it is not as it was before; for now the same poison may be added to it with impunity. In this respect, at least, it has been changed: it is no longer liable to the influence of that which, lately, could disturb the whole order of its life. What the change is that has passed on the blood in these and many similar cases,* we know not; but the change, once effected, may be maintained through life. And herein seems to be a proof of the assimilative force in the blood; for there seems no other mode of explaining these cases than by admitting that the altered particles have the power of assimilating to themselves all those by which they are being replaced: in other words, all the blood that is formed after such a disease deviates from the natural composition, so far as to acquire the peculiarity engendered by the disease: it is formed according to the altered model.

Again, as regards the maintenance of the body by the development of the successive germs or cytoblasts of previous structures, or of the offspring of persistent germs or germinal centres,—this may be established (at least as a reasonable hypothesis) by such cases as those of the human teeth, and hair, and the like. In these, each productive organ, while developing itself, gives off that which may serve for its reproduction, *i. e.* for the construction of its successor; and, from the analogy of the ordinary development of germs, we may say that in this rudimental structure there is the power necessary for the production of a new organ. We may, indeed, be nearly sure of it; because, if the germ be uprooted, the new organ is not formed.

With such evidence, we may admit the existence of the forces which are assumed in the doctrine of organic assimilation, and of the succession of tissue-germs. Still it is, I think, proveable that such forces are not sufficient for the maintenance of the body in its perfection; and that, even where they do tend towards that end, or are essential to it, they act in subordination to that power which we recognise as determining the impregnated germ in its development, and as diffused through all the structures issuing from the germ.

For, in the first place, it is to be observed, that these usually received explanations of the maintenance of the several parts of the body in nutrition assume the existence, either of some structure to which, as to a model, the new materials may be made like; or, else, of something of the nature of a tissue-germ, which may be developed after the model of that from which itself was formed. Both assume a present, or lately present, model. But there are many instances in which new structures are formed for the maintenance of the body, where there is no model according to which the forming matter may shape itself, nor any parent-cell from which a reproducing germ may spring. Such are all the instances of formation for which, in a former course of lectures,* I suggested the term of "nutritive repetition," to distinguish them from the examples of nutritive reproduction such as I have just mentioned. I then referred, for illustration, to the

* Such as are enumerated in the "Lectures on Nutrition," &c. in the MEDICAL GAZETTE, 1847.

* MEDICAL GAZETTE, 1847.

different modes in which sets of teeth may succeed each other. In our own case, as the first or deciduous tooth is being developed, a part of its productive capsule is detached, and serves as a germ for the development of its successor; in which successor the first tooth may be said to be reproduced. But in such jaws as the shark's, and most other fishes, in which we see row after row of teeth succeeding each other, the row behind is not formed of germs derived from the row before, but the front row is repeated in the second, the second in the third, and so on.

This instance of nutritive repetition is one of a large class of similar facts. The new blood-corpuscles, that are being constantly formed for the renovation of the blood, are not developed from germs given-off from the old ones; neither are they formed by any assimilative force exercised by the old ones. By watching the stages of their construction, we may really see that the development of each is an independent repetition of the process by which the first was formed.* And so with the successive developments of ova and epithelial cells, and many others,—each is developed independent of the rest, and each repeats the changes through which its predecessor passed.

It is useless to multiply instances; else they might be very numerously cited; and, numerous as they are, the theory of nutrition by assimilation, or by the development of successive cytoblasts, is inapplicable to them all,—not merely insufficient, but inapplicable; for a postulate of this theory is the existence of a present model or germ for the construction of the forming part; and in all these cases no such germ or model can be found.

But, on the other hand, when it appears that the development of each new part is a repetition of the development of its predecessors, and even of the first-formed among them, then surely we may admit that they are all, from first to last, formed by the continuous operation of the same power,—the power which begins to work in the impregnated germ, and continues acting for the maintenance or the successive orderly changes of the forms it first constructed.

But I have said that, in instances in which we may discern the operation of an assimilative force, or the existence of cytoblasts or tissue-germs, we must also admit that these are controlled by the same power derived from the embryo-germ. I will adduce but two examples. I have mentioned, as the best instance of an assimilative force, the persistence of alterations once produced by disease in the blood or any tissue; but we know that after a time these alterations are often obliterated, and the blood or tissue returns to its perfect state. By what power? —Not by that of assimilation: that should keep it always the same; we cannot understand assimilation as effecting only a near resemblance; it must produce the very image. By what power, then, is the natural state restored? surely it must be by the same power which determined the whole course of development, from the very germ, which was for a time subjugated by the effects of the disease, but now again brings the diseased part to the same condition as it would have been in, had no morbid change been effected in it.

Again, we speak of the germs of tissues as enough to explain the formation, or reproduction, of the second tooth, and the successive generations of hairs, of muscular fibres, and some other tissues. But, to take the second tooth for an example of this class of cases: it is not like the first, from whose formative organs it derived its germ, but like the corresponding second tooth of the parent. What, then, determined this difference? Not, surely, the independent power of the germ or gemmule derived from the sac of the first tooth, for it is the essential character of germs to imitate precisely in their development those forms from which they sprang.

The teeth herein present an instance of a general rule, that changes supervene as the replacing elements of tissues succeed to one another. In every tissue, for example, the progress of age makes differences. In the continual mutation of particles by which each tissue is maintained in ordinary nutrition, there is a gradual change of form or composition, and the old tissues are manifestly different from the young. Such changes are equally inconsistent with the doctrine of assimilation, and with that of the successive development of tissue-germs; for the powers assumed in these hypotheses could do nothing but produce from first to last the self-same forms.

Thus, then, in nutrition we find many instances in which the doctrines of assimilative force and of tissue-germs are quite inapplicable: in many more, where such forces as they assume do operate, they yet seem insufficient for the end attained. But the same things which thus prove the insufficiency of these doctrines, are evidences for the truth of that which I have endeavoured to maintain. Especially so are those gradual changes which ensue as life advances; for these, you will observe, answer to all those which were noted as characters of the operation of germ-power. Thus, they are all, in each individual, repetitions of the changes which, in corresponding times, occurred in its progenitors. These changes,

* The process is described in Kirkes' Physiology, p. 65, from the Lectures on the Life of the Blood, delivered in 1848.

as much as any of the stages of earlier development to perfection, occur in conformity with a specific law: they are as much marks of specific character as are any of the earlier transitions, or the perfect features of the individual. In all instances, moreover, the formative processes of the full and later life are limited, as in the germ, to certain periods and methods of development or degeneration; in all, the changes that ensue are concurrent and commensurate in many parts, yet, in each, they are independent of the rest; and they are all effected without any present model.

On the whole, then, since we see that the continual mutation of particles for the growth and maintenance of the living body by nutrition manifests, in all essential things, the peculiar features that characterised the first formation of the same body from the germ, we seem justified in holding that it is one and the same power which, being maintained continuously from the germ to the latest period of normal life, determines all organic formation. Whatever be the properties of the germ from which this formative power emanates, they must, in due measure, be communicated to all the materials that the germ appropriates, and, successively, to all that enter into the construction of the developing body; so that in all its living parts there is a measure of the same power as was most vividly concentrated in the germ. Under this power, the organic assimilative force, in some instances, and the production of successive tissue-germs in others, appear to work as subordinate agents; but in many instances, as in the formation of blood, the power seems to act more directly upon amorphous organic matter, which in the perfect body, as in the germ, it informs according to the law of specific character.

If what has been said appear sufficient to prove the operation of the germ-power in the ordinary maintenance of the body, *i. e.* for the reproduction of particles which are absorbed or cast off at the term of their natural life, then more than sufficient evidence for the same opinion will appear in the phenomena of repair and reproduction after injuries. These, occupying, as it were, a middle place between the phenomena of embryonic development and those of ordinary nutrition, have of late been alternately, or in different instances, referred to one or the other of the different powers by which those phenomena are supposed to be governed. But, probably, the likeness of the phenomena of reproduction to those of both nutrition and embryonic development should have suggested, as they did to Blumenbach and Treviranus,* that all the three are manifestations of one and the same power. That they are so, will be evident, I think, in what I shall have to describe in the following lectures. For, 1st. it will be clear that repair and reproduction cannot be in any case explained as the result of assimilation or by the succession of tissue-germs. In grave injuries and diseases, the parts that might serve as models for the new materials to be assimilated to, or as tissue-germs to develope new structures, are lost or spoiled; and yet the effects of injury and disease are recovered from, and the right specific form and composition are regained. And, secondly, if we watch the manner in which the recovery is achieved, we shall discern in it all those characters which mark the operations of the power of the germ. We shall see that the reproduced parts are formed, not according to any present model, but according to the appropriate specific form, and often with a more strikingly evident design towards that form, as an end or purpose, than we can discern in the natural construction of the body. We shall see, too, that in this re-formation there is an independent, though concurrent, development of many parts; and that the whole process is limited by the same restrictions of time, and space, and exact method, as those observed in the original development of the parts. This, also, may be added to the arguments already adduced to prove the continuous action of the germ-power through life, and its slight variation therein; that when, in an adult animal, a part is reproduced after injury or removal, it is made conformable, not to that condition which was proper to it when it was first formed, or in its infantile life, but to that which is proper according to the time of life in which it is reproduced—proper, because like that which the same part had, at the same time of life, in members of former generations. In the reproduction of the foot or the tail of the lizard, they grow, as it were, at once into the full dimensions proper to the part, according to the age of the individual. Spallanzani expressly mentions this: — that when a leg is cut from a full-grown salamander, the new leg and foot are developed, as far as form and structure are concerned, just as those of the larva were; but as to size, they from the beginning grow and are developed to the proper dimensions of the adult. The power, therefore, by which this reproduction is accomplished, would seem to be, not the mere revival of one which, after perfecting the body, had lapsed into a dormant state, but the self-same power which, before the removal of the limb, was occupied in its maintenance by the continual mutation of its particles, and now engages itself, with more energy, in the reconstruction of the whole.

* Biologie, iii. 522.

The power to repair the damages sustained by injury, and to reproduce lost parts, appears to belong, in some measure, to all bodies that have definite form and construction.' It is not an exclusive property of living beings; for even crystals will repair themselves when, after pieces have been broken from them, they are placed in the same conditions in which they were first formed. I know not what amount of mutual illustration, if any, the repair of crystals and living bodies may afford; but, in any case, we may trace here something like an universal property of bodies that are naturally and orderly constructed: all, in favourable circumstances, can repair at least some of the damages to which they are liable from the violence of external forces.

But, to speak only of the repair and reproduction that occur in the several orders of the animal kingdom: among these they exist in singularly different degrees, and in such as can be only partially included in rules or general expressions. The general statement sometimes made, that the reparative power in each species bears an inverse ratio to its position in the scale of animal life, is certainly not proved; and many instances are contrary to it, such as the great reparative power possessed by the Triton and other lizards, and the apparently complete absence of it in the perfect insects. Rather, the general rule which we may expect to find true, and for which there is already much evidence, may be, that the reparative power bears an inverse proportion to the amount of germ-power consumed in the development and growth of the individual, and in its maintenance in the perfect state.

Our ideas of the consumption of power in the organization of matter, are, perhaps unavoidably, very vague: yet are there facts enough to prove that the power which can issue from the mysterious properties of a germ is limited; that it is not ever communicated to an indefinite quantity of matter; and there are enough to justify the hypothesis, that the germ-power, thus limited, is in some measure consumed in the development of every new structure, and, in a less measure, in the growth and maintenance of those already formed. The instances to which I shall refer are explicable on this hypothesis, and are, therefore, evidences of its probability.

First, then, it appears constantly true, that the reparative power is greater in all parts of the young than of the older individuals of all species. Even when we compare individuals that have all attained their highest development and growth, this rule seems to be true. We know it from general observations of the results of similar injuries and diseases in persons of different ages: numerous as the exceptions may be, the general rule seems true. And it is yet more evidently proved in the case of some lower animals. Spallanzani mentions it expressly in regard to the reproduction of the tail of the tadpole. The quickness with which the work of reproduction is both begun and perfected, was always, in his experiments, in an inverse ratio to the age of the tadpole. He says the same for the reproduction of the legs of salamanders, and it is only in young frogs and toads that any reproduction of the limbs will take place. So, too, in experiments on the repair of fractures, the union of tendons and the like, in the Mammalia: one may see abundant evidence that the vigour and celerity of the process are in an inverse proportion to the animal's age. There is, indeed, some reason to believe, that in the very early period of embryonic life, a true reproduction of parts of limbs may take place, even in the human species; for (not to speak of the possibility that supernumerary members may sometimes have been formed in consequence of accidental fission of the budding limbs of the embryo), there are some cases in which fingers are found on the stumps of arms in such circumstances as justify the belief that after a limb had been accidentallly amputated in the uterus, these had been produced on its remaining portion.

All these facts agree well with the belief that the germ-power is gradually diminished in the acts of organizing matter for the maintenance of the body; and the difference between the reparative power in children and that in adults appears so much greater than the difference in adults of different ages, that it is probable the germ-power is more diminished by growth than by mere maintenance.

However this may be, it seems certain that the capacity for the repair or reproduction of injured parts is much more diminished by development than by growth or maintenance of the body; *i. e.*, much more by those transformations of parts by which they become fitted for higher offices, than by the multiplication or maintenance of those that are already perfect in their kind and function. In other words, to improve a part requires much more, and more perfect, formative power, than to increase it does.

This, as a general principle, is exemplified in many instances. In the greater part of congenital malformations we find arrest of development, but no hindrance of growth; as a heart, in which a septum fails to be developed, yet grows to its full bulk. So, if tadpoles be excluded from due light and heat, their development will be much retarded, but their growth will be less checked. So, too, in the miscalled cultivation and improvement of flowers, growth is increased, but development is hindered; and an excess of coloured leaves is formed, instead of the due number of male and female organs. Or again, in an old ulcer or a sinus, cells may be continually reproduced, maintaining or even increasing the granulations, yet they will not develope themselves into cellular tissue and cuticle for the healing of the part; and so, even when repair and reproduction have gone far towards their ultimate achievement, that which takes a longer time, and oftener fails, is the improvement, the perfecting, of the new material, by its final development. This is observed in all cases of reproduced limbs, and even in ordinary scars.

These facts (and there are many others like them) seem to justify the expression that, not only more favourable conditions, but also a larger amount of organizing force, is expended in development than in growth. If we may thus interpret the facts, they will be collateral evidence for the belief that, in different species of animals, the reparative power will bear an inverse ratio to the amount of development already passed through; so that, for each species, in its perfect state, the reparative power might be measured by the degree of likeness between the embryonic and the perfect form, structure, and composition. The greater the sum of dissimilarities in all these respects between the embryo and the perfect animal, the less seems to be the reparative power in the latter.

It is consistent with this that the highest amount of reparative power exists in those lowest polypes, in which, as my Colleague has so ably argued, the materials of the germ-mass yet remain, not transformed, but multiplied, and, as it were, grouped into the shape of their bodies. In the fresh-water Hydra, the power of the germ appears communicated without loss to all the cells that descend by multiplication from the original germ-cells; provided only the cells are not developed into higher forms or into subserviency to special functions. In the Hydra viridis, and Hydra fusca, it seems literally true that any minute cluster of cells, derived by mere multiplication from those of the germ-mass, may, after being separated from the perfect body, reproduce the perfect form. This is the general truth of the numerous experiments performed on Hydræ by Trembley, Roesel, and others. They have been so often quoted, that I need not do more than mention the greatest instances of reproductive power that they showed.

Trembley cut an Hydra into four pieces: each became a perfect Hydra; and while they were growing, he cut each of these four into two or three. These fractions of the quarters being on their way to become perfect, he again divided these, and thus he went on, till from the one hydra he obtained fifty. All these became perfect; he kept many of them for more than two years, and they multiplied by their natural gemmation just as much as others that had never been divided. So that a division by fifty did not perceptibly diminish the power of the germ present in the polype that was thus subdivided. Again, he cut similar polypes longitudinally, and in an hour or less each half had rolled itself, and seamed up its cut edges, so as to be a perfect Hydra. He split them into four,—he quartered them,—he cut them into as many pieces as he could, and nearly every piece became a perfect Hydra. He slit one into seven pieces, leaving them all connected by the tail, and the Hydra became seven-headed, and he saw all the heads eating at the same time. He cut off the seven heads, and, hydra-like, they sprang forth again. And even the fabulist dared not invent such a prodigy as the naturalist now saw. The heads of the Lernæan Hydra perished after excision: the heads of this hydra grew for themselves bodies, and multiplied with as much vigour as their parent-trunk.

Now these instances may suffice to show that in the lowest polypes the process of reproduction after injury confounds itself with that of their natural generation by gemmation, or, as it probably more rarely happens, by spontaneous fission. We cannot discern a distinction between them; and there are some things which seem to prove the identity of the power which operates in both. Thus, in both alike, the formative power is limited according to the specific characters of the Hydra: immense as the power of increase is, which may be brought into action by the mutilations of the Hydra, yet that power cannot be made to produce an Hydra of much more than ordinary size, or to raise one above its ordinary specific characters. And again, the identity of the power is shown in this,—that the natural act of gemmation retards that of reproduction after injury. Trembley particularly observes, that when an Hydra, from which the head and tentacula had been cut off, gemmated, the reproduction of the tentacula was retarded soon after the gemmule appeared.

The instance of the Hydra is only one of many proving it to be a general law, that a large power of repair and reproduction after injury exists in the species in which propagation by spontaneous fission, or by gemmation, is possible. I need not say how consistent this is with Professor Owen's doctrine,—that Partheno-genesis, or the capacity of generating without previous impregnation of the parent, is dependent on a retention of a part of the original germ-cells, or of their direct and untransformed descendants, within the body of that parent. Wherever such cells are, there is the power, without the need of impregnation, of producing a new individual; and in all the instances in which such cells form part of the general substance or parenchyma of the body, an injury may be said to act only as a stimulus, exciting the premature exercise of a ready power, which, in the natural case, appears as the generative, but, in the accidental case, appears as the reparative power.

I need not enumerate the species which manifest this coincidence of the power of propagating by gemmation or fission, and of reproducing large portions of the body, and even of reconstructing, from fragments, the whole body. They include, as chief examples, the Actiniæ, which after bisection form two perfect individuals,—and the Holothuriæ, which, as Sir J. G. Dalyell has observed, when hurt or handled, will eject all their viscera, leaving their body a mere empty sac, and yet in three or four months will have all their viscera regenerated. They include, also, from among the Anellata, the young Nereids, and those species of Nais, on which Bonnet, Spallanzani, and others, made their marvellous experiments,—experiments of which the climax seemed to be achieved when a Nais was cut by M. Lyonnet into thirty or forty separate pieces, and there were produced from those fragments as many perfect individuals.

Instead of dwelling on these instances, let me mention some observations, made by Sir J. G. Dalyell, upon other polypes, which seem calculated to illustrate in a remarkable manner the general laws of the reparative processes in even the higher animals.

In the Hydra Tuba,—the species of which he has traced that marvellous development into Medusæ,—he has found that when cut in halves, each half may regain the perfect form ; but this perfect form is regained only very slowly, and, as it were, by a gradual improvement of parts that are, at first, ill-formed. The diagram, copied from his plate, shows these stages of improvement. The fact may possibly be explained (as he suggests) by the mutilation having disturbed the progress of the Hydra in its development of young Medusæ ; for the experiment was made in March, nearly at the time when the series of changes should have commenced. But, if I may venture not to accept the suggestion of so admirable an observer, I should suspect rather that this is an instance of gradual recovery of perfection, such as we see more generally in the repair of injuries and diseases in the higher animals.

He has noticed something of the same kind, and more definite, in the Tubularia indivisa, one of his experiments on which is illustrated by this diagram, copied from his representation of it. A fine specimen was cut near its root, and after the natural fall of its head, the summit of its stem was cloven. An imperfect head was first produced, at right angles to the stem, from one portion of the cleft ; after its fall, another and more nearly perfect one was regenerated, and, as it grew, improved yet more. A third appeared, and then a fourth, which was yet more nearly perfect, though the stem was thick, and the tentacula imperfect. The cleft was almost healed ; and now a fifth head was formed quite perfect ; and after it, as perfectly, a sixth and seventh head. All these were produced in fifteen months.

The lower half of this specimen had been cut off four months after the separation of the stem. Its upper end bore—first, an abortive head ; then secondly, one which advanced further in development ; a third, much better ; and then, in succession, other four, which were all well formed.

The upper portion of this lower half of the stem now shewing signs of decay, a portion was cut from its lowest part, and further manifested the reproductive power of the stem ; for three heads were produced from the upper end of the piece cut off, and four from the lower end of the upper piece which had seemed to be decaying. In 550 days this specimen had grown 22 heads.

Now, I cannot but think that we have, in these instances of gradual recovery from the effects of injury, a type of that gradual return to the perfect form and composition, which are noticed in the higher animals. Our theory of the process of nutrition leads us to believe that in the constant mutation of particles in nutrition, those elements of the blood, or of any structure that have been altered by disease, in due time degenerate or die, and are cast off or absorbed, and that those which next succeed to them partake, through the assimilative force, of the same morbid character ; but that, every time of renewal, the new particles, under the influence of the germ-power, approach a step nearer to the perfect state. Thus, as it were, each generation of new particles is more nearly perfect, till all the effects of the injury or the disease are quite obliterated. Surely, in the gradual recovery of perfection by these polypes, we have an apt illustration of the theory,—one which almost proves its justice.

The power of reconstructing a whole and perfect body, by the development of a fragment, is probably limited to the species that can propagate by spontaneous fission or gemmation, or that increase their size, as some of the Anellata do, by the successive addition of rings that are developed after the manner of gemmules from those that precede them. Where this power is not possessed, there, whatever be the position of the species in the animal scale, the reparative power appears to be limited to the reproduction of lost members, — as legs, claws, a part of the body, the head, an eye, the tail, and the like: yet, within this limit, the rule seems again to hold good,—that the amount of reparative power is in an inverse ratio to that of the development, or change of structure and mode of life, through which the animal has passed in its attainment of perfection, or on its way thitherward.

Here, however, even more than in the former cases, we need, not perhaps more experiments, but experiments on a larger number of species. It appears generally true, that the species whose development to the perfect state is comparatively simple and direct, have great reparative powers; while many, at least, of those in which the development is with such great changes of form, structure, and mode of life, as may be called metamorphosis, retain in their perfect state scarce any power for the repair of losses. Yet we want more instances of this; and especially, it were to be wished that we had the results of experiments upon the lowest animals that pass through such metamorphoses *e. g.* on the Hydra Tuba, not only in its Hydra state, but in all the changes that succeed, till it attains its complete Medusa form.

In the absence of such evidence as experiments of this kind might furnish, the best examples of this rule are furnished by the experiments of Mr. Newport. They show that among the insects, the reparative power, in the complete state, is limited to the orders in which that state is attained by a comparatively simple and direct course of development—as the Myriapoda and Phasmidæ, and some of the Orthoptera. These can reproduce their antennæ, and their legs, after removal or mutilation; but their power of reproduction diminishes as their development increases, — and, even in the Myriapoda, whose highest development scarcely carries their external form beyond that of the larvæ of the more perfect insects,—even in these, such reparative power apparently ceases, when, after the last casting of their integuments, their development is completed.

In the higher hexapod insects, such reproduction has been seen in only the larval state,—none of them, in its perfect state, can reproduce an antenna, or any other member. The Myriapoda, then, are, in their reparative power, equal to the larvæ of the higher insects, and nearly all the germ-power which these manifest, appears to be exhausted in the two later metamorphoses.

The case is the stronger, as illustrating the expenditure of germ-power in metamorphoses, when the higher insects are compared with the Arachnida; for in these, which attain their perfect state through more direct development, the reparative power remains equal to the reproduction of limbs and antennæ. A yet stronger contrast is presented between the higher insects and the several species of salamander in which so profuse a reproduction of the limbs has been observed; for though they be so much higher in the scale of animal life, yet the amount of change in external form and habits of life through which they pass in their development from the embryo to the perfect state appears less than that accomplished in the metamorphoses of insects.

Many instances, besides those which I have cited, appear to support this rule, that the reparative power in each perfect species, whether it be higher or lower in the scale, is in an inverse proportion to the amount of change through which it has passed in its development from the embryonic to the perfect state. And the deduction we may make from them is, that the power for development from the embryo is identical with that exercised for the restoration from injuries: in other words, that the power is the same by which perfection is first achieved, and by which, when lost, it is recovered.

This is, again, generally confirmed in the instances of the Vertebrata; but of the repair in these, or at least in the highest of them, I shall have to speak so exclusively in the future lectures, that I will now only say that, in the highest Vertebrata, and in man, a true reproduction after loss or injury seems limited to three classes of parts:—

1. To those which are formed entirely by nutritive repetition,—such as the blood and the epithelia.

2. To those which are of lowest organization, and (which seems of more importance) of lowest chemical character,—as the gelatinous tissues, the cellular and tendinous, and the bones.

3. To those which are inserted in other tissues, not as essential to their structure, but as accessories, as connecting or incorporating them with the other structures of vegetative or animal life,—such as nerve-fibres and blood-vessels.

With these exceptions, injuries or losses in the human body are capable of no more than repair, in its more limited sense; *i. e.* in the place of what is lost, some lowly organized tissue is formed, which fills up the breach, and suffices for the maintenance of a less perfect life.

I may thus state the sum of what I have endeavoured to establish. We recognise in the impregnated germ properties which, in favourable conditions, issue in the manifestation of a power capable of developing it into the perfection of a certain specific form and structure: that perfection is maintained through part of the life of the complete being, and is maintained by means, to the explanation of which the accepted doctrines of the assimilative force and of the successive development of tissue-germs are either inapplicable or insufficient. But its maintenance is explicable with the hypothesis that the same power as that which was manifested in the development from the germ is still in action, and actuates, as it did in the germ, all organization in conformity with the law of the specific character. So, too, the gradual changes that ensue in the course of life, after the attainment of the most perfect state, may be referred to the continuous operation of the same power, modified in each individual according to the specific type which has been observed in all the members of the same species. And, finally, the same power, working with an apparently increased energy, determines the restoration of lost parts, and the repair of injuries,—working, in all cases, towards the restoration of the perfection of the specific form, by the same means, and in the same method, and within the same limits.

There are yet some topics which I will crave your indulgence that I may suggest for your consideration, if only as an apology for a lecture in which I may seem to have been discussing doctrines that can hardly be applicable to our daily practice, and with illustrations drawn from objects in which, as surgeons, we may have but little interest. Let me, then, express my belief that, if ever we are to escape from the obscurities and uncertainties of our art, it must be through the study of those highest laws of our science, which are expressed in the simplest terms in the lives of the lowest orders of creation. It was in the search after the mysteries — that is, after the unknown highest laws—of generation, that the first glance was gained of the largest truth in physiology—the truth of the development of ova through partition and multiplication of the embryo-cells. So may the study of the repair of injuries sustained by the lowest polypes lead us to the clearer knowledge of that law, in reliance upon which alone we dare to practise our profession,—the law that lost perfection may be recovered by the operation of the power by which it was once achieved. Already, in the facts that I have quoted from Sir Graham Dalyell, we seem to have the foreshadowing of the facts through which the discovery may be made.

And let us not overlook those admirable provisions which we may find in the lives of all that breathe, against injuries that, but for these provisions, would too often bring them to their end before their appointed time, or leave them mutilated to complete a painful and imperfect life. We are not likely to undervalue, or to lose sight of, the design of all such provisions for our own welfare. But we may better appreciate these if we regard them as only of the same kind as those more abundantly supplied to creatures whom we are apt to think insignificant: indeed, so abundantly that, as if with a consciousness of the facility of repair, self-mutilation is commonly resorted to for the preservation of life. When the Ophiura, or any of the brittle Star-fishes, break themselves to fragments, and disappoint the grasp of the anxious naturalist, they probably only repeat what they are instinctively taught to do, that they may elude the jaws of their more ravenous enemies. But death would be better than such mutilation, if their rays could not be reproduced almost as easily as they can be rejected. The experimentalist, too, who cuts off one or the other end of any of the Anellata, perhaps only puts them to a necessity to which they are liable from the attacks of their carnivorous neighbours. Almost defenceless, and so easily mutilated, their condition, were it not for their faculty of reproduction, might be more deplorable than that of any other creature; and even their existence as species might have been endangered long ago. It would almost seem as if the species that have least means of escape or defence from mutilation were those on which the most ample power of repair has been bestowed;—an admirable instance, if it be only generally true, of the beneficence that has provided for the welfare of even the least (as we call them) of the living world, with as much care as if they were the sole objects of the Divine regard.

Lastly, if I may venture on so high a theme, let me suggest that the instances of recovery from disease and injury seem to be only examples of a law yet larger than that within the terms of which they may be comprised,—a law wider than the grasp of science,—the law that expresses our Creator's will for the recovery of all lost perfection. To this train of thought we are guided by the remembrance that the healing of the body was ever chosen as the fittest emblem of His work whose true mission was to raise man's fallen spirit and repair the injuries it had sustained; and that once, the healing power was exerted in a manner purposely so confined as to advance, like that which we can trace, by progressive stages to the complete cure. For there was one, upon whom, when the light of Heaven first fell, so imperfect was his vision, that he saw, confusedly, "men, as trees walking;" and then, by a second touch of the Divine Hand, was "restored, and saw every man clearly." Thus guided by the brighter light of revelation, it may be our privilege, while we study the things of which I have been speaking, to gain, by the illustrations of analogy, a clearer insight into the Oneness of the plan by which things spiritual and corporeal are directed. Even now, we may trace some analogy between the acts of the body and those of man's intellectual and moral nature. As in the development of the germ, so in the history of the human spirit, we may discern a striving after perfection,—after a perfection, not viewed in any present model (for the human model was marred almost as soon as it was formed), but manifested to the enlightened Reason in the "Express Image" of the "Father of Spirits." And so, whenever, through human frailty, amid the violences of the world, and the remaining "infection of our nature," the spirit loses aught of the perfection to which it was once admitted, still its implanted Power is ever urgent to repair the loss. The same Power, derived and still renewed from the same Parent, working by the same appointed means, and to the same end, restores the fallen spirit to nearly the same perfection that it had before. Then, not unscarred, yet living—"fractus sed invictus"—the Spirit still feels its capacity for a higher life, and presses to its immortal destiny. In that destiny the analogy ends. We may watch the germ-power developing the body into all its marvellous perfection and exact fitness for the purpose of its existence in the world; but, this purpose accomplished, it passes its meridian, and then we trace it through the gradual decay of life and death. But, for the human Spirit that has passed the ordeal of the world, there is no such end. Emerging from its imprisonment in the body, it soars to the element of its higher life: there, in perpetual youth, its powers expand, as the vision of the Infinite unfolds before it; there, in the very presence of its Model, its Parent, and the Spring of all its Power, it is "like Him, for it sees Him as He is."

LECTURE II.

The materials provided for the repair of injuries in the human body. Division of injuries into open and subcutaneous. Modes of healing of open wounds—by immediate union—by primary adhesion—by granulations—by secondary adhesion—by scabbing. Modes of healing of subcutaneous wounds — by immediate union—by connection, mediate union, or bonds of new substance.

Part taken by extravasated blood in the healing of injuries—its frequent absence—its various disposal when present—its ejection, absorption, or organization. Coagulable lymph the general material for repair by new substance—its chemical and vital properties. Probability of the existence of two varieties of lymph, characterized by their different modes of developement into connective tissue—the one, as formed in open wounds, being developed through nucleated cells; the other, as formed in subcutaneous wounds, through nucleated blastema. Similarity of these modes to the developements of the same tissue in other instances—relations of each of them to the process of inflammation and to suppuration.

In the present lecture, I propose to give a general account of the materials employed for the repair of some of the injuries inflicted on the human body.

I hope I do not err in thinking that the most advantageous mode of treating this subject will be to confine myself to that class of injuries which may be called visible breaches of continuity; such as wounds and fractures. For, in regard to the recovery from diseases, our knowledge of the effects of any disease seems, as yet, too imperfect for us to trace the stages by which the morbid state reverts to that which is healthy. We may be sure it is in conformity with the same general laws as those of recovery from injury, and almost sure that it is by the operation of the remaining germ-power, improving gradually the particles that in succession replace those altered by disease. But the whole details of the process have yet to be discovered.

Even within the narrower field of the repair of breaches of continuity, I must yet assign to myself a closer limit. A future lecture will be devoted to the healing of fractures; in this, therefore, I shall speak almost exclusively of the healing of divided soft parts; and I shall take as the chief and typical examples the repairs of wounds made in operations. References to the healing of other injuries may, however, be made by the way, and for collateral illustration.

Recent improvements in surgery have shown how right Mr. Hunter was, when, in the very beginning of his discussion concerning the healing of injuries, he points out, as a fundamental principle, the difference between those two forms of injuries of which one is subcutaneous, the other open to the air. He says: "The injuries done to sound parts I shall divide into two sorts, according to the effects of the accident. The *first* kind consists of those in which the injured parts do not communicate externally, as concussions of the whole body, or of particular parts, strains, bruises, and simple fractures, which form a large division. The *second* consists of those which have an external communication, comprehending wounds of all kinds, and compound fractures."* And then, he says, "The injuries of the first division, in which the parts do not communicate externally, seldom inflame; while those of the second commonly both inflame and suppurate."

In these sentences Mr. Hunter has embodied the principle on which is founded the whole practice of subcutaneous surgery; a principle of which, indeed, it seems hardly possible to exaggerate the importance. For, of the two injuries inflicted in a wound, the mechanical disturbance of the parts, and the exposure to the air of those that were covered, the exposure, if continued, is the worse. Both are apt to excite inflammation; but the exposure excites it most certainly, and in the worse form; *i. e.* in the form which most delays the process of repair, and which is most apt to endanger life. Abundant instances of this are shown in the difference between a simple and a compound fracture, though the former may have been produced by the greater violence; or, between a single fracture, even with much violence, extending into a joint, and an open wound, never so gently made into one. Or, for parallel instances, one may cite the rarity of suppurations after even extensive ecchymoses, and their general occurrence when wounds are left open.

I have lately had frequent occasion to observe these differences, in a series of experiments made for the illustration of the healing

* Works, vol. iii, p. 240.

of divided muscles and tendons. Some of these were divided through open wounds, and some by subcutaneous section; and the present specimens afford a fair example of the difference of results that often ensued. In the same rabbit, the tibialis anticus and extensor longus digitorum were divided on the right side with a section through the skin; on the left, with a subcutaneous section, through a small opening. Twelve days afterwards the rabbit was killed. The wound on the left side is shown well repaired, and with comparatively little trace of inflammation; the gap on the right is closed in with a scab, and an imperfect scar, but under these is a large collection of matter, and no trace of a reparative process. The contrast is the stronger, because in all these cases there is, unavoidably, more mechanical violence inflicted in the gradual subcutaneous division than in the simple open wound. And, it must be added, that a speedy closure of the external wound made in an open section may bring the case into more favourable conditions, than those of a subcutaneous wound made with more violence. This, also, I saw in some of the experiments: a clumsy subcutaneous division of one Achilles-tendon excited great inflammation about it; while the open section of the other tendon in the same rabbit was quickly and well repaired, because the external wound had been speedily united, and had sufficiently soon converted the open into a subcutaneous injury.

Still, what Mr. Hunter said is true: subcutaneous wounds seldom inflame; open wounds generally both inflame and suppurate. It will be a principal object of this lecture to show something like an anatomical reason for this difference, in the fact that the materials produced for the repair of open wounds are not the same, or, at least, do not develope themselves in the same manner, as those for the repair of closed or subcutaneous ones.

Before speaking of the materials for repair, I must briefly state that the healing of open wounds may be accomplished by five different modes—namely, 1. By immediate union; 2. By primary adhesion; 3. By granulations; 4. By secondary adhesions, or the union of granulations; 5. By healing under a scab. The repair of subcutaneous wounds may be effected by immediate union, but is generally accomplished by connection, or the formation of bonds of union between the divided and retracted parts. Very rarely it is effected by means of granulations without suppuration.

Of these modes, which I hope to describe hereafter in detail, it is the peculiarity of the first, or process of immediate union, that it is accomplished by the mere re-union or re-joining of the divided parts, without the production or interposition of any new material. In all the others, new material is produced and organized. This process of immediate union corresponds with what Mr. Hunter called "union by the first intention." It is not the same as that which, in modern surgery, is called union by the first intention; for that is the same as Mr. Hunter named "union by adhesion," or "by the adhesive inflammation," and is effected, as he described it, by the organization of lymph interposed between two closely approximated wounded surfaces. Mr. Hunter maintained that union by the first intention is effected by means of the fibrine of the blood extravasated between the surfaces of the injured part, which fibrine, there coagulating, adheres to both the surfaces, becomes organized, and forms a vascular bond of union between them.* Doubtless, Mr. Hunter was, in this, in error; but, as the blood extravasated in wounds is not without influence on their repair, I will endeavour to state the several modes in which it may, when thus effused, be finally disposed of.

In my last course of lectures, I stated the evidences for believing that masses of effused, or stagnant and coagulated, blood may be organized; *i. e.* may assume the characters of a tissue, and may coalesce with the adjacent parts and become vascular. Among these evidences, several cases were mentioned in which such organization of blood had been distinctly traced; they included cases of blood effused in serous sacs, especially in the arachnoid, clots in veins organizing into fibrous cords, or, after less organization, degenerating into phlebolithes, clots organizing into tumors in the heart and arteries, and the clots so organized above ligatures on arteries as to form part of the fibrous cord, by which the obliterated artery is replaced. These last cases afforded the most conclusive evidence, because they had been very carefully investigated in a series of experiments and microscopic observations, by Dr. Zwicky.† In the course of last year I had the opportunity of examining a specimen which, more fully than any other I had seen, confirmed his account of the mode in which blood-clots become organized. It supplied, too, some facts which appear to me important to the present subject.

The specimen was obtained from an insane person, by my friend Mr. Holmes Coote. A thin layer of pale blood-coloured and ruddy membrane lined the whole internal surface of the cerebral dura mater, and adhered close to it. Its colour, the existence of patches of blood-clot imbedded in it, and all its other characters, satisfactorily proved that it had been a thin clot of blood,—an example of such as are effused in apoplexy of the cerebral

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* Works, vol. iii. 253.

† Ueber die Thrombus; Zurich, 1846.

membranes, of such as Mr. Prescott Hewett has so fully described in his paper in the Medico-Chirurgical Transactions. Numerous small vessels could be seen passing from the dura mater into this clot-membrane, and with the microscope, while they were still full of blood, I made a sketch from which the diagram was copied. The arrangement of blood-vessels bears a close resemblance, but, perhaps, more in its irregularity than in any positive characters or plan, to that which exists in false membrane formed of organized lymph: but the vessels were, I think, generally larger.

Such were the blood-vessels of this organized clot. Its minute structure showed characters which are of peculiar interest, because of their resemblance to those observed in the material that is commonly formed in the repair of subcutaneous injuries. In the substance of what else appeared like a filamentous clot of fibrine, sprinkled over with minute molecules, the addition of acetic acid brought into view corpuscles like nuclei, or cytoblasts, very elongated, attenuated, and, in some instances, like short strips of flat fibre. Of course, such corpuscles are not to be found in any ordinary clot of fibrine; neither are they seen in any stage of the organization of such lymph as is commonly effused in inflammation; but they exactly resemble such as may be found in certain examples of rudimental cellular tissue, and (among these) in the material for the repair of subcutaneous injuries. In short, the minute structure of this clot now organized was an example of what I shall have often to refer to under the name of "nucleated blastema."

With such evidence as this of the organization of a thin layer of blood-clot, and of the developement of its fibrine being apparently identical with that of the material commonly formed for the repair of subcutaneous injuries, it was with much surprise that I found that extravasated blood can, commonly, have no share at all in the repair of injuries.

One of the best proofs of this is, that scarcely the smallest portion of blood is effused in the cases in which the largest quantity of reparative material is produced in the shortest time, and in which the healing process is most perfectly accomplished. In twenty cases in which I have lately divided the Achilles tendon in rabbits, I have only once found, in the subsequent examinations, a clot of extravasated blood in the track of the wound. In this case, I believe, the posterior tibial artery was wounded: for in all others, and in similar divisions of muscles, unless a large arterial trunk, such as the anterior tibial, were cut, the only effusion of blood was in little blotches, not in separate clots, but effused or infiltrated in the cellular tissue near the wound. In some cases there was blood-stained infiltration of the inflammatory products, but in none were there such clots as could be organized into bonds of union. In short, parts thus divided scarcely bleed: what blood does flow escapes easily through the outer wound, as the surrounding tissues collapse into the space left by the retracting parts; or, what remains is infiltrated into the tissues, and forms no separate clot.

It is the same with fractures. In a large proportion of these, one finds no clots lying between the fragments where they are to be united, and only very small spottings of blood, like ecchymoses, in or beneath the periosteum. The abundant extravasations that commonly exist in the subcutaneous tissue are generally confined to it: they are not continued down to the periosteum or bone.

In all these cases, then, we have sufficient proof that extravasated blood is not necessary for union by the first intention, or for any other mode of repair, in the simple fact that where the repair is best, and the material for it most ample, no blood is so extravasated as to form a clot that could be organized.

But, though this may be the usual case, the question still remains—When blood is effused between wounded surfaces, and clots there, how are the clots disposed of? For often, though not generally, such clots are found in wounds, or between the ends of a broken bone, or a divided tendon when an artery by its side is cut; and in most operation-wounds, one sees blood left on them, or flowing on their surfaces, after they are done up. How, then, is this blood disposed of?

If effused in large quantity, so as to form a voluminous clot, and especially if so effused in a wound which is not perfectly excluded from the air, or if effused in even a subcutaneous injury in a person whose health is not good, it is most likely to excite inflammation; and the swelling of the wounded parts, or their commencing suppuration, will push it out of the wound. Thus we often see blood ejected.

But in more favourable circumstances it may be absorbed; and this may happen whether it have formed separate clots, or, more readily, when it is infiltrated in the tissues. What I have seen, however, in the experiments to which I have already referred, leads me to dissent from the account commonly given of the absorption of blood thus effused. The expressions generally used imply that the first thing towards the repair of such a wound is the absorption of the extravasated blood; and that then, in its place, the lymph or reparative material is effused. But this can hardly be the case; for the absorption of blood is a very slow process, and commonly requires as much time as would suffice for the complete healing of a wound, or even of a fracture. Not to mention the very slow absorption of the extravasations of blood in apoplexy, or in serous sacs, I have found the blood effused in the subcutaneous tissue and the muscles scarcely changed at the end of five weeks after a simple fracture; that in a tied artery as little changed after seven weeks; and even in common leech-bites we may sometimes find the blood-corpuscles in little ecchymoses unchanged a month after their extravasation: yet in much less time than this it is commonly implied that all the blood extravasated in an injury is cleared quite away, that lymph may occupy its place. My impression is that this opinion rests on imperfect observations. Blood is supposed to be effused in all subcutaneous injuries; and where it is not found, it is supposed to have been absorbed; the truth, rather, being that where no blood appears, none ever was.

The true method of the absorption of blood seems to be, that it is enclosed within the effused reparative material, and absorbed by the vessels of that material as its organization proceeds. The best instance in support of this that I have seen was in the case of an Achilles tendon divided subcutaneously six days before death. The reparative process had proceeded favourably, and as strong a band of union as is usual at that period was formed of the new reparative material effused between the retracted ends. On slitting open this band, I found within it a clot of blood, such as must have come from a large vessel; and this clot was completely enclosed within the new material, not closely adherent to it, nor changed as if towards organization, but rather decolorized, mottled, and so altered as clots are in apoplexy before absorption.

I believe that this case only showed in a very marked manner what usually happens with blood thus effused and not ejected; for it is quite common, after the division of tendons, to find new reparative material, if not containing distinct clots, yet blotched with the blood that was infiltrated in the tissue in which the reparative material is deposited: and even when the repair of a fracture was nearly perfect, I have still found traces of blood-corpuscles enclosed in the reparative material, and degenerating, as if in preparation for absorption.

Ejection and absorption are, doubtless, the usual means by which blood effused in injuries is disposed of; yet I feel nearly sure it may in some instances become organized and form part of the reparative material. The cases of manifest organization of blood already referred to leave no doubt of the possibility of this happening: its occurrence can no longer be set aside as a thing quite improbable. The only question is, whether the organization of blood effused in injuries has been seen. Now I think no one familiar with Hunter's works will lightly esteem any statement of his as to a matter of observation. He may have been sometimes deceived in thinking that he saw blood becoming organized in subcutaneous injuries (for subcutaneous granulations are sometimes very like partially decolorized clots); yet I believe he was more often right: for sometimes one finds clots of blood about the fractured ends of bones which have every appearance of being in process of organization. They do not look mottled, or rusty, or brownish, as extravasated blood does when it is degenerating, preparatory to its absorption; but they are uniformly decolorized to a pinkish yellow hue. They have less appearance of filamentous structure than recent clots have, and they are not grumous or friable, like old and degenerating ones, but have a peculiar toughness, compactness, and elasticity, like firm gelatine. When clots are found in this condition, I believe it is a sign that they were organizing, for this is the condition into which, commonly, the clot in a tied artery passes in its way to be fully organized; and (which is very characteristic) you may find clots in the track of wounded parts thus changing, as if towards organization, while those about them, and out of the way of the reparative process, are degenerating.

On the whole, then, I believe we may thus conclude concerning the part that blood, when it is extravasated, takes in the repair of injuries:—

1. It is neither necessary nor advantageous to any mode of healing.

2. A large clot, at all exposed to the air, irritates and is ejected.

3. In more favourable conditions the effused blood becomes enclosed in the accumulating reparative material; and while this is organizing, the blood is absorbed; and—

Lastly, it is probable that the blood may be organized and form part of the reparative material; but even in this case it probably retards the healing of the injury.

I proceed now to the consideration of the material which is produced for the repair of injuries that are not healed by the immediate union. It is that to which the general name of lymph, or coagulable lymph, is given.

Our notions concerning the properties of this substance, when once effused for the repair of injuries, are derived almost entirely from examinations of the lymph effused in acute inflammations, with which it is supposed to be identical. The identity is far from being proved, but their similarity is in many particulars evident, and especially in that both manifest, by their spontaneous coagulation, that they contain fibrine. The coagulum which is spontaneously formed in reparative material is, in microscopic characters, identical with that of fibrine: chemically, too, they appear the same; and the organization of the fibrine of the blood in the complete clot, as well as all the other circumstances which lead to the opinion that fibrine is the principal material for organization into tissues,* justifies the belief that the lymph effused for purposes of repair has fibrine for its principal constituent. However, when we speak of fibrine as the chief reparative material, we must not have in mind the pure organic compound that minute chemistry might obtain, but rather that which exists in the natural, and seemingly rough, state,—as fibrine, with some fatty matter, and some incidental saline constituents; for all these are found in all the specimens of coagulable lymph that have been examined; and doubtless they are essential, as the so-called "incidental" principles always are, to the due construction of the substance to be organized.

Regarding its vital properties, the essential character of the coagulable lymph is its tendency to develope itself,—a tendency which it has of its own properties. It thus displays itself as a plasma or blastema—a fluid to be classed with those others that manifest the capacity to assume organic structure,—such as the lymph and chyle that develope themselves to blood; the semen, which, at first fluid, gradually developes itself into more and more complex structures.

The natural tendency of coagulable lymph is to develope itself into the fibrous, or the common fibro-cellular or connective, tissue—the lowest form of vascular tissue, and the structure which, in nearly all cases in man, constitutes the bond by which disunited parts are again joined. This is commonly formed, whatever be the tissue upon which the lymph is placed, whether containing cellular tissue in its natural structure or not. This, therefore, we may regard as the common or general tendency of lymph; but in certain cases the development of lymph passes beyond this form, or deviates from it into another direction, in adaptation to the special necessity of the part to be repaired. Thus, for the repair of bone, the lymph may proceed a certain distance towards the developement of fibrous tissue, as if for a common healing; but this fibrous tissue may next ossify; or, not forming fibrous tissue at all, the lymph may proceed at once to the formation of a nearly perfect cartilage, and this may ossify. In general, moreover, the character of the connective tissue that is formed in repair is adapted to that of the parts that it unites. The bond for the union of a tendon is much tougher than that for a common scar in the skin; that in skin is tougher and less pliant than that in mucous membrane, and so on.

It has been thought a nice question, whether these variations in the developements of the same material—*i. e.* of the lymph—in adaptation to the purposes it has in each case to serve, be due to the assimilating influence of the parts among which it is deposited, or to a specific power, like the germ-power, which determines in each case the special result, as in embryonic developement it determines the formation of the several dissimilar organs out of similar materials. I have little doubt it is such a germ-power. In favour of this view, are all those general facts concerning the continuousness of its operation from the germ onwards, which I mentioned in my last lecture; and we may commonly observe that the developement of special structures in the reparative material takes place at considerable distances from the structures by whose assimilative force some have supposed the developement to be determined. Thus, *e. g.* in the repair of fractures, one may find, sometimes, plates of bone formed in new fibrous material external to the periosteum of the old bone; and in the formation of the tough fibrous tissue which is made for the repair of tendons, one may always notice that the developement is equal and commensurate through the whole length of the new bond of union. Such a developement cannot be determined by the contact, or even by the contiguity, of the original tendinous structure, or by anything like an assimilative force issuing from it.

But, passing by, for the present, the instances of special developement of the reparative material, in adaptation to special purposes or injuries, let me speak of its developement into fibrous, fibro-cellular, or connective tissue. I have said that, in its first production, the reparative material is like the lymph of inflamed serous membranes,—at least, no characteristic difference between them is yet known; neither are there yet any observations to show a difference in the characters of the materials effused for the repair of injuries of different parts, or in different circumstances; and yet such a difference, in even the original characters of the lymph, is indicated by the fact that in different circumstances it may proceed to the same end—the formation of fibrous tissue—by two different ways of developement. The lymph, or new material, which is produced for the repair of open wounds, generally developes itself into fibro-

* See especially Carpenter's Physiology, page 81, &c.

cellular tissue through nucleated cells; that formed for the healing of subcutaneous wounds as generally developes itself into the same tissue through the medium of nucleated blastema.

Now both these are repetitions of natural modes of developement of the same forms of tissue. In the embryo and fœtus you may trace very well the developement of subcutaneous cellular tissue through nucleated cells, and that of tendons and other *formed* fibro-cellular or fibrous tissues through nucleated blastema.

It must not appear an objection that there should be two modes of developement to the same perfect tissue; for this is usual, and has been observed in nearly all the tissues. I spoke of it last year in relation to the developement of the blood-corpuscles, of which a first set are formed from part of the embryo-cells that form the germinal area, or the whole body of the embryo, and the second set are formed exclusively from the corpuscles of lymph and chyle; and so it is with the cartilage, the muscular, and other tissues that are formed in the earliest periods of embryo-life. At first they are developed from some of the embryo-cells; yet in later life, no such cells are seen among them, but others appropriate to them, and of widely different form. So also in the bones, which at first are developed through cartilage, but in their subsequent growth are increased by ossification of fibrous tissue; and in the repair of which we shall find even more numerous modifications of these different developements.

The developement of the fibro-cellular or connective substance through nucleated cells may be observed in the material of granulations, or in that of inflammatory adhesions, whether in a serous sac or in a wound healing by primary adhesion, in inflammatory indurations, and in the naturally developed fibro-cellular tissue of at least many parts. The process is, with slight and apparently not essential modifications, the same in all, and is, I believe, almost exactly as described by Schwann.

The cells first formed are round, very slightly granular, from 1-1500th to 1-2500th of an inch in diameter; and (if not at once, yet as soon as water is added) they display a well-marked cell-wall, and a clearly defined round nucleus. Whether in granulations, or in inflammatory exudations, such cells present a striking resemblance to the white corpuscles, or lymph-corpuscles, in the blood. Indeed, the only usual difference between them is in the character of the nucleus, which, in these new-formed cells presents a well-defined dark-edged wall, and clear contents; but, in the white blood-corpuscles, appears rather as a mass of colourless, but nebulous substance, with no decided distinction of wall and contents. Such a difference may be connected with the different destinations of the nuclei; in the cells of which fibro-cellular tissue is to be formed, they take a principal share in the developement; but, in the lymph-corpuscles developing into mammalian blood-corpuscles, the mass of the nucleus is diffused into the cell-contents, and becomes uniform with them.*

In the developement of cellular tissue from these cells, whether in the natural structures or in those that are formed in disease or after injury, the first apparent change is in the nucleus. It becomes oval (even before the cell does), and at the same time becomes clearer, brighter, like a vesicle tensely filled with pellucid substance. One or two nucleoli now appear distinctly in it, and soon it attenuates itself; but this it does later, or in a less degree, than the cell: for a common appearance is that of elongated cells bellied-out at their middle by the nucleus.

While these changes are ensuing in the nucleus, each cell also is developing its structure; first becoming more minutely, yet more distinctly, granular or dotted, then having its cell-wall thinned, or even losing it. It elongates at one or both ends, and thus are produced a variety of lanceolate, caudate, or spindle-shaped cells, which gradually elongate and attenuate themselves towards the filamentous form. As they thus change, they also group themselves, so that, commonly, one may find the swollen part of each, at which the nucleus lies, engaged between the thinner parts of the two or more adjacent to it. Thus, the filaments into which the cells are developed are clustered or fasciculated: each cell forming, I think, usually, only one filament,† and long filaments being sometimes formed by the attachment of the ends of two or more, each developed from a single cell.

The final disposal of the nuclei of these cells is hard to discern. Doubtless, in many instances, they are developed into filaments, like those of elastic tissue, such as Henle has well named nucleus-fibres. But in the developement of the cellular tissue formed in inflammation or granulating wounds, the nuclei seem, rather, to waste, and be absorbed.

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* Perhaps the similarity between these primary cells is only an evidence of the general likeness of the cells from which, after the earliest developement of the embryo, all the tissues that are developed through cells are formed. The similarity of the pus-cells to the cells for fibro-cellular tissue, and to the white blood-corpuscles, will be mentioned in a future lecture.

† Schwann describes each elongated cell as splitting up into several filaments. I have not seen clear indications of such a process: but it may occur in some parts in which I have not examined the developement.

Certainly such nucleus-fibres are not found in scars lately formed, though common in those of old standing. But although the nuclei may thus be formed for only a brief existence, yet in their time they display more organic activity than the cells,—for they take the initiative, not only in the developement of the filament, but also in the multiplication of the cells. In granulations, one may may often find large compound cells, of oval form, and as much as 1-250th of an inch in diameter, containing eight, ten, or more, nuclei. These have been derived by subdivision from the nucleus of the simple cell, and are probably destined to be the nuclei of as many separate cells; affording an instance of conformity with that same law of multiplication of cells by partition of the nucleus, which is traced as the constant method for the construction of the germ-mass in the ovum.

Such, briefly, is the process for the developement of fibro-cellular tissue through nucleated cells. Some modifications of it may be observed in certain cases—especially in regard to the proportion that the cells bear to the substance in which they lie. In some forms of granulations, and in some natural parts of the embryo, this substance is abundant; and I think it may be developed so as to take part in the formation of filaments. But none of the modifications affect the essential characters of the process.

The developement of fibro-cellular or fibrous tissue through nucleated blastema is observed in the natural developement of tendons and ligaments; and, as I have already said, in the organization of the material by which, in most cases, the bonds of connection after subcutaneous wounds are formed. It is the same which Henle* regards as the only mode of developement of the fibro-cellular and fibrous tissues. Schwann, on the other hand, believes that that there is no other mode than that which I have just described. My account will not appear less probable, while it shows that both these admirable anatomists are right in what they severally affirm, though, it may be, not in what they doubt or deny. Certain it is that both these modes of developement of fibro-cellular or fibrous tissue may be traced; nor can any better example be selected than in the formation of scars from granulations, and of the bonds that unite subcutaneously divided tendons.

Of the union of divided tendons I hope to speak in a future lecture. For the present purpose, and in relation to the developement of fibro-cellular or fibrous tissue from nucleated blastema, it may be enough to state, that when the first effusion of the products of the inflammation, excited by the violence of the wound, is completed, then a quantity of finely molecular or dimly-shaded substance, like homogeneous or dotted fibrine, begins to appear in the space in which the bond of union is to be formed. This substance is infiltrated in the tissue that collapses into the space between the retracted ends of the tendon. At first there is no appearance of nuclei or cytoblasts in it: it seems to be merely a blastema of fibrine; but as it acquires firmness and distinctness, the nuclei appear in it; they seem to form out of collecting clusters of granules, and presently appear as oval bodies, with dark hard outlines, soon becoming elongated, with clear contents, without nuclei, irregularly scattered, but so firmly imbedded in the blastema that, in general, they cannot be dislodged. They may be seen in very fine fragments without reagents; but, commonly, the application of acetic acid is necessary to make them distinct, by making the intermediate substance transparent, while the nuclei themselves acquire dark edges and shrivel up a little. The nuclei undergo little change, while the blastema in which they are imbedded is acquiring, more and more distinctly, the filamentous appearance, and then the filamentous structure,—only they appear to elongate, and to attenuate themselves, and to grow more irregular in their outlines as if by shrivelling.

The blastema may become at length perfect fibro-cellular or fibrous tissue,—tissue not to be distinguished from that found in normal conditions. The final disposal of the nuclei is doubtless sometimes, as Henle describes it, that they are developed into the nucleus-fibres, and constitute some of the various forms in which elastic yellow tissue is found mingled with the proper white filaments. But, in the process of repair by tissue thus developed, as well as by that which is formed through cells, my impression is that the nuclei finally shrivel,—gradually contracting into little crooked or branched lines,—and at length disappearing: for, as I have already said, well-formed nucleus fibres, or such elastic yellow fibres as might be developed from them, do not generally occur in cicatrices of recent formation, or in the large bonds of union by which divided tendons are healed.

I have been thus minute in the account of these two modes of developement of fibro-cellular tissue, prevailing alike in the natural structures, and in the materials of repair, because the knowledge of them may enable us to settle some questions respecting all the modes of healing, and because it seems to point out the essential anatomical difference in the

* Allgemeine Anatomie. A similar process is described by Reichert, Zwicky, and Gerlach.

healing of open and of subcutaneous wounds, with disconnection of divided parts.

The general truth appears to be (as already stated) that the material of repair for subcutaneous wounds is developed into cellular tissue through the formation of nucleated blastema; while that for repair by primary adhesions, and by granulation, is developed into the same through nucleated cells. Now, since both these methods of developement are, as I have already said, imitations of natural methods, we might suppose that they are therefore both alike natural or healthy processes,—both alike independent of inflammation,—alike sure to pass to their purposed end, safe from disease or degeneration.

But, if we consider also the morbid conditions in which these two methods of developement of cellular or fibrous tissue occur, then we can see that the developement through cells is characteristic of inflammatory processes—at least, as far as the origin of the cells is concerned. For, of such cells, in various stages of developement, are formed not only long-suppurating granulations, but also the walls of abscesses, inflammatory infiltrations, producing succulence, indurations, and thickenings of soft parts; the lymph produced in inflammation of serous membranes, which organizes itself into false membranes.

On the other hand, the developement of cellular tissue through nucleated blastema, is, in morbid processes, observed in instances in which there are commonly no signs of inflammation,—as *e. g.* in warts and condylomata, in the simple fibro-cellular tumors of the subcutaneous tissue, in nasal polypi, in organizing clots of blood.

These instances, then, may enable us to conclude respecting the existence or non-existence of inflammation in the healing of injuries. The material of repair in union by primary adhesion and granulations is the same, in appearance and mode of developement, as we find produced in other conditions which all are agreed to call inflammatory. But, in the healing of subcutaneous wounds, we find a different material of repair, which resembles, in both appearance and mode of developement, that which we find forming growths whose production is not attended with any signs of inflammation. On these grounds, therefore,—and they are corroborated by the appearances of the injured parts during the process of healing,—we are justified in holding, generally, that inflammation ensues in the healing by adhesion and by granulations, but does not exist in the healing of subcutaneous wounds.

I shall again have occasion to consider the relation between the healing processes, and that of inflammation. I will now only briefly say, that, although inflammation may be deemed necessary for the production of the lymph that may form adhesions or granulations, yet we have no evidence that the continuance of inflammation is necessary for the organization of the lymph. Rather, the persistence of inflammation seems to hinder the organization of the lymph, to keep it in a low state of developement, or to favour its degeneration. Thus, to name but one example, granulations over an irritating body suppurate abundantly, and remain for years unhealed; — that is, they are imperfectly organized; they stop short of their developement into the cellular tissue and cuticle proper to cicatrices, or degenerate into pus.*

I may also add, that, although I have described the two modes of developement of fibro-cellular or fibrous tissue for the healing of wounds as if they were always as separate as they are distinct, yet they may co-exist, and probably often do so. In the repair of many wounds, the two materials—namely, that which is to be developed through nucleated cells, and that whose progress is to be through nucleated blastema—may be mixed. Thus, in subcutaneous wounds and injuries—as, for example, in the case of divided tendons,—the first consequence of the mechanical violence is the effusion of a common inflammatory product, which makes the cellular tissue œdematous, and organizes itself into nucleated cells. Thus you find the space between the retracted parts for about two days. But, then, the more proper and purer material of repair is produced; and this, increasing in an inverse proportion to the degree of inflammation, soon overwhelms the former product of inflammation, and is developed into the nucleated blastema. Still, for many days, traces of the inflammatory product may be discerned mingled with the blastema, confusing its appearance, but, I believe, finally organizing with it into the bond of union. So, in divided muscles, and in simple fractures, the inflammatory exudation, produced in consequence of the first violence, appears to mingle and develope itself with the more proper material of repair; but they bear an inverse proportion to one another, and the more manifest the signs of inflammation, the less is the quantity of the proper

* In thus considering inflammation as necessary to the production of such lymph as may form adhesions or granulations, but as injurious to its organization or further developement, we may perhaps reconcile two completely opposite views on this point. The expressions generally used imply that inflammation is commonly considered to exist through the whole process of adhesion,—in, for example, a serous cavity. Dr. Macartney (Treatise on Inflammation, p. 37), maintains, on the contrary, that the formation of such adhesions is not at all an effect of inflammation. The one opinion seems to make the inflammatory process of too much avail; the other, of too little.

reparative material, and the slower, in the end, the process of repair.

On the other hand, I think that in the ordinary healing of open wounds, which are soon brought together by sutures, or other appropriate means, there may be less than the commonly observed formation of nucleated cells, and some of the reparative material may be developed through the nucleated blastema. Or, when the different materials are not mingled at the same spot, yet, in one wound, different parts may be healed by the organization of one or other material, according to the degree of inflammation that is in each part present during the production of the lymph. But all these things need further inquiry.

LECTURE III.

Healing by immediate union: its relation to Hunter's "Union by the first intention." Description of cases. Essential characters of the process: the conditions necessary for it.
Healing by primary adhesion; its similarity to Hunter's "Union by the adhesive inflammation." General account of the process, and of its relation to other modes of healing.
Healing by granulations. General stages of the process. Periods of repose and of increased vascularity. Production of new substance. Formation of granulation-cells, and their developement into cellular or connective tissue and cuticle; their deviations from this process.

I PROCEED now to the description of the several modes of healing of wounds, and shall at present speak of only such wounds as are externally open. Among the modes which I enumerated, the first was that which, as I stated in the preceding lecture, is effected by immediate union. It corresponds with what Mr. Hunter called union by the first intention; but since that term has been applied more recently to another mode of healing, I have adopted the term "immediate union" from Dr. Macartney, who, so far as I know, was the first to observe clearly that the healing of wounds may be effected "without any intervening substance, such as blood or lymph."* He says—"The circumstances under which immediate union is effected, are the cases of incised wounds that admit of being, with safety and propriety, closely and immediately bound up. The blood, if any be shed on the surfaces of the wound, is thus pressed out, and the divided blood-vessels and nerves are brought into perfect contact, and union may take place in a few hours; and as no intermediate substance exists in a wound so healed, no mark or cicatrix remains behind.

"We have familiar examples of this mode of healing in slight cuts received on the fingers, which, after being bound up, if no inflammation be induced, perfectly heal without the individual having any unpleasant sensation in the part after the moment of the infliction of the wound. A case has been lately communicated to me, of a considerable cut of the hand having been cured by this mode of direct union, without any sensation of pain, and in the short space of four or five hours."

* Treatise on Inflammation, p. 59.

It is singular that Dr. Macartney should speak of the process of immediate union occurring in so few and very trivial instances as these; for it seems certain that many even very large wounds are usually, in favourable circumstances, thus healed. The characteristics of this mode are, that the divided parts, being placed in exact contact, simply conjoin or re-unite: no blood or new material is placed between them for a connecting bond, and no sign or product of inflammation is present. All these characteristics meet in such cases as the favourable union of flaps of skin, which have been reflected from the subjacent parts, and are then replaced or transferred to some other adjacent wounded surface.

The instances in which I have best observed it have been after operations for the removal of the mammary gland. In these operations, as you know, the usual proceeding is to remove some of the skin, including the nipple, and to uncover the rest of the surface of the gland by reflecting from it an upper and lower flap of skin. Then, the gland being removed, these flaps, which are often of considerable extent, are laid down upon the parts on which the base of the gland rested, chiefly upon the fascia over the great pectoral muscle.

A specimen which I have here will illustrate the healing that may now ensue. It was taken from a woman 33 years old, who had her breast and several axillary glands removed for cancer. Her general health seemed good, and all went on well after the operation. The flaps, which were of course very large, had been carefully laid down, strapped with isinglass plaster, and well tended. They appeared to unite in the ordinary way, and there remained only a narrow space between their somewhat retracted edges, in which space granulations arose from the pectoral muscle. Three weeks after the operation these were making good progress towards cicatrization; but erysipelas and phlebitis ensued, and the patient died in four or five days.

I cut off the edges of the wound with the subjacent parts, expecting to find the evidences of union by organized lymph, or, possibly, blood. But neither existed; and the state of parts cannot be better described than by saying, that scarcely the least indication remains of either the place where the flap of skin was laid on the fascia, or of the means by which these parts were united. It was not possible to distinguish the relation which these parts held to each other from that which naturally exists between subcutaneous fat and the fascia beneath it. There was no unnatural adhesion; but, as the specimens will still show, the subcutaneous fat which did lie over the mammary gland is now connected with the fascia over the pectoral muscle, just as (for example) the corresponding fat below the clavicle is naturally connected to the portion of the same fascia that lies there. I could find small points of induration where, I suspect, ligatures had been tied, or where possibly some slight inflammation had been otherwise excited; and one small abscess existed under the lower flap. But with most careful microscopic examination, I could discover no lymph- or exudation-corpuscles, only small quantities of what looked like the débris of such oil-particles or corpuscles of blood as might have been between the surfaces when the flaps were laid down. In short, we cannot otherwise or more minutely describe this healing than by the term "immediate union:" it is immediate, at once in respect of the absence of any intermediate substance placed between the wounded surfaces, and in respect of the speed with which it is accomplished.

Opportunities of examining wounds thus healed being rare, I made three experiments on rabbits (with my friend Mr. Savory), and found the description I have just given quite confirmed. The specimen I have here affords a good example. A portion of skin that my extended fingers would just cover, was raised from the back of a rabbit, replaced and fastened down with a few sutures. Three days afterwards the rabbit was killed: the edges of the wound were slightly retracted, and the space between them was covered with scab; for about half an inch under the edge of the replaced flap of skin, the tissue was inflamed and infiltrated with exudation-matter; but beyond this no trace of the injury or of its healing could be seen. The parts appeared as they had appeared before the operation. Even the microscope could detect only a slight infiltration of inflammatory matter, which one might certainly ascribe to the wound being open at its edges, and to some hairs having by accident been enclosed under the flap when it was replaced.

Of course, it is only from such examinations as these after death, that we can speak certainly of the absence of inflammation and of all intermediate uniting substances, yet confirmatory evidence may be obtained from the examination of any such wound during life,—I mean any such case as that of a flap of skin raised up, then laid down on the subjacent wounded surface, and there uniting favourably; or any case of that kind of plastic operation in which a flap is raised, and then made to slide to some further position. In such cases, with favourable progress, no sign of inflammation is observed; though, if the skin were in even a small degree inflamed, it could scarcely fail to be manifested by the ordinary appearances of redness and heat. If the flap be pressed, no fluid oozes beneath its edges (I speak, of course, of only such cases as are making favourable progress), and after one or two days, according to the extent of the wound, the flaps will move on the subjacent parts,—not with the looseness of a part separate from them, nor with the stiffness of one adherent through inflammation, but with the easy and pliant sliding which is peculiar to the natural connection of the skin with the subjacent fascia.

Such is the nature of "immediate union," the best imaginable process of healing. Two conditions appear essential to it—first, exactness of the coaptation of the wounded surfaces; and secondly, the absence of all inflammatory process.

To obtain the former, the simple replacement of the raised pieces of skin may sometimes be sufficient. But there is a class of cases to which this mode of healing is peculiarly applicable, and in which more than this may be required: I refer to the removal of large subcutaneous tumors,—fatty tumors and the like,—where, after the operation, large cavities are left, and commonly left to granulate. In these cases I venture to express my belief that modern surgery does not often enough employ the older method of carefully and softly padding the parts, and of so bandaging them that the exposed surfaces may be held in contact for the one, two, or three days necessary for immediate union. Many surgeons, I know, commonly employ these means; but by many,—and, I think, the majority,—they are avoided, through fear of exciting inflammation by over-heating the parts, or hindering the discharge of secreted fluids. Doubtless, no single rule of management would be safe; but I think with regard to this fear of exciting inflammation, it need not be entertained, if the means I have alluded to be employed only during the first two or three days after the infliction of the wound. For one may generally observe that, for at least two or three days after such an injury as an amputation, the raising a flap of skin in a removal of the breast, or the like, scarcely any reparative process appears in the parts that are kept from contact, no granulations are formed, no pus secreted, only a little serous-looking fluid oozes from them. Now, during this calm, which would certainly never be disturbed by the parts being softly padded and kept in perfect rest, the immediate union may be accomplished: if, through any untoward circumstance, it be not in this period completed, its occurrence is, I believe, impossible, and then the means more appropriate for other methods of healing may be employed.

The attainment of the other necessary condition,—the absence of inflammation,—is quite consistent with these means for insuring perfect and continued contact of the wounded surfaces. How the condition is to be fulfilled I need not say: the means are some of those that are commonly laid down for preventing inflammation from being, as it is said, more than is necessary for the union by the first intention; and the best of them are temperance and rest. The necessity of observing them will appear the greater, if it is remembered that what is wanted for immediate union is, not a certain undefined slight degree of inflammation, but the complete absence of inflammation;—for, the probability of the occurrence of immediate union may be reckoned as being in an inverse ratio to the probability of inflammation occurring in the time necessary for its accomplishment.

I pa s now to the second mode of repair that I enumerated—that, namely, *by primary adhesion.*

This is the process which Mr. Hunter named union by adhesion, or union by the adhesive inflammation. My reasons for preferring the term "primary adhesion," will presently appear. He says (vol. iii. p. 253,) "Where the former bond of union," [*i. e.* the union by blood or by the first intention], "is lost in a part, to produce a new one, a second operation takes place—namely, inflammation." Observe how carefully Mr. Hunter distinguishes the case in which inflammation ensues, from that in which none is necessary: and presently after, "if the divided parts are allowed to remain till the mouths of the divided vessels are entirely shut, inflammation will inevitably follow, and will furnish the same materials for union which are contained in extravasated blood, by throwing out the coagulated lymph; so that union may still take place, though some time later after the division of the parts. This inflammation I have called the adhesive." On this sentence, Mr. Palmer, expressing the opinion entertained by all the pathologists of ten or twelve years ago, says—"It is now generally considered that union by the first intention and adhesive inflammation are essentially the same processes, modified by the degree of inflammation. Union by the first intention is uniformly attended with some degree of pain and swelling, together with increased heat and vascularity, which, taken conjointly, constitute the definition of inflammation." And again: "According to the modern views, the modes of union above detailed" [*i. e.* the modes of union included by Mr. Hunter under the union by the first intention], "are always accompanied by adhesive inflammation . . . . The parts are united, not by the extravasated blood becoming vascular, but by the effusion and organization of coagulable lymph."

After what I have said respecting the process of immediate union, it may appear that Mr. Hunter was more nearly right than his successors. It would be an instructive piece of the history of surgery to show, exactly, how this truth being mixed with error came, therefore, to be thrown away, and to make room for an error which had less truth mixed with it. The stages of transition in opinions seem to have been that—first, sufficient reason was found for disbelieving his statement, that blood forms the bond of union by the first intention; then, as it was assumed that there must always be some intermediate bond, this, it seemed, could be none but coagulable lymph. Now, coagulable lymph being known only as the product of inflammation, it followed that inflammation must be necessary for the healing of every wound; and then there ceased to be any distinction between the union by the first intention and the union by adhesion; both alike seemed to be the result of lymph, the product of inflammation, being effused between the wounded surfaces, and united to them both.

The typical examples of union by primary adhesion may be watched in the cut edges of skin that are brought close together. Here, when the cut surfaces are not in exact contact, the wound is exposed, and lymph is formed, and fills up the space; or, when they are in contact, the sutures, or other means employed to keep them so, excite inflammation enough for the production of some lymph between them. The lymph organizing itself, and becoming vascular, connects the two edges or surfaces, and forms between them a thin layer of cellular tissue, on the surface of which, if it be exposed, a very delicate layer of cuticle is developed. The smooth shining surface of this cuticle gives the peculiar character of the scar, and one that scarcely changes, except in the alteration of apparent colour when the new material becomes less vascular.

The lymph effused in the healing by primary adhesion always, so far as I know, developes itself through nucleated cells, as the lymph of acute inflammation does; doubtless, the whole process is very similar to that of the adhesion of inflamed serous membranes.

It may be very quickly accomplished. Lately, a boy died eighty hours after receiving a lacerated wound of the abdomen; and, for forty-eight hours of these eighty, he was so manifestly dying, that I think no reparative process could have been going on. A portion of the edges of the wound was united with lymph, which presented well-marked cells, like those of granulations, and contained new-formed blood-vessels.

But it may be accomplished more quickly

than in this case. If a small abscess be opened, and the edges of the opening are not gaping or inverted, they may be found united, except at the middle, within twenty-four hours. I have seen them so united with a distinct layer of soft, pinkish, new substance, in a wound made seventeen hours previously.

There are no cases in which the process of primary adhesion can be better observed than after operations for hare-lip. Possibly the inner portions of the wounds made in them may be healed by the immediate union, when the surfaces have been in exact coaptation; but the edges of the skin and mucous membrane seem always united by the adhesive inflammation, for a scar is always visible,—a scar formed by the lymph organised into cellular tissue and epithelium—a scar which, as well as any, shows how little of assimilative force can be exercised by adjacent tissues; for, narrow as it may be, it does not become quite like the adjacent skin, nor, like it, bear perfect epidermis and hair.

The history of union by primary adhesion cannot be conveniently completed till an account has been given of the healing by granulations and by secondary adhesion. Of these I will next speak: now I will only say of this union by primary adhesion, that it is less desirable than that of immediate union, because—1st, it is, probably, not generally so speedy; 2dly, it is not so close, and a scar is always formed by the organization of the new matter; and 3dly, the formation of lymph-cells is a process so indefinitely separated from that of the formation of pus-cells, that union by primary adhesion is much more likely to pass into suppuration than any process is in which no lymph is formed.

In describing the modes of healing by *granulations* and by *secondary adhesion*, I shall venture again to take my account from certain typical examples: such as cases in which, after amputation of the limbs, the surfaces of the wound are not united by either of the means already described, but, as the expression is, are "left to granulate;" or such cases as the removal of a breast, and subsequent suppuration of the flaps and the exposed fascia; or such as wounds into inflamed parts, when the edges gape wide asunder, and the spaces left between them are filled up with granulations. These may serve as examples of a process which, although in all cases it may preserve certain general features of similarity, is yet in detail almost infinitely, and often so inexplicably, diversified, that any more than a general account of it might fill volumes.

Granulations will generally arise on all wounded surfaces that are left open to the air and are not allowed to dry; they will do so whether this exposure be continued from the first infliction of the wound, or commence after the edges, which have been brought together, have been again forced asunder by the swelling of the deeper-seated parts, or by hæmorrhage, or secretion of fluid, between them. Exposure of a wound to the air is not prevented by any ordinary dressings: the air that is enclosed beneath them, or that can penetrate them, appears to be quite enough to determine all the difference of the events that follow open and subcutaneous injuries.

The simplest case for illustration is that of an open gaping wound, which, from the time of its infliction, is only covered, as in ordinary practice, with water dressing, or some soft and moist substance. Blood gradually ceasing to flow from the surface of such a wound, one may see still some blood-tinged serous-looking fluid oozing from it; and the material on the surface of the wound, examined with the microscope, will be found to contain an abundance of the white corpuscles of the blood, imbedded apparently in a fibrinous film. The existence of these corpuscles on the surface of the wound, especially on those of wounded muscles and fasciæ, appears to depend only on their peculiar adhesiveness. One sees them adhering much more firmly than ever the red corpuscles do to the walls of the capillary blood-vessels, and to the glass on which they are examined; and I should think we may thus explain their collecting on cut surfaces; while the other constituents of the blood flow away, the white corpuscles, and probably, also, some of the fibrine, quickly coagulating, adhere to the surface, which, in comparison with what they naturally flow over, is very rough, and therefore favourable to the quick coagulation and entangling of the fibrine.*

I am not aware of any facts that would prove what share the white corpuscles thus accumulated may take in the healing of a wound. They do not hinder it; for it is by many believed to be favourable to union by adhesion, to leave cut surfaces exposed till they appear glazed over with a whitish film, and then to put them into contact. This glazing consists of fibrine and white blood-corpuscles. It is probable the corpuscles are organised; but I know of no facts bearing

* Reinhardt, by whom, I think, the fact was first clearly noticed (Traube's Beitrage, H. ii. p. 188), supposes the white corpuscles may exude separately from the vessels. Perhaps the truth is, that their peculiar adhesiveness makes them flow less readily from the bloodvessels, when the bleeding is about to stop; so that at last, when the vessels finally close and empty themselves, a large proportion of these corpuscles may issue from them and adhere to the cut surface over which they slowly roll.

on the point, and it is one which I think experiments on animals could hardly be made to illustrate.

But if a wound be still left open, this glazing remains on such parts as it may have formed on, especially on the exposed muscles. No evident change ensues in it, except that it appears to increase slowly, and makes the surface of the wound look as if covered with a thin greyish layer of buffy coat. This increase of glazing is the prelude of the formation of granulations; but while it is going on there is, in and about the wound, an appearance of complete inaction,—a sort of calm, in which scarcely anything appears except a slight oozing of serous fluid from the wound. The calm continues from one day to eight, ten, or more, according to the nature and extent of the wounded part, and the general condition of the body. In a cut or sawn hard bone, ten days at least will generally elapse before any change is manifest; in cancellous bone the change ensues a few days more speedily: on the under surface of a large flap of skin, with subcutaneous fat, three days may thus pass without change; on the cut or excoriated surface of the more vascular part of the skin, two days or three.

These periods of repose after severe injury are of equal interest in physiology and in surgery; but in the former it is only the interest of mystery. Observations on injuries of the frog's web* make it probable that the blood is stagnant for some little distance from the wound during several days after the injury: but why it is so, and what are the changes ensuing in and about it, preparatory to its again moving on, we cannot tell. The interest to the surgeon watching this period of repose is more practical: the calm may be the brooding time for either good or evil; whilst it lasts, the mode of union of the wound will, in many cases, be determined: the healing may be perfected, or a slow uncertain process of repair may be but just begun; and the mutual influence which the injury and the patient's constitution are to exercise on one another appears to be manifested more often at or near the end of this period than at any other time. Moreover, in general, the time at which, on each tissue, granulations are produced, is determined by this calm; for they begin to be distinctly formed at its end. Thus, on a stump, after a circular amputation, one may find the margin of the skin and the surface of the muscles well covered with granulations, while the surface of the fat reflected with the skin is barren of them, and the sawn walls of the bone are dry and bare. But from the sawn end of the medullary tube there may already protrude a florid, mushroom-shaped mass of granulations, overhanging the adjacent walls: as if parts in which nutrition is habitually carried on under restraint within hard and rigid boundary-walls were peculiarly apt to produce abundant organizable material as soon as they are released.*

But suppose the period of calm after the violence of the injury to be well overpast—How does the right process of repair set in? Apparently, first of all, by the supply of blood to the injured part being increased.

The experiments on injuries made on the webs of frogs, to which I have already referred, have shown that immediately after the infliction of an injury, the blood in the adjacent parts remains for some days quite stagnant; and we may believe the same occurs, but for a shorter time, in our own case. During this stagnation, materials may ooze from the vessels enough to form the glazing of the wounded surfaces of certain parts; but before granulations can be formed, the flow of blood must again begin, and its supply must be increased by enlargement, and perhaps by multiplication, of the vessels in the injured part. Now, we cannot often see this increase so well in soft parts as in bone exposed after injury. If, in this condition, compact bone be closely watched, there may be seen, two or three days before the springing up of granulations, rosy points or minute blotches, which gradually deepen in their hue, and become larger. From these, presently, granulations will arise. The same process may be well seen when a portion of the skull has been exposed, as by suppuration under the pericranium. In such a case, which was under my care for a time last autumn, nearly one-third of the upper part of the skull was bared, and it became dry and yellowish, and looked quite lifeless; but after some days a few rosy points appeared on its surface, and these multiplied and enlarged, and from each of them granulations grew up till the whole surface of the skull was covered. We watched them nearly every day, and it was evident that, in all cases, an increased supply of blood preceded the production of the new material from which granulations were to be formed.

Doubtless just the same happens in soft parts as in bone; so that it may be stated generally that the first visible change that ensues after the period of calm,—the period of incubation, as it is called,—is an increased

* See especially those detailed by Mr. Travers in his Essay on Inflammation and the Healing Process.

* One may sometimes observe a similar fact in the growth of granulations out of the very centre of the cut end of a divided tendon, while its margins are unchanged. The abundant growth of substance, like brain covered with granulations, in cases of hernia cerebri, is of the same kind.

supply of blood to the parts in which repair is to ensue. This, probably, corresponds exactly with the increased afflux of blood which ensues in inflammation; and Mr. Travers' and other observations on the healing of the frog's web, make it nearly sure that this increased afflux is attended with slower movement of the blood, or at first even with stagnation of the blood in the minute vessels nearest to the cut edges or surface.

Of the force by which this increased afflux of blood is determined, I believe that as yet no sufficient explanation can be rendered; but the fact serves to show that the ordinary process of granulation is, in its commencement, morbid—beneficial, indeed, in its end or purpose, but morbid in its method—comparable with the process of inflammation more than with any of those that are natural to the body. The process of granulating displays herein two points of resemblance to inflammation, and of dissimilarity from natural processes:—namely, 1st, that the increased quantity of blood moves more slowly than in health, while in the naturally increased supply its movement is not retarded; and 2dly, that the increased supply precedes the increased production of material. For, in the discharge of natural functions, the increased supply of blood to a part appears always to be a secondary event, the consequence of some increase in the formation of the part. As in the embryo, many parts form themselves before blood appears—and the growth of these and other parts always a little precedes the proportionate supply of blood to them,—so always, subsequently, the increase or diminution of growth, or any other organic act, appears to precede, by some small interval, the proportioned change in the supply of blood. But with unnatural and morbid processes it appears to be different: in these, with inflammation for their type and chief example, the increased afflux of blood precedes the increased production of material to be organized, and the decrease of blood precedes the decrease of organic processes.

That which next follows, after the increased afflux of blood, is the effusion of the material that is to be organised into granulations. This is added to the glazing that already exists upon some surfaces, and where none such exists, as on fat or bone, is accumulated on the bare surface of the wound. No account of this process of effusion, so far as it is visible to the naked eye, can be better than Mr. Hunter's (iii. 491). "I have often been able," he says, "to trace the growth and vascularity of this new substance. I have seen upon a sore a little white substance, exactly similar, in every visible respect, to coagulating lymph. I have not attempted to wipe it off, and the next day of dressing I have found this very substance vascular; for by wiping or touching it with a probe it has bled freely. I have observed the same appearance on a bone that was laid bare. I once scraped off some of the external surface of a bone of the foot, to see if the surface would granulate. I remarked, the following day, that the surface of the bone was covered with a whitish substance, having a tinge of blue: when I passed my probe into it I did not feel the bone bare, but only its resistance. I conceived this substance to be coagulating lymph thrown out by inflammation, and that it would be forced off when suppuration came on; but, on the succeeding day, I found it vascular and appearing like healthy granulations." To this, little can be added more than the microscope has shown. In the minute structure of granulations, or at least of such growths of new substance as present all the characters that we imply by that term,—the bright ruddy texture, the pointed and granulated free surface, the succulency and abundant supply of blood,—in these, we may discern two varieties, corresponding with the varieties of lymph that I have already spoken of. For, in subcutaneous injuries or diseases, granulations sometimes form which develope themselves into cellular tissue, through nucleated blastema; so I found in a case of simple fracture in which the ends of the bone remained long ununited: they were enclosed in a cavity formed by condensation of the surrounding tissues, but containing no pus, and were covered with a distinct layer of fluid granulations. It was just such a case as that which Mr. Hunter had in view, and preserved,* as an instance of the formation of granulations without suppuration, in the repair of subcutaneous fractures and other injuries.

But in by far the greater proportion of cases, granulations are only formed in exposed injuries: in these they consist of cells that may develope themselves into fibro-cellular tissue; and of such as these I will now exclusively speak.

Cells upon cells, such as I have already described, are heaped up together in a layer from half a line to a line thick, without apparent order, and connected by very little intermediate substance. Singly they are colourless; but in clusters they are ruddy, even independent of the bloodvessels. In granulations that are making healthy progress, one can especially trace that multiplication of nuclei of which I have already spoken. In the same, too, one can conveniently trace the cells in various stages, according to the position they occupy: the

* College Museum, No. 16.

deeper-seated ones being always most advanced, and often much elongated, or nearly filamentous; while the superficial ones are still in a rudimental state, or near the edges of the granulating surface are acquiring the character of epithelium-cells. The cellular tissue thus constructed by the developement of the granulation-cells finally assumes all the characters of the natural examples of that tissue. Thus it is found in the layer of substance of which scars that are formed in the place of granulating wounds are composed. After some time, also, elastic tissue is mingled with the fibro-celullar; but this, as I have already said, appears to be effected by a later process. I found in one case no elastic tissue in scars that had existed, the one twelve months, the other eighteen months; but in scars several years old I have always found it.

The cuticle, also, that forms on granulations gradually approximates more nearly to the perfect characters, and, like the fibro-cellular tissue that it covers, presents the interesting fact of adaptation to the purposes of the part on which it is placed. Thus in granulating wounds or ulcers on the sole of the foot, one may often see that, from the first, the new cuticle is more opaque and thicker than it is on other parts, on which the natural cuticle, in adaptation to the protection required from it, is naturally thinner: and let it be observed that this peculiar formation of the new cuticle is in adaptation to conditions not yet entered upon. It justly excited the admiration of Albinus* when he saw in the fœtus, even long before birth, the cuticle of the heel and palm thicker than those of other parts,—adapted and designed to that greater friction and pressure to which in future time they would be exposed. It is the same when, in adult life, new cuticle is to be formed on the same parts: while it is forming, all pressure and all friction are kept away, yet is it constructed in adaptation to its future exposure to them. Surely such a provision is, beyond all refutation, an evidence of design; and surely in this fact we may discern another instance of the identity of the powers that are put in operation in the acts of first construction and of repair.

But before I end this lecture, let me add, that although one may so clearly trace, in the developement of granulation-cells, and in the end which they achieve by the formation of fibro-cellular tissue and cuticle, an imitation of the natural processes and purpose of the corresponding developements in the embryo, yet is there a remarkable contrast between them, in regard to the degrees in which they are severally liable to defect or error. We can scarcely find examples of the arrests or errors of developement of mere structure in the embryo, but such events are quite common in the formation of granulations, as well as of all other new products. All the varieties in the aspect of granulating wounds and sores, which the practised eye can recognise as signs of deflection from the right way to healing, are so many instances of different diseases of the granulation-substance, — diseases not yet enough investigated, though of much interest in the study of both the healing process and the organization of new products in inflammation. A comparatively few observations enable one to trace morbid conditions of these new structures closely answering to those long known in the older and more perfect tissues. Thus, one may find simply arrested developement of granulations; as in the indolent healing of wounds and ulcers, whether from locally or generally defective conditions. Herein even years may pass, and the cells will not develope themselves beyond one or other of their lower forms. There is probably a continual nutrition of particles among such cells, as in common nutrition,—or they may increase, as in growth; but no developement ensues, and the wound or the ulcer remains unhealed.

In other cases, the cells not only do not develope themselves, but they degenerate, becoming more granular, losing the well-marked characters of their nucleus, and acquiring all the structures of the pus-cell; thus are they found in the walls of fistulæ and sinuses. Or, worse than this, the granulation-cells may lose all structure, and degenerate into a mere layer of débris and molecular substance. Thus they may be found on the surface of a wound for a day or so before death in exhaustion, or in erysipelas, or fever. With more active disease granulations become turgid with blood, or œdematous: such are the spongy masses that protrude beyond the openings leading to diseased bone; or they inflame, and abundant large inflammatory granule-cells are found among their proper structures; or they suppurate internally, and purulent infiltration pervades their whole mass.

All these are among the many hindrances to healing: these are the dangers to which the healing by granulations is obnoxious: it is the proneness to these things that makes it even slower and more insecure than, in its proper course, it might be. But to these I must again refer when I speak of the formation of pus, and the relation of its cells to those of granulations.

* Annotationes Academicæ.

LECTURE IV.

Developement of blood-vessels in granulations; their modes of formation in the embryo: their formation in granulations and similar new productions, by outgrowths and channelling.

Healing by secondary adhesion, or union of granulations.

Healing by scabbing; its several modes, and advantages.

Process of suppuration. Relation of the pus-cells to granulation-cells and inflammatory exudation-cells, and of the liquor puris *to fibrinous blastema. Probable degeneration of other cells into pus-cells.*

Characters of scars: their contraction and gradual perfection.

With the structural developement of the granulation-cells, described in the last lecture, there coincides a chemical change which seems to be the contrary of developement; for the granulation-substance, being converted from albuminous into horny and gelatinous principles, becomes, in chemical composition, less remote than it was from the constitution of inorganic matter. At its first effusion, the reparative material has the characters of fibrine; afterwards, when in the form of granulations and of young fibro-cellular tissue, its reactions are so far altered that it presents the characters of pyine, a somewhat indefinite principle, yet an albuminous one; finally, in its perfect developement, the new formed fibro-cellular tissue is gelatinous, and the cuticle appears to be like other specimens of horny matter.

These changes are in conformity with what appears to be a general rule—namely, that structures which are engaged in energetic developement, self-multiplying, the seat of active vital changes, are generally of the highest organic chemical composition; while the structures that are already perfect, and engaged in the discharges of functions such as are attended with infrequent changes of their particles, are as generally of lower composition. The much higher chemical developement (if I may so call it) of the blood than of the greater part of the tissues that are formed from it, is a general instance of this: in it albumen and fibrine predominate, and there is no gelatine; in them gelatine is abundant, and fatty matter: and both these, through their affinities to the saccharine and oily principles, approach the characters of the lower vegetable and inorganic compounds.

The granulation-substance is a good instance in point: while lowly developed, but in an active vegetative life, it is albuminous; when perfect in its developement, its perfected structures are gelatinous or horny. In this state its particles have probably a longer existence: they exchange a brief life of eminence for longevity in a lower station.

I have spoken hitherto of the developement of only those structures which form the proper material of granulations, and of the scars that remain after the healing of wounds. But, commensurately with these, bloodvessels, and perhaps, also, nerves, are formed. Of these, therefore, I will now speak.

In the last lecture I referred to the changes that ensue in the circulation of a wounded part. At first, it appears that the blood stagnates in the vessels immediately adjacent to the wound. This is evident in the wounds made in frogs' webs, and is most probable in the case of wounds in our own tissues; for else we could hardly understand the total absence of bleeding from a surface on which, as in every large wound, myriads of small vessels must be cut and lie exposed. But after a time, of various duration in the different tissues, the movement of the blood is renewed, though not to its former velocity; the vessels of the wounded parts enlarge, and they all appear more vascular. Then the material of granulations, already in part effused, accumulates, and very soon blood and bloodvessels appear in this material.

By what process are these new vessels formed? Mr. Hunter's opinion was, (and it appears still to be often entertained) that both the blood and vessels form in the granulation-substance, as they do in the germinal area of the chick; and that, subsequently, they enter into communications with the vessels and blood of the part from which the granulations spring. But it certainly is not so; although the developement of vessels is according to a method equally natural with that described by Mr. Hunter.

In embryos, we may discern three several modes according to which bloodvessels are formed—a good example of the manifold ways by which, in developement, the same end may be reached. In the first and earliest method, they are constructed around the blood-corpuscles, which being gradually developed from some of the embryo-cells, are laid-out in the plan of the earliest and simplest circulation of the blood. Thus, in the larvæ of Batrachia, as in the common tadpole, before even the walls of a heart are formed, one sees a crowd of embryo blood-corpuscles collected where the heart is to be; and, in the substance of the out-growing external branchiæ, are looping lines of blood-corpuscles, around which as yet no walls can be discerned. It is so, also, with the blood and vessels of the warm-blooded vertebrata: the corpuscles are rapidly developed from some of the cells of the germinal area, and are laid out in the plan of the heart, and the terminal sinus, and their communicating channels. But at first it is only as a plan: the blood does not move, and is not walled-in. Then, as the heart and vessels are formed around the blood, its circulation in these simple channels is established. In this case, the vessels appear to be formed of the plasma or fluid material which lies between the cells, and gradually assumes the condition of a membrane, and is then developed into the more complex structures of the bloodvessels.

After this earliest period of embryo-life, it is probable that blood is never formed except within the vessels already constructed. It would seem as if none but the original embryo- or germ-cells could be directly transformed into blood-corpuscles; all those that are later made derive their materials through a process of gradual elaboration in lymph- or blood-vessels, to which process no resemblance can be discerned in the substance of granulations. To increase the extent and number of vessels that must be added in adaptation to the enlargement and increasing complexity of the embryo, two methods are observed; of which the one appears chiefly appropriate to the interstitial formation of new vessels, the other, for the construction of those of superadded or out-growing parts.

For the former, one finds, in the interspaces of vessels already existing, primary cells, which enlarge and elongate, and send out branches in two or more directions,—branches sometimes so exceedingly slender, that one might take them for mere threads of embryonic fibro-cellular tissue. But they are hollow: and while some of them are directed into anastomosis with each other, others extend towards, and open with dilatations, into the vessels already formed and carrying blood. Then, these fine branches of each stellate cell becoming larger, while the main cavity of the cell, from which they issued, attenuates itself, they are altogether transformed into a network of nearly uniform calibre, and through these the blood, entering by the openings of communication with the older vessels, makes its way.

Thus the wide spaces of the network formed in the primordial circulation are subdivided into smaller meshes, and each part receives a more abundant supply of blood. Such a developement (as shown in the diagrams) may be seen in the soft gelatinous matter within the amnion of embryo-sheep, and in the tissue of the tail of the tadpole; though in this last the developement is often abortive.

But, for parts that are formed by superaddition or out-growth, another mode of developement of blood-vessels is observed; and this, I believe, is the only mode in which new blood-vessels are ever formed for granulations, or for superficial deposits of lymph, adhesions, and the like. The sketch is made from what may be seen in the growing parts of the tadpole's tail: it accords with what Spallanzani observed of the extension of vessels into the substance of the tail when being reproduced after excision. Mr. Travers and Mr. Quekett* watched the same in the new material formed for the filling up of holes made in the frog's web: the same process is indicated in the specimens illustrating the repair of similar wounds which were purchased by the College from the Museum of the late Dr. Todd, of Brighton; and there is no reason to suppose that any other method prevails for the supply of blood-vessels to any granulations, or similar new productions. For, though the process in granulations or in lymph cannot be exactly watched during life, yet every appearance after death is consistent with the belief that it is the same as I have described, and no appearances are found which would justify a suspicion that either of the other methods of developement has occurred.

The method may be termed that by *out-growth* from the vessels already formed. Suppose a line or arch of capillary vessel passing below the edge or surface of a part to which new material has been superadded. The vessel will first present a slight dilatation in one, and coincidently, or shortly after, in another point, as if its wall yielded a little near the edge or surface. The slight pouches thus formed gradually extend, as blind canals or diverticula, from the original vessel, still directing their course towards the edge or surface of the new material, and crowded with blood-corpuscles, which are pushed into them from the main stream. Still extending, they converge; they meet; the partition-wall, that is at first formed by the meeting of their closed ends, clears away, and a perfect arched tube is formed through which the blood, diverging from the main or former stream and then rejoining it, may be continuously propelled.

In this way, then, are the simplest blood-vessels of granulations and such out-growths formed. The plan on which they are arranged is made more complex by the similar out-growths of branches from adjacent arches, and their mutual anastomoses; but, to all

* On Inflammation, and the Healing Process.

appearance, the whole process is one of out-growth and developement from vessels already formed. And I beg of you to consider the wonder of such a process; how, in a day, a hundred or more of such loops of fine membranous tube—less than 1-1000th of an inch in their diameter—should be upraised, not by any mere force of pressure, though with all the regularity of the simplest mechanism, but each by a living growth and developement, as orderly and exact as that which we might trace in the part most essential to the continuance of the life. Observe, that no force so simple as even that of growth or mere assimilation can determine such a result as this: for, to achieve the construction of such an arch, it must spring with due adjustment from two determined points, and then its flanks must be commensurately raised, and these, as with mutual attraction, must approach and meet exactly in the crown. Nothing could accomplish such a result but a power determining the concurrent developement of the two out-growing vessels, in conformity with the same law as that according to which the same power actuates the germ. We admire the intellect of the engineer, who, after years of laborious thought, with all the appliances of weight and measure, and appropriate material, can begin at points wide apart, and force through the solid masses of the earth one tunnel, and can wall it in secure from external violence, and strong to bear some ponderous traffic;—and yet he does but grossly and imperfectly imitate the Divine work of living mechanism that is hourly accomplished in the bodies of the least conspicuous objects of creation—nay, even in the healing of our casual wounds and sores.

The wonder of the process is, perhaps, in some degree, enhanced by the events that will follow what may seem to be an accident. When the new vessel has begun to project, it sometimes bursts; and the diagram shows what then will happen. (I have to thank Mr. Quekett for the sketch, which he made while assisting Mr. Travers, in the examinations of which he has published the results in his work on Inflammation and the Healing Process.) The blood-corpuscles that issue from the ruptured pouch or diverticulum collect in an uncertain mass within the tissue, like a mere ecchymosis; but, before long, they manifest a definite direction, and the cluster bends towards the line in which the new vessel might have formed, and thus opens into the other portion of the arch, or into some adjacent vessel. For this mode of formation from vessels, the name of *channelling* seems more appropriate than that of out-growth; for it appears certain that the blood-corpuscles here make their way in the parenchyma of the tissue, unconfined by membranous walls. That they do so in a definite and purposive manner, though their first issue from the vessel has appeared so accidental, may be due to the fact that, in the more regular developement by out-growth, the cells of the parenchyma concur with the extension of the new vessels, by clearing away from them as they approach; so that, even before the out-growth, the way for it, or for its contents (should they happen to escape), is, in some measure, determined.

The occurrence of such a process of channelling as is here indicated loses all improbability, when we remember that in insects the blood habitually flows, in a considerable and important part of its course, through sinuses, spaces, or channels without proper walls, such as are here supposed to exist only for a time. In such channels, too, it seems very probable that the blood moves in part of its course through some of the softer medullary and other morbid growths: at least, in these I have often found it impossible, with the microscope, to detect even the rudiments of such vessels as could carry their great supplies of blood.

The general plan of arrangement of the blood-vessels in granulations agrees with this account of their developement by out-growth. Some of Sir A. Cooper's preparations in the Museum* of the College show how the new vessels extend from the parts on which the granulations lie, in lines directed vertically towards their surface, not often dividing, but communicating on their way by frequent transverse or irregular branches. Of these branches, some probably represent the loops or arches successively formed in the deepening layer of granulation-cells, while others must be formed by offshoots from the sides and other parts of the several arches. Near the surface of the granulations, at a very little distance below the outermost layer of the cells, the vessels communicate much more frequently, and form their loops or terminal arches—arches of junction between the outgoing and the returning streams of blood.

On the same plan are formed the vessels of the walls of abscesses lined with granulations; but here (at least in the specimens I have been able to examine) the vertical vessels are not so long, and the whole number of vessels is generally greater. I believe the vessels of granulating ulcers are always similarly arranged; so they are represented by Mr. Liston† in a common ulcer; so, also, Sir A. Cooper‡ described them in

* Museum of the College of Surgeons, Nos. 19, 20, 356.

† Medico-Chirurgical Transactions.

‡ Catalogue of the Pathological Museum of the College, vol. i. p. 110, Specimen No. 246.

granulations from an ulcerated scirrhous cancer; and I have found the same general plan in the warty ulceration of soot-cancer on the scrotum.

The structure of the new vessels formed in granulations also agrees with the described mode of development. In the earliest period of their appearance they present no indication of being formed by the fusion, or any transformation of the granulation-cells, but consist of thin membrane, in which, if it be not quite simple, nuclei or cytoblasts are imbedded. These nuclei pass through the same stages of development, by narrowing and elongation, as those I have described in the nucleated blastema; and thus they become like the pieces of flat fibre that one sees on the walls of the original vessels of the same size. Like them, also, they are arranged, some longitudinally and some transversely to the axis of the vessels, giving them, as the diagram shows, a character altogether peculiar.

Respecting the purpose of the supply of blood thus sent to granulations, one traces, in the developement of vessels, a series of facts exactly answering to those in ordinary embryonic developement. Organization makes some progress before ever blood comes to the very substance of the growing part; for the form of cells may be assumed before the granulations become vascular. But, for their continuous active growth and developement, fresh material from blood, and that brought close to them, is essential. For these the blood-vessels are formed; and their size and number appear always proportioned to the volume and rapidity of life of the granulations. No instance would show the relation of blood to an actively growing or developing part better than it is shown in one of the vascular loops of a granulation, imbedded among the crowd of living cells, and maintaining their continual mutations. Nor is it in any case plainer than in granulations, that the supply of blood in a part is proportionate to the activity of its changes, and not to its mere structural developement: the vascular loops lie imbedded in the simplest primary cells, or, when granulations degenerate, in structures of yet lower organization; and as the structures are developed, and fibro-cellular tissue formed, so the blood-vessels become less numerous, till the whole of the new material assumes the paleness and low vascularity of a common scar.

Of the developement of Nerves in granulations I know nothing: I have never been able to see any in either granulations or cicatrices. The exquisite pain sometimes produced by touching granulations would indicate the presence of nerves: but it would be more satisfactory to see them; for the force of contact, or the change that it produces, may be propagated through the largest granulations, and stimulate the nerves beneath them, as contact with the exterior of a tooth excites the nerve-filaments in its pulp. The sensibility that granulations seem to have may, therefore, be really that of the excited tissues from which they spring.

Lymphatics do not exist in granulations. Professor Schroeder van der Kolk has demonstrated them in false membranes by mercurial injections: * but, in a letter recently received he tells me that they cannot, either by these or any other means, be traced in either scars or granulations; and, he adds, "they cannot be demonstrated in the skin, even in the healthy state, except in the scrotum."

The subject of suppuration should perhaps be considered now; but I had rather defer it till I have spoken briefly of the two remaining modes of healing open wounds—those, namely, by *secondary adhesion*, and by *scabbing*.

The healing by secondary adhesion, or union of granulations, has been long and often observed; yet it has been only casually described, and having never been distinguished by a specific name, has not received that attention to which its importance in practice seems to entitle it. It occurs wherever surfaces of granulations, formed in the manner just described, well-developed, but not yet covered with cuticle, are brought into contact, and so retained at rest. As often as this happens, the cells of which the surfaces are composed adhere together; vessels passing through them form mutual communications; and the surfaces, before separate, are connected; out of the two layers of granulations, one is formed, which pursues the normal developement into fibro-cellular tissue.

In all its principal characters, therefore, the process of secondary adhesion is like that adhesion for which, to mark at once their likeness and their differences, I have suggested the term of primary. In the primary adhesion, the layer of lymph, placed between the wounded and bare surfaces, is probably formed equally from both, and being developed in the same manner as the granulations, of which I have spoken, probably receives vessels from both surfaces, and so becomes the medium through which the vessels communicate and combine the severed parts. In the process of secondary adhesion, the superficial cells on the surfaces of two layers of granulations are placed together, and receiving vessels from both combine them into one.

* Lespinasse, De Vasis Novis Pseudo-membranarum, figs. iii. iv.

Mr. Hunter had observed this process, and says of it—"granulations have the disposition to unite with one another when sound or healthy; the great intention of which is to produce the union of parts, somewhat similar to that by the first intention, although possibly not by the same means" (iii. 493). And "I have seen two granulations on the head—viz. one from the dura mater after trepanning, and the other from the scalp, unite over the bare bone which was between them so strongly in twenty-four hours, that they required some force to separate them, and when separated they bled."

In illustration of the process he put up this preparation,* which in his MS. Catalogue,† he described as "granulations under the skin in an abscess in the leg, which were opposed by others on the muscles, and which were to unite. Those under the skin only are saved and folded towards each other, to show the opposition of two granulating surfaces."

There are several circumstances in which the healing by secondary adhesion should be attempted,—such, for example, as I witnessed in a case which was lately in St. Bartholomew's. After an ordinary circular amputation of the thigh, no immediate union and no primary adhesion had taken place, and the whole interior of the stump was granulating. Had it been, as the expression is, left to granulate, or to fill up with granulations, the healing process would have occupied at least a month or five weeks more, and would have greatly exhausted the patient, already weakened by disease. But Mr. Stanley ordered the stump to be so bandaged that the opposite surfaces of granulations might be brought into close contact: they united, and in a week the healing of the stump was nearly perfected.

In all such cases—and I need not say that they are very frequent—the healing by secondary adhesion may be attempted without danger, and with manifest advantage.

Again: Mr. Hunter operated for hare-lip, and no primary adhesion of the cut surfaces ensued. He let them both granulate: then brought the granulations together, as in the common operation, and they united, and healed soundly.

Or, again: Mr. Skey, not long since, operated for fissure of the soft palate. The very edges of the wounds sloughed and retracted, and the case seemed nearly hopeless; but he kept in the sutures, and granulations sprang up from the edges of the cleft, after the separation of the sloughs: they met in the mid-space of the cleft, and coalesced, and formed a perfect scar.

* Museum of the College of Surgeons, No. 27.

† Pathological Catalogue of the Museum of the College of Surgeons, Vol. i. p. 16.

Doubtless, cases like these are of no rare occurrence: but I am induced to mention them as illustrations of a process of which the importance and utility are not generally considered, and which is rarely applied in practice.

In applying it in practice, certain conditions are essential to success; especially that—first, the granulations should be healthy, not inflamed, or profusely secreting, or degenerated, as those in sinuses commonly are; 2dly, that the contact between them should be gentle but maintained; and perhaps they should be as much as possible of equal developement and alike.

The treatment of wounds by scabbing may be regarded, as Mr. Hunter* says, as the most natural one—for it requires no art. It is the method by which one sees nearly all open wounds healed in animals; for in them, even in the warm-blooded, it is difficult to excite free suppuration from the surfaces of wounds: they quickly become coated over with a scab formed of the fluids that ooze from them and entangle dust and other foreign bodies; and under such a scab the scar is securely formed.

In general, the scabbing process is effected by some substance effused on the surface of the wound, drying there, and forming a hard and nearly impermeable layer. The edges of this substance adhere over those of the wound, so as to form for it a sort of air-tight covering, under which it heals without suppuration, and with the formation of a scar, which is more nearly like the natural parts than any scars formed in wounds that remain exposed to the air, and which does not, like them, contract, so as to produce deformity of the parts about it.

The scab may be formed of either dried blood, dried lymph and serum, or dried purulent fluid. Instances of the healing of wounds under dried blood are not rare. It is especially apt to occur in the cases of wounds in which a large flat surface is exposed, as after the removal of the mammary gland. The most remarkable case of this kind is recorded by Mr. Wardrop,†—the largest wounded surface he ever saw, remaining after the removal of a diseased breast, almost entirely healed under a crust of blood, which remained on for more than thirty days.‡ But the most common examples of healing under blood scabs are in small wounds—such as are made in bleeding, or more rarely in some compound fractures.

* Works, Vol. iii. 262.

† In his Lectures on Surgery, in the Lancet for 1832-3, Vol. ii.

‡ Mr. Henry Lee tells me that a similar case has lately occurred in his practice. An excellent instance of healing under blood-scabs is also related by Dr. Macartney (Treatise on Inflammation, p. 208.)

The excellent, though nearly obsolete, practice of laying on such wounds a pad of lint soaked in the blood, was a good imitation of the most natural process of their repair.

If a blood-scab be not formed over a wound, or if such an one have been detached after being formed, then at once a scab may be derived from the serum and lymph that ooze from the surface of the wound. Thus it is commonly with wounds in animals that are left to themselves, and in many small wide-open wounds in our own case. Thus, also, I imagine, the best healing of burns and scabs is effected, when the exposed surface is covered with cotton-wool or other substance, which, as the oozing fluids become entangled with it, may help them to form a scab.

At a yet later period, the pus produced from exposed granulating wounds may concrete on them, and they will heal under it excluded from the air. Such a process may also ensue in the healing of ulcers, and has been successfully imitated in Mr. Stafford's plan of filling deep ulcers with wax*. In any case the healing process is probably just the same as that under scabs of blood or serum; but, I believe, it has not yet been exactly determined what are the changes that ensue in the surface beneath the scab. So far as one can discern with the naked eye, the wounded surface forms only a thin layer of cuticle on itself; no granulations, no new cellular tissue, appears to be formed; the raw surface merely skins over, and it seems to do so uniformly, not by the progressive formation of cuticle from the circumference towards the centre, as is usual in open wounds.

The healing of a wound by scabbing has always been thought a desirable process; and when one sees how quickly, by means of this process, wounds in animals are healed, and with how little general disturbance, one may well wish that it could be systematically adopted. But to this there seems some hindrance. Many surgeons have felt, as Mr. Hunter did, that the scabbing process should be permitted much oftener than it is, in the cases of both wounds and ulcers; but none have been able to lay down sufficient rules for the choice of the cases in which to permit it. Probably, the reason of this is that, at the best, in the human subject, the healing by scabbing is an uncertain process. When the scab is once formed, and the wound covered-in, it is necessary that no morbid exudation should take place. Whenever, therefore, inflammation ensues in a wound or sore covered with a scab, (and this, I need hardly say, is a very common event) the effused fluid, collecting under the scab, produces pain, compresses the wounded surface, or forces off the scab, with great discomfort to the patient and retardation of the healing.

* On the Treatment of the Deep and Excavated Ulcer. 1829.

I suspect that the many instances of disappointment from this cause have led to the general neglect of the process of scabbing in the treatment of wounds. The observance of perfect rest, and of the other means for warding off inflammation, might, however, yet make it an available auxiliary in the treatment of wounds, especially of large superficial ones; for, in the treatment of small wounds, collodium appears sufficient to accomplish all that scabbing would do.

Such are the several methods of healing observed after wounds of soft parts;* and in connection with them, two subjects remain to be considered, namely, the process of suppuration, and that of the perfecting of scars.

Respecting the process of suppuration, it cannot be necessary that I should give a particular account of pus, or of its general or chemical characters. I will rather endeavour to show its relations to the healing process, by illustrating the points of resemblance and of difference between it and the material of which granulations are formed.

Let me remind you that the formation of granulations is not necessarily attended with the production of pus. I have already referred to this fact in speaking of the formation of subcutaneous granulations, such as are sometimes seen on the ends of bones that do not unite, in the ordinary way, after simple fractures. Mr. Hunter also expressly describes these cases; and the same kind of granulations without suppuration may be sometimes seen springing from the ulcerated articular surfaces of bones, in cases of diseased joint without any external opening.

It would be an interesting fact if it were found that the granulations that do not suppurate are those that are formed of nucleated blastema: they are so in some cases, I know; but it is not proved of all. However, the common instances of suppurating granulations are those that are formed of nucleated cells; and with these pus may be formed, whether on an open surface, or on the walls of an abscess, or on the walls of an inflamed serous cavity, when, as in empyema, the lymph acquires a free granulated surface.

To illustrate the relations between pus and granulations, at least so far as their component cells are concerned, this diagram may serve, which was copied from sketches that I made, at the same time, of some granu-

* I have not been able to recognize what Dr. Macartney has named the *modelling process*, as a method of healing distinct from that which ensues in the most favourable instances of healing by granulations. I have, therefore, not enumerated it among the modes of healing; yet it may occur in some conditions that I have not met with: I would not, with only my present experience, impute confusion to so good and independent an observer as Dr. Macartney.

lation-cells from the walls of a sinus, and some pus-cells from a healthily granulating wound. I chose these sources purposely, that I might be able to compare ill-developed granulation-cells with well-constructed pus-cells: and a comparison of them shows that, whether as seen without addition, or as changed by the action of water and acetic acid, they are not to be distinguished from one another. Had I not seen the vessels in the tissue that these granulation-cells formed, I might, in the first examination, have almost thought I was deceived in thinking they were not pus-cells. Six varieties of the appearances of the cells from each source are here shown, and they severally exactly correspond. Other varieties of form might have been drawn from both sources; but these may suffice to show the apparent identity of structure between well-formed pus-cells and the ill-developed or degenerate granulation-cells, such as are found in the walls of sinuses and the like half-morbid structures. I do not mean to say generally that granulation-cells and pus-cells cannot be distinguished; for between well-formed granulation-cells, such as are found in healing wounds, and any particles that can be found in pus, certain distinctions are almost always manifest. The pus-cells are darker, more and more darkly granular, more various in size, and more various, not in shape, but in apparent structure, more often containing particles like fatty molecules, more rarely showing a nucleus when neither water nor acid is added, and much more commonly showing a tripartite or ill-formed nucleus under the action of the acid: above all, not showing any molecular movement of their contained particles when they are distended with water. This last character, of which I was informed by Mr. Quekett, is certainly the best for the determination of pus-cells, however formed. I am not sure that it ever fails to be a sufficient mark of diagnosis for them; still, neither it nor all the rest of the characters I have enumerated are indicative of essential difference; and between even the widest extremes there are all possible gradations, till distinction is impossible; so that when you place, as I have often done, ill-developed or degenerate granulation-cells on one side of the microscope-field, and pus-cells on the other, there is not a form of corpuscle on the one which is not repeated on the other.

From this, one cannot but draw the conclusion that the cells of pus are ill-developed or degenerate granulation-cells. Some of them may be degenerate, *i. e.* they may have been, as granulation-cells, attached for a time to the surface of the granulation-layer, and, having been to a certain point properly developed, and having lived their time, may, in ordinary course, have been detached and shed, as epithelial cells continually are from healthy surfaces. They may be thus detached after more or less degeneration, and hence may result some of the modifications of form that they present; but some also, I imagine (at least in the healing of wounds), may be ill-developed, —that is, imperfectly formed of the material which exudes from the surface of the granulations, and which, being exposed to the air, or being too remote from the supply of blood, cannot attain its due developement, and, in an imperfectly developed state, is soon cast off. It cannot but be that organizable matter is constantly oozing from such a surface as that of granulations; but the conditions into which it enters on that surface are such as are very likely to hinder any but the lowest and an imperfect organization.

The many characters of degeneracy that pus-cells show accord with this view; such as the general imperfection of their nuclei, —the abundance of large and fatty-looking granules in them,—the large quantity of fatty matter that chemical analysis detects, —and their limitation to certain forms, beyond which they are never found developed, though none of these forms is more highly organized than that of the youngest or most rudimental granulation-cell.

A further confirmation of the opinion that pus-cells are ill-developed or degenerate granulation-cells, is furnished in the numerous cases in which pus-cells are produced after, or together with, inflammatory exudation-cells; as in abscesses, inflammation of serous membranes, and the like. Now exudation-cells are not distinguishable in apparent structure from granulation-cells, and, like these, may show every gradation of form to that of the pus-cell; so that, from both cases, we may conclude that the true relation which the cell in granulations or in inflammatory lymph holds to the pus-cell, is that of a well-organized structure to the same structure either ill-developed or degenerate after having, up to a certain point, been duly formed. To this we are guided by the comparison of the granulation-cell, in its earliest and most imperfect state, with the pus-cell in its best condition; and the contrast becomes the stronger while we trace the one, in its vigorous life, developing itself into new and higher structures,—the other, in its decay, degenerating to lower forms and lower chemical composition.*

* Valentin, Gerber, and many others, have held nearly the same view as this of the character of pus-cells; but I think they have not sufficiently, if at all, dwelt on the probability that some pus-cells are ill-developed, others degenerate from a previously higher developement. The many varieties of form, and the many differences of the conditions in which they occur, may be thus explained. I think, too, that the characters of degeneracy, or imperfect developement in the liquor puris, have been too much overlooked.

But it is not only in the cells that we may trace this appearance of the degeneracy of pus: it is equally shown in the fluid part, or *liquor puris*, which, unlike the solid fibrinous intercellular substance of granulations and inflammatory lymph, is always albuminous, and incapable of organization, even when, by evaporation or partial absorption, it assumes the solid form.

Now this liquor puris answers to the solid and organizable blastema of granulations; and as undue liquidity is among the most decided marks of ill-formed pus, so the abundance of the blastema, in proportion to the cells, is one of the best signs that granulations are capable of quick developement.

An observation, which any one may easily make, seems to indicate that the liquor puris may be the product of the degeneration and liquefaction of the solid blastema, as the pus-cells appear to be of the granulation- or exudation-cells imbedded in it. If the formation of abscesses be watched, one may see, on one day, a large solid and inflamed swelling, firm and almost unyielding, giving no indication of containing any collection of fluid; but next day, one may detect in the same swelling the signs of suppuration: the border may feel as firm as before, but all the centre and the surface may be occupied with an ounce or more of matter. And observe,—this change from the solid to the liquid state may have ensued without any increase of the swelling. Such an increase must have occurred had the pus been secreted in a fluid state into the centre of the solid mass: and the changes cannot, I think, be explained except on the admission, that the inflammatory product, which was effused and infiltrated through the tissue in a solid form, has been liquefied: its exudation-cells degenerating into pus-cells, its blastema into liquor puris.*

Such, briefly, is the account which may be rendered of pus in its relation to the granulating process; nor can I find any facts which are inconsistent with this view. I will only add a suspicion that other rudimental forms of tissues may, in degeneration, sometimes assume the characters of pus-cells. The easy transition from some forms of mucus-cells to pus-cells would imply that much of the pus so readily secreted from inflamed mucous membranes is formed, not of degenerate lymph, but of their natural products, degenerated or ill-developed. And the equally indefinite line of distinction between the white or rudimental corpuscles of the blood and the pus-cells, may suggest that that most obscure affection, purulent diathesis or pyæmia, may have its essential anatomical character in the degeneration of the white blood-corpuscles. The arrested developement of these blood-corpuscles appears to be a constant occurrence in all inflammations; if to this were added a degeneration of them after the arrest, I believe the suppuration of the blood would be, so far as its anatomical characters are concerned, accomplished.

* Such a liquefaction is not that assumed in the older doctrines, which held that pus was partly formed of the dissolved materials of the original tissues. The orginal tissues doubtless remain, unless partially absorbed: yet there appears to be thus much of liquefaction in the formation of an abscess, that the inflammatory product, first formed as a soft solid, degenerates and becomes fluid.

Can we assign any use or purpose to the process of suppuration? In the case of abscesses and acute inflammations we may discern no more of purpose than in any other disease. But in the case of granulating wounds, the use commonly assigned to pus, that it serves as a protection to the granulations, is probably ascribed to it with reason. It does this even in the fluid state; but the devices of surgical treatment, having regard to present comfort, rarely let us see how much better it protects a wounded surface when, as in animals, it is allowed to dry into a scab.

Let us now consider the case of a wound completely healed, and the scar that occupies its place.

It is hard to describe in general terms the characters of scars, varying as they do in accordance with the peculiar positions, and forms, and modes of healing of wounds. But two things may be constantly observed in them: namely, their contraction and their gradual perfecting of their tissues.

A process of contraction is always associated with the developement of granulations. Mr. Hunter has minutely described it, and preserved several specimens to illustrate it: among which are two stumps,* in which its occurrence is proved by the small size of the scars in comparison with that of the granulating surfaces which existed before them. This healing of stumps, especially after circular amputations, will always show the contraction of the granulations, even before the cicatrix is formed; for one sees the healthy skin drawn in and puckered over the end of the stump, before any cuticle is formed on the granulations, except perhaps on the very margin. And many injuries, but especially burns, show the contraction of the scar continuing long after the apparent healing is completed.

To what may we ascribe this contraction of both the granulations and the scars? It has been regarded as the result of some vital power of contraction; and possibly it may be so in some measure. Yet, on the

* Nos. 28 and 29 in the Museum of the College.

whole, it seems rather to be the necessary mechanical effect of the changes of form and construction that the parts undergo. The same change ensues in the organization of all inflammatory products: as, *e. g.*, in false membranes, indurations, thickenings of parts, and the like consequences of the effusion and organization of lymph.

Now, in all these cases, the form of the cell, while developing itself into a filament, is so changed that it will occupy less space. The whole mass, too, of the developing cells becomes more closely packed, and the tissue that they form becomes much drier; with this, also, there is much diminution of vascularity. Thus, there results a considerable decrease of bulk in the new tissue as it developes itself; and this decrease, beginning with the developement of the granulation-cells, continues, and I think sufficiently accounts for the contraction, without referring to any vital power.

The force with which the contraction is accomplished is often enormous. One sees its result in the horrible deformities that follow the healing of severe burns; and I have here a specimen, in which I have no doubt, that, as in one described by Mr. Curling, deep scarred and seamed depression of the outer table of the skull was caused by the contraction of granulations over it.

The improvement and perfecting of the tissue of the scar is, again, a very slow process. It is often thought remarkable, that nerves and some of the higher tissues should require so long time for their repair; but scarcely less is necessary for the perfecting of a common scar. The principal changes by which it is accomplished include the removal of all the rudimental textures, the formation of elastic tissue, the improvement of the fibrous or fibro-cellular tissue, and of the new cuticle, till they are almost exactly like those of natural formation, and the gradual loosening of the scar, so that it may move easily on the adjacent parts.

All these changes are very slowly accomplished. One sees their effects, it may be, only after the many years in which, as it is said, the scars of childhood gradually wear out; *i. e.*, in which the new formed tissues gradually acquire the exact similitude of the old ones. Thus, the remains of the rudimental cellular tissue, imperfectly developed, may be found in apparently healthy scars of ten months' duration. After second operations, in which the scar of some former wound was removed, I have still found imperfectly developed granulation-cells in the tissue of the scar. Elastic tissue, also, I think, is not commonly formed in the first construction of a scar, but appears in it sometimes as much as twelve months after its first formation, and then gives it the common structure of the mixed fibro-cellular and elastic tissues which exist in the cutis.

But, an occurrence which may appear more singular than this is, in all good scars, as they are called, that gradual loosening of the tissue that at first unites the scar to all the adjacent parts. Thus, in such a wound as is made for tying a deep artery, or in lithotomy, at first, the new tissue, the tissue of the scar, extends down to the bottom of the wound, equally dense in all parts, and fastening the skin to the parts at the very deepest portion of the wound. But after a time this clears up. The tissue of the scar in the skin becomes more compact and more elastic; but that beneath it becomes looser and more like natural cellular tissue; and the morbid adhesions of one part to another are freed.

Now, in all this we may trace, I think, a visible illustration of the recovery from the minute changes of disease, —I mean, in this gradual return of tissues to the healthy state, — in the gradual approach of the new particles that are successively produced to a nearer conformity with the specific character of the parts they should replace, till repair becomes almost reproduction. And how can all this be reconciled with any theory of assimilation? How could assimilation alter the characters of a scar? or make one part of it assume one character, and another part a character quite different? so that, at length, that which looked homogeneous as a mass of new-formed tissue, acquires, in separate parts, the characters of the several tissues in whose place it lies, and whose office it is destined, though defectively, to discharge.

LECTURE V.

Repair of Fractures—Differences between the process in man and that in lower animals. Absence of provisional callus in the repair of fractures in man. Evidence from cases of complete repair, and of repair in progress. Position of the reparative materials in fractures in the human subject. Probable reasons of the differences in the two processes.

Modes of Ossification of the reparative material. Natural modes of ossification: through cartilage and fibrous tissue. More numerous modes in the repair of fractures. Usual characters of the new bone, and its later changes. Arrest of the reparative process.

I SHALL not endeavour in the present lecture to treat fully of the Repair of Fractures. No one acquainted with the extent of the observations already made on this subject, and with the reputation of those who have been occupied with them, will blame me if I almost limit myself to the endeavour to explain only two or three points in the history of the repair of injured bones. The chief points that I have chosen are—1st, the particulars in which the process of repair of fractures, observed in the human subject, deviates from that described from experiments upon lower animals; and secondly, the nature of the reparative material previous to its ossification.

On the first point, I must express my conviction that the description drawn by Dupuytren and others, from examinations of fractures in dogs, rabbits, birds, and other animals, cannot be applied without great deductions to the case of fractures in the human subject. True as the pictures are of the cases of the animals examined, they are exaggerations of the process in our own case. With a few exceptions, all that is written in these accounts of external and internal, provisional and definitive, callus, of the formations of cartilage and bone within the medullary tube and beneath the periosteum, can be traced only, as it were, in rudiment in the fractures of the human bones.

My impression of this was first obtained while describing the large collection of fractures for the Catalogue of the Museum of the College.

With the concurrence of Mr. Stanley, who had long held a similar opinion,* I then wrote—" There is scarcely a specimen in the Museum of such a provisional callus formed in the repair of a fractured human bone; in nearly every case of such fracture, the material of repair, whether cartilage or bone, is only inlaid between the broken surfaces, or between the adjacent parts of the fragments, and unites them by being fixed to both. In favourable conditions this appears to be the usual mode of repair, even though the fragments of the broken bone be very much displaced."

" But the formation of a provisional callus, completely encircling the broken ends and adjacent parts of the fragments, is usual in the repair of fractures of the bones of other mammalia, and of birds. . . . A similar, but less perfect process is also shown in the accumulations of cartilage or bone which are often formed about fractures of the ribs, and of some other bones in the human subject, the fragments of which have not been held steady. It is probable, therefore, that the difference between the modes in which fractures are commonly united in man and other animals respectively, depends in part on the movement to which the fragments are subjected in the latter,—but, probably, in part also on the greater readiness with which, under all circumstances, bone is formed in the animals lower than man."†

Since that was written, I have examined many more specimens, and find the same rule true—namely, that in the ordinary repairs of simple fractures in the human subject, the reparative material, or callus, is merely inlaid between the several fragments: it fills up the interspaces between them and the angles at which one fragment overhangs another; but it does not encircle or ensheath them, in the manner implied in the description of provisional callus: nor is it in any considerable quantity, if at all, deposited either

* Since the delivery of the lecture, Mr. Stanley has published his account of the Repair of Fractures in the descriptions of his beautiful " Illustrations of the Diseases of the Bones," p. 27.

† Pathological Catalogue of the Museum of the College of Surgeons, vol. ii. p. 37.

beneath the periosteum or within the medullary tube. In birds, dogs, and other ordinary subjects of experiments, the formation of a provisional, or, as it may, perhaps, be better called, an *ensheathing* callus, is usual. It is illustrated by numerous specimens on the table ; yet even in animals it is not constant. To obtain what would be called good specimens of provisional callus, the injuries must be inflicted upon young animals, and among these I cannot but suspect that particular instances have been selected for description,—those in which less callus was formed having been put aside as imperfect instances of repair, though, in truth, they may have displayed the more natural process.

For fractures in the human subject, the evidence that union is accomplished by the reparative material being placed between, not within and around, the fragments—*i. e.* as an intermediate, not an ensheathing callus—this evidence may be obtained by the examinations of such fractures even long after they are completely healed. In as many as you like to examine you will find the new bone formed exclusively between the fragments. Whether they were in apposition, or nearly so, or wide apart, still there is no appearance of new bone being formed on the outer side of any fragment,—I mean on that side which is turned away from the other fragments. And this is the case even in those instances in which there is so much displacement of the fragments, and so much distortion, that we can hardly suppose the repair to have proceeded very quietly. Neither in any of these do you find new bone within the medullary tube. It may be objected by some to these specimens, that the fragments were once ensheathed and blocked-up with callus, and that it has been since absorbed. But this is not probable, seeing that in many cases there remain, on the outer surfaces of the fragments, certain marks of their original form and slight irregularities. In one of the specimens which I present,* we have traces of the healing of a long fissure, which appears now as a sunken groove, making it nearly certain that no new bone was formed over it. In another, is a detached piece of the wall of a femur turned quite round, so that its periosteal surface lies on the periosteal surface of the principal fragment; yet on the outer surface of this piece (which was the inner surface of its wall) the thin plates forming the boundary of the medullary tube are still unchanged.†

But if any deem these and the like characters insufficient to prove the absence of ensheathing callus, and of callus extending into the medullary tube, yet recent specimens are not open to such doubts. I add, therefore, that (with the exceptions presently to be mentioned) in all the specimens of fracture that I have been able to examine, in the human subject, within six months of the time of the injury, there has been the same absence of provisional or ensheathing callus. The specimens here present are—a radius, four weeks after the fracture*; another, four or five weeks† ; a tibia, five weeks‡ ; a femur, six weeks§ ; another of the same date‖ ; a third, I should think, about eight or nine weeks¶ ; a radius, of somewhat later date** ; a tibia, eight weeks†† ; a fibula, eleven weeks‡‡ ; a tibia, twelve weeks§§ ; and a tibia, sixteen weeks after the injury.‖‖ Here are, also, others of various but unknown dates, all in process of apparently natural repair. All these were cases of simple fractures, and they include (with a few exceptions presently to be mentioned) all the specimens of such recent fractures, in the human subject, as are in the Museums of the College and of St. Bartholomew's Hospital. The displacements and other conditions following the injury have been manifestly various ; but all agree in this,—that the fragments are united by intermediately placed reparative substance, and that this, whether soft or osseous, in no case surrounds or ensheaths the fragments, or does more than just close in the medullary canal. When present in the largest quantity, it is only enough to smooth off the chief irregularities, and to fill up the interspaces and the angles or corners, between the fragments.

Such, then, appears to be the natural mode in which the reparative material is deposited for the union of fractures of human bones. And, regarding the particular position which it may in each case occupy, I do not know that it can be more exactly described, than by saying, that it is deposited where it is most wanted for the strengthening of the bone,—so that, whatever would be the weak part of the bone, if unhealed, there is the new material placed, in quantity as well as in position just adapted to the exigencies of the case, and restoring, as much as may be, the original condition and capacities of the bone.

If now it be inquired why this difference

* Museum of St. Bartholomew's Hospital, Ser. 3, C. 5.

† Museum of the College of Surgeons, No. 454.

* Museum of St. Bartholomew's Hospital, Series iii. 94.

† The same Museum, Series iii. 95.

‡ The same Museum.

§ The same Museum.

‖ Museum of the College, No. 412-415.

¶ Museum of St. Bartholomew's, Ser. iii. 103.

** The same Museum, Ser. iii. 78.

†† From Mr. Lonsdale's Museum.

‡‡ Museum of St. Bartholomew's, Ser. iii. 80.

§§ The same Museum, Ser. iii. 67.

‖‖ Museum of the College, No. 438, and of St. Bartholomew's, Ser. iii. 113.

should exist in the corresponding processes in man and other animals, I believe still that it must be ascribed principally to the two causes already quoted from the Catalogue —namely, the quietude in which fractures in our bones are maintained, and the naturally greater tendency to the production of new bone which animals always manifest. Even independently of surgery, in the case of fractures of the lower extremity, the human mode of progression almost compels a patient to take rest; and in fractures of the upper extremity, the circumstances of human life and society permit him to do so far more than other animals can. The whole process of repair is, therefore, more quietly conducted; and, as we may say, there is comparatively little need of the strength which the formation of provisional callus would give a broken limb.

The exceptions to the rule of difference in the repair of human bones and those of animals confirm it as thus explained; for the only bones in which, in the human subject, a provisional callus is generally or naturally formed, for the repair of fractures, are the ribs. In cases of fractured ribs one may see, indeed, a very close imitation of that which is described, from experiments on animals, as the ordinary mode of union. The provisional callus is well formed under the periosteum, and encircles, like a broad ring or ferrule, both the fragments, and may almost completely ossify before their union is accomplished, or even apparently begun.

Another bone for the repair of which, but more rarely, callus is formed around the fragments, is the clavicle; and the best specimen in which I have here seen it is one* in which the fracture was not detected, and the fragments were allowed to move on one another, till the patient died twelve weeks after the injury.

Except in such cases as these of fractures not kept at rest, I doubt whether a natural formation of callus beneath the periosteum, or within the medullary tube of a human bone, would ever occur. In disease, the occurrence is not so rare; for, when the natural process of union fails altogether, the loose ends of the bones may be inclosed within a case formed wholly or in part of bone; or an imitation of callus may be made by a gradual morbid accumulation of bone around a fracture, even after its natural union.† (St. B. H. C. 29.)

* Museum of St. Bartholomew's, Ser. iii. 92.

† Museum of St. Bartholomew's, iii. C. 29.—In the same Museum (Ser. iii. 65-66), is a humerus, with a quantity of bony callus accumulated round a fracture of its shaft. It was taken from a man who died some weeks after the fracture, and whose arm had, for a long time after the injury, been the seat of severe spasms. See Mr. Stanley's "Illustrations of Diseases of Bones," Pl. xxiii. fig. 3.

But I think the comparative restlessness of animals is not alone sufficient to account for all the difference in the processes. The remainder may be ascribed to their greater tendency, in all circumstances, to the formation of new bone. Not in fractures alone, but in necrosis this is shown. It is very rarely that such quantities of new bone are formed in even children, as are commonly produced after necrosis of the shafts of bones in dogs or other animals; nor is there in the human subject any such filling up of the cavities from which superficial sequestra have been separated, as the experiments of Mr. Hunter showed, after such exfoliations from the metatarsal bones of asses.*

Other examples might be quoted; but these may suffice to show that, after injuries, new bone is formed more abundantly in animals than in man. And I hope enough has been said to prove that the generally received account of provisional callus, and other parts of the healing of fractures, is an exaggeration of what occurs in man. If it be asked what it is that is felt like a callus after fractures, I would say that, in such cases as I could examine after death, I have usually found that the overlapping ends of the bone, being both at once grasped, had been taken for the enlargement of callus. Sometimes, also, the thickening and induration of the parts around the fracture infiltrated with serous and bloody fluid, or with lymph, have been mistaken for it.

The next point on which I proposed to speak, concerned the structure of the reparative material thus deposited within the fragments. In reference to this, it seems essential that I should refer to those recent observations on the natural process of ossification, which have shown that bone is as commonly and as naturally formed through fibrous or membranous tissue as through cartilage.

Dr. Robert Nesbitt appears to have been the first who described the ossification of certain bones, especially those of the vault of the skull, as being effected in membrane. He did this, in 1731, in "two lectures, read in the Anatomical Theatre of the Surgeons of London;" for in these, which were afterwards published with the title "Human Osteogeny," he says, even in his title page, that "the general notion, that all bones are formed from cartilages, is demonstrated to be a mistake."

His account of the difference between the ossification of the bones of the skull and that of the vertebræ, the pelvis, and the bones of the limbs, is so far accurate, that it appears strange it should not have directed

* Museum of the College, Nos. 641 to 653.

subsequent inquirers much more than it did. But the distinction that he pointed out was, after his time, only occasionally insisted on ;* and till very recently the opinion generally accepted was,—that the bones of the vault of the skull are formed by the ossification of cartilage, and that their developement differs from that of the other bones only in this,—that there is no complete cartilaginous basis formed for each bone before ossification, but that cartilage is formed in the membranous coverings of the brain, just previous to the formation of the bone. Thus, *e. g.*, in the parietal or any of these bones in process of ossification, it was held that a thin border of cartilage might be always found projecting beyond the bone ; and that at the same rate as this border ossified, so another, cartilaginous like it, would be formed in preparation for the next step of ossification ; the formation of the cartilage only just keeping in advance of its ossification, till the formation of the whole bone was perfected. Such was the account given by E. H. Weber and Miescher, and adopted by Henle,† and, I believe, all anatomists of note.

But even while this opinion was gaining ground from observations in the Mammalian fœtus, doubts of its truth were arising from examinations, instituted by Von Baer, into the construction of the primordial cartilaginous skulls of fish. These inquiries, begun in 1822, were, however, little regarded till, in 1835, Dugès published his researches on the Osteology of the Batrachia. In these he showed that the skull of the naked, tail-less, Amphibia is originally entirely cartilaginous ; and that the bones of the perfect skull develope themselves in part from the cartilage of the fœtal skull, and in part on the exterior of that cartilage, in the perichondrium. Thus he gave strength to the opinion which Von Baer had entertained of the developement of the skulls of fish, and directed the observations of many subsequent inquirers — especially of Vogt, Agassiz, Jacobson, and Rathke. I need not enter on the consideration of the various extensions into detail which these gave to the discovery of Von Baer. It may be sufficient for me to state, from an admirable memoir recently published on this subject by Kölliker,‡ that it is now proved "that in all vertebrata the bones of the skull are divisible into two categories : into primary bones, and secondary, overlying or tectile bones, of which the former proceed from the cartilaginous *primordial* skull, and are preformed in cartilage ; while the latter are formed outside the cartilage, from soft blastema between the cartilage and the skin."

* See Hildebrandt's Anatomie, i. 333.

† Allgemeine Anatomie, p. 831.

‡ In the Berichte vom zootomische Anstalt zu Wurzburg, p. 49.

The bones included in each category he enumerates ; but, for my present purpose, it is, perhaps, of yet more interest to add, that by microscopic examinations Dr. Sharpey has not only fully confirmed these views, respecting the ossification of the bones of the vault of the skull, but has added this important fact,—that the ossification by which the long bones increase in their circumference takes place, not in layers of cartilage successively formed beneath the periosteum, but in layers of fibrous substance: in short, that the peripheral growth of bones that are formed in the first instance by ossification of cartilage, is effected by ossification of membrane. In regard to the bones of the skull, observations similar to Dr. Sharpey's appear to have been made at nearly the same time by Spöndli and Kölliker ; and, in regard to the long bones, Kölliker has not only confirmed Dr. Sharpey's observations, but has, more lately, added that the same law holds for the vertebræ, the ribs, and, in short, for all the other bones of the skeleton that are formed from cartilage, with the exception of the ossicula of the ear, which attain their full size in the cartilaginous state.

Thus, then, it will appear that the peripheral growth and ordinary maintenance of all bones, after the ossification of their primordial, and for a time growing,* cartilage is completed, is effected by the ossification of membranous or fibrous tissue. I would call it fibrous rather than membranous, because in some instances, as the patella and other sesamoid bones, and in the union of fractures, and the growth of some tumors, a mass of tissue, rather than a membrane, ossifies.

Thus much of preface seemed necessary to explain the cases in which the material for the repair of fractures is transformed into bone through the developement, not of cartilage, but of fibrous tissue.

What I have just said of the later growths of bones being accomplished by ossification of fibrous tissue, not of cartilage, might lead one to expect that all ossification for the repair of fractures, after the termination of the usual period for ossification through cartilage, would be accomplished through the formation of a fibrous substance. But it is not so : rather, in the examination of many specimens, one finds the new bone

* The cartilage probably grows between the chief mass and the epiphysis of a bone as long as the bone increases in length, its growth only just preceding its ossification: hence it may be said generally, that the growth of a bone in length is by ossification of cartilage,—its growth in thickness by ossification of fibrous tissue, as Kölliker says (p. 44). But when once the growth in length is completed, and the cartilage is exhausted, then all natural ossification, whether for common maintenance or for growth, appears to take place in fibrous tissue.

formed in some through fibrous tissue, in some through cartilage, in some through fibro-cartilage, or a mixture of the two; and, in yet further deviation from any single rule of developement, the bone may be formed through either cartilage or fibrous tissue, in either a rudimental or a perfect state.

The changes that ensue directly after a simple fracture are in accordance with what I have already described in relation to the general repair of injuries. A period of rest follows the injury; and for a week or ten days no change may be observed, at least in fractures in the adult long bones: and here, at once, is a point of contrast with the consequences of fracture in the lower animals; for these specimens,* showing the consequences of fracture of the tibia in rabbits six, ten, and fourteen days after the injury, prove that a perfect cartilaginous callus is in them formed in a shorter time than would elapse before the commencement of any distinct reparative process in man.

Especially, for contrast, one may notice the unchanged state of the periosteum round the broken human bones: for this, in ordinary cases, is neither raised by deposit beneath it, nor in any way altered—except, it may be, by slight thickening—during the whole healing of the fracture.

The first new material produced after simple fracture consists of the lymph and serum, which are effused in consequence of the inflammation that the violence of the injury excites. But these, as in the repair of other subcutaneous injuries, are presently overwhelmed and enclosed (as the effused blood also is) by the more proper reparative material. How this is placed I have already said. In a plan, wherein one cannot overlook the evidences of particular design and of appropriate purpose, it is inlaid between the fragments, wherever, when the limb comes to be used, the most new bone will be necessary for its strength. Thus, it may take the various forms of groins and buttresses, arches, beams, or bridges, according to the mode and degree of displacement of the fragments.

Thus placed, its developement proceeds. I cannot tell the conditions which will determine, in each case, the route of developement towards bone that the new material will take; nor whether the differences that may be observed are to be ascribed to the seat or nature of the injury, or to the condition of the patient. All these things have yet to be determined; and I believe that years of patient and well-directed investigation will be requisite for them. I can do little more than point out the modes in which the ossification may be accomplished.

And, first, it may be accomplished through perfect fibrous tissue. Thus I found it in a case of fracture of the lower part of the femur, and in a fracture of the radius; thus, too, I think, whatever new bone is formed after fractures of the skull is developed; and thus, too, one may find, in the neighbourhood of fractures and other injuries of bone, ossifications of inter-osseous fibrous membranes, and of the tissue of the periosteum, or just external to it.*

But, secondly, the bone may be formed by ossification of the fibrous tissue in a rudimental state. And this rudimental state may be that of either nucleated cells or nucleated blastema. Through nucleated cells, as the embryo-forms of fibrous tissue, bone is formed when granulations or inflammatory effusions ossify. The process may be often seen in the union of compound fractures, or of simple ones when much inflammation has been excited; but, best of all, the ossification of nucleated cells, in granulations, may be observed when bone is formed in the mushroom-shaped mass of granulations that is protruded through the medullary canal of a bone sawn across in an amputation. In all these cases there appears to be a direct transformation into bone, without the intervention of either cartilage or perfect fibrous tissue.

The ossification of nucleated blastema, such as I have described as a rudimental form of fibrous tissue, may also be seen in simple fractures; and my impression is, that it is the ordinary mode of ossification in simple fractures of long bones that unite well and quickly. In such a case, in a fracture of the tibia, I found, in long-continued examinations, that the bone is formed without any intermediate state of cartilage; a finely and very closely granular osseous deposit taking place in the blastema, and gradually accumulating so as to form the delicate yet dense lamellæ of fine cancellous tissue. The nuclei of the blastema appeared to be enclosed in the new-forming bone, and I thought I could trace that they became the bone-corpuscles; but I could not be sure of this, nor, indeed, could I, in either this or any other examination, satisfy myself that the origin of these corpuscles is in any structures previously existing in the soft or unossified tissue. Their first appearance in the forming new bone is too obscure, I think, to warrant any positive opinion; neither could I trace how the nucleated blastema, or other structure which is in-

* Museum of the College, Nos. 418, 419, and 420.

* The thin plate of bone which closes-in the exposed medullary canal of the end of a fractured long bone, where one fragment overlaps another, will usually, I think, present a goo example of ossification of fibrous tissue.

cluded within the new cancelli, is transformed into the later and more perfect medulla; only, one sees fatty matter gradually accumulating.

Such are instances of the ossifications, for the repair of fractures, that may be accomplished through fibrous tissue; and all these are possible without the intervention of the smallest portion of cartilage.

But perfect cartilage, with its characteristic homogeneous intercellular substance, and its well-formed cells, and all the characters of the purest fœtal cartilage, may be produced. Through the ossification of such cartilage, Miescher* and Vœtsch,† and others, describe the repair of fractures as accomplished in dogs, pigeons, and other animals. I have not yet found the very same process in the human subject; but I should think it would occur in favourable instances of simple fractures in children. In youths and adults I have found only varieties of fibrous cartilage; but these have presented numerous gradations of structure, from the fibrous towards the perfect cartilaginous structure. In different specimens, or sometimes even in different parts of the same, the reparative material may display—in one, fibrous tissue, with a few imbedded corpuscles, like the large nearly round nuclei of cartilage cells; in another, a less appearance of fibrous structure, with more abundant nucleated cells, having all the characters of true cartilage cells; and in a third, a yet more nearly perfect cartilage. Through any of these structures, and apparently by the same method through all, the reparative new bone may be formed. It may be formed, first, where the reparative material is in contact with the old bone, and thence extending, it may seem as if it grew from the old bone; or it may be formed in the new material in detached centres of ossification, from which it may extend through the intervening tissues, and connect itself with the old bone.

The new bone, through whatever mode it be formed, appears to acquire quickly its proper microscopic characters. Its corpuscles, being first of simple round or oval shape, and then becoming jagged at their edges, subsequently acquire their canals, which appear to be gradually hollowed out in the preformed bone as minute channels communicating with one or more of the corpuscles. The laminated canals for blood-vessels, I think, are later formed. At first, all the new bone forms a minutely cancellous structure, much like that of the fœtal bones in their first construction; but this gradually assimilates itself to the structure of the bones that it repairs, while its outer portions assume a compact laminated structure, and its inner or central portions acquire wider cancellous spaces and a more perfect medulla. But, in regard to many of these later changes in the bonds of union of fractures, there are so many varieties in adaptation to the peculiarities of the cases, that no general account of them can be rendered. Only, specimens and drawings, one and all, show the most striking evidences of design in the adaptation of the reparative process to the particular exigencies of each case; so that it might be said, with complete truth, of every instance, that whatever is necessary,—whatever may best, under the circumstances, repair the damage,—that is done.

Let me, in conclusion, remind you how this account of the ossification of fibrous tissue, in the repair of fractures, illustrates the most usual condition of fractures of which the repair is incomplete. They are united by ligament—that is, by fibrous tissue: to the formation of this tissue the process goes on naturally, but at this point it is arrested; the fibrous tissue does not ossify, and its fibrous state, imperfect for the purpose of repair, is perpetuated.

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* De Inflammatione Ossium, 1836.

† Die Heilung der Knochenbrüche, 1847.

LECTURE VI.

Repair of injuries of cartilage. Relation of cartilage and bone in the series of animal tissues.

Repair of tendons and muscles, divided in open and subcutaneous sections. Inflammatory effusion following the injury; effusion of reparative material; its organization and gradual perfection; its strength.

Repair of divided nerves: the primary and secondary conjunction of their fibres.

General considerations on the relations between the processes of repair and those of inflammation and developement. Bearing of the facts observed in repair on the question of the constancy of specific characters.

My last lecture must necessarily be somewhat fragmentary, while I purpose to devote it to the consideration of the modes of healing of several different tissues,—modes which, although they be all consistent with what has been said of the general rules and methods of the healing process, yet present each some peculiarity that seems worthy of observation.

And first (though it matters little which I begin with)—of the healing of wounds and other injuries of cartilage.

There are, I believe, no instances in which a lost portion of cartilage has been restored, or a wounded portion repaired, with new-formed permanent cartilage, in the human subject. When a fracture extends into a joint, one may observe that the articular cartilage remains for a long time unchanged, or else has only its broken edges a little softened and rounded-off. At length the gap is filled with a tough fibrous tissue; or rather, the gap becomes somewhat wider and shallower, and the space thus formed is so filled-up. Among the many experiments made by Dörner and others,* who cut and variously injured the articular cartilages of dogs, none showed any sign of reproduction; and Mr. Skey has told me that when, in experiments, he cut away portions of the cartilages of a dog's knee-joint, no repair of the cartilage ever appeared to ensue, though the joint did not materially suffer from the injury, and recovered its free capacity of motion.

Even in the smallest wounds of cartilage, the same union by fibrous tissue or ligament alone obtains, as a specimen here shows. A man, long before death, cut his throat, and the wound passed about half an inch into the angle of his thyroid cartilage. In the very narrow gap thus made—a gap not more than half a line in width—there is only a layer of tough fibrous tissue; and with the microscope I could detect no appearance of a renewed growth of cartilage. On the contrary, the edges of the cartilage, to which the fibrous tissue was attached, were as abrupt, as clean, and as straight as those would be of a section of cartilage just made with a very sharp instrument. The cut cartilage was unchanged, though the union between it and the new-formed fibrous tissue was as close and as firm as that of the several parts of a continuous tissue.

In some instances (but I suppose in none but those of cartilages which have a natural tendency to be ossified in advancing years) the fractures of cartilage are united by bone. This commonly happens in the fractures of the costal cartilages (as the specimens show*); and it has been noticed in fractures of the thyroid cartilage. The union of a fracture of the cartilaginous portion of a rib is effected, as that of one in the osseous portion is, by an enclosing ring of bone, like a provisional callus; and the ossification extends to the parts of the cartilage immediately adjacent to the fracture.

The imperfect repair of cartilage contrasted with the perfect repair which bone, after similar injuries, undergoes, may seem opposed to the general rule,—that the more highly a tissue is developed, the less is its capacity for repairing the injuries it may sustain; for it is usual to speak of cartilage as being *developed* into bone, and to regard bone as the more developed and more highly organised of the two tissues. But I think it is only in a very limited sense that this mode of expression is just. In some admirable remarks† on the cartilaginous state of the endo-skeleton of Chondropterygian fishes, my colleague has said—" I know not why a flexible vascular animal substance should be supposed to be raised in the histological scale because it has become impregnated, and, as it were, petrified, by the abundant intussusception of earthy salts in its areolar tissue. It is perfectly intelligible that this accelerated progress to the

* See Hildebrandt's Anatomie, Bd. i. p. 306.

* Museum of St. Bartholomew's, Ser. iii. 48, 73.

† Owen; Lectures on Comparative Anatomy, vol. ii. p. 146.

inorganic state may be requisite for some special office of such calcified parts in the individual economy; but not, therefore, that it is an absolute elevation of such parts in the series of animal tissues." Now all that one sees of the life of cartilage, in the narrower survey of the higher mammalia, is conformable with this view, and would lead us to speak of its change into bone as a degeneration, rather than a developement. The change is effected not only in the vigour of life, but as constantly, in certain parts, in its decay; and wherever it is effected, the part that has become bone ceases to grow, except by superaddition: the interstitial changes of normal nutrition are reduced to their lowest stage, or altogether cease. The cartilage, too, as I have said, is less frequently repaired after injury, and its repair is commonly effected by the production of bone; yet it is contrary to all analogy for a lower tissue to be repaired by the formation of a higher one. And it may be added that the granular, and in some instances even crystalline, form, in which the earthy matter of bone is deposited, is inconsistent with the supposition that its animal matter has acquired a higher developement than it had before in the state of cartilage. So far, then, as its position in the series of animal tissues is concerned, bone should be placed below cartilage, as a tissue which has passed into a state of less active life, and has acquired characters that approximate it to the more lowly organised and to the inorganic substances. An osseous skeleton is, indeed, proper to the most highly developed state of the individual, and in this view bone appears superior to cartilage: but, with as much right, in the same view, the atrophied thymus gland, and the renal capsules almost arrested in their growth, might claim to be regarded as developements from their fœtal state; for these, also, are normal parts of the more perfect organism.

Healing of Tendons. — I have already often referred to the phenomena that follow the division of tendons by subcutaneous and by open wounds; but the practical interest of the subject will, I hope, justify my giving a connected account of the process, as I observed it in a series of numerous experiments performed, with the help of Mr. Savory, on rabbits from three to six months old. Such experiments are, I know, open, in some measure, to the same objection as I made in the last lecture to those on fractures in the lower animals; but the few instances, in which examinations have been made of human tendons divided by subcutaneous section, have shown that the processes in man and in animals are not materially different. At the most, we may believe that, as in the repair of bones, the production of reparative material is more abundant, and its organization more speedy, in animals than in man.

I have already, in the second lecture, stated generally the differences in the several consequences of open and subcutaneous wounds. In the case of divided Achilles-tendons, the disadvantages of open wounds —*i. e.* of wounds extending through the integuments over and on each side of the tendon, as well as through it—were as follows:—1. There were always more inflammation in the neighbourhood of the wound, and more copious infiltration of the parts, than in a subcutaneous division of the tendon in the same rabbit; 2. Suppuration frequently occurred, either between the retracted ends of the divided tendon or beneath its distal end; 3. The skin was more apt to become adherent to the tendon, and so to limit and hinder its sliding movements when the healing was completed; 4. The retracted ends of the tendon were more often displaced, so that their axes did not exactly correspond with each other, or with that of the reparative bond of union.

Such mishaps were often observed in the open wounds, but were rare after the subcutaneous operations. In the cases of open wounds, they were avoided as often as the wound through the integuments healed quickly; and, whenever this happened, the case proceeded like one in which the subcutaneous division had been made. It was evident that the exposure of the wounded parts to the air did little harm, if it was continued for only a few hours,—a fact which may be usefully remembered when operations must be performed on tendons which it is not convenient to divide unseen.

These same cases of speedy healing of the opening in the integuments served to show, that it is unimportant for the healing of divided Achilles-tendons, whether the cellular sheath or covering of the tendon be divided or not. In all the cases of open division in these experiments, it was completely cut through; yet, when the external wound healed quickly, the union of the divided tendon was as speedy and as complete as in any case of subcutaneous division in which it might be supposed that the sheath of the tendon was not injured.

I will describe now the course of events after subcutaneous division of the Achilles-tendon; stating only what was generally observed, and what the specimens and diagrams before me will serve to illustrate.*

* The account here given agrees in all essential respects with that by Lebert, in his Abhandlungen der praktischen Chirurgie, page 403. Neither do the accounts materially differ, except in being less minute, which are given by Von Ammon (De Physiologia Tenotomiæ), Duval (Bull. de l'Acad. Royale de Médecine, 1837), and Duparc (Nederlandsch Lancet, 1837).

At the instant of the division, the ends of the tendon separate to a distance of nearly an inch, the upper portion of the tendon being drawn up the leg by the action of the gastronemius and soleus muscles. The retraction is comparatively much greater than in operations on the human Achilles-tendon; for where these are done, the muscles are seldom capable of strong or extensive contraction. It is in all cases to be remembered that the separation is effected entirely by the withdrawal of the upper portion of the tendon: the lower, being not connected with muscle, remains with its end opposite the wound. To this we may ascribe the general fact, that the reparative process is more active at the upper than at the lower portion of the tendon: for the latter lies in the very centre of the chief inflammatory action; while the former is removed far from it, being drawn away, at once from the seat of the injury, and from even the slightest exposure to the air.

I have already said that very little blood is effused in the subcutaneous operations. The first apparent consequence of the division of the tendon is the effusion of a fluid or semi-fluid substance, which, like the product of common inflammation, quickly organizes itself into the well-known forms of exudation-cells,—forms nearly like those of the white corpuscles of the blood and the granulation-cells. These, speedily becoming more distinctly nucleated and elongated, undergo the changes which I mentioned in describing the developement of granulations. The effusion makes the tissues at and near the wound succulent and yellow, like parts infiltrated in anasarca. Together with the enlargement of their vessels, it swells the parts, so that the skin is scarcely at all depressed between the separated ends of the tendon. But in well-made subcutaneous sections, this inflammatory effusion is of small amount, and takes, I believe, little or no share in the healing of the injury; for the effusion ceases after the first twenty-four hours, and I think that its cells are not developed beyond the state in which they appear spindle-shaped. I have never seen indications of their forming filaments of cellular or fibrous tissue.

In rabbits, forty-eight hours usually elapse before there are distinct signs of the production of the proper reparative material. This is deposited in the fibro-cellular tissue that lies between and close round the separated ends of the tendon, as well as in the interspaces of the tendinous fasciculi of those ends. It thus swells up the space between the separated ends, and makes the ends themselves somewhat soft and succulent. Some portion, at least, of it being deposited where the inflammatory effusion was, one finds their constituents mingled; but I believe that, while the proper reparative material developes itself, the product of the inflammation is either arrested in its developement, or even degenerates,—its cells shrivelling up, and gradually wasting.

I need not now describe the mode of developement of the reparative material provided for divided tendons; for I have taken it as a typical example of the developement of lymph into nucleated blastema, and thence into fibrous tissue.* To the naked eye it appears after three days as a soft, moist, and greyish substance, with a slight ruddy tinge, accidentally more or less blotched with blood, extending from one end of the tendon to the other, but having no well-marked boundary—undefined, merging gradually into the surrounding parts. In its gradual progress, the reparative material becomes commensurately firmer, tougher, and greyer, the ruddiness successively disappearing from the circumference to the axis: it becomes, also, more defined from the surrounding parts, and after four or five days forms a distinct cord-like vascular bond of connection between the ends of the tendon, extending through all the space from which they have been retracted, and for a short distance ensheathing them both.

As the bond of connection thus acquires toughness and definition, so the tissue around it loses its infiltrated and vascular appearance: the inflammatory effusion clearing up, and the integuments becoming looser, and sliding more easily. In every experiment, one finds cause for admiration at the manner in which a single well-designed and cord-like bond of union is thus gradually formed, where at first there had been an uniform and seemingly purposeless infiltration of the whole space left by the retraction of the tendon.

With the increase of toughness, the new substance acquires a more decidedly filamentous appearance and structure; so that after the seventh or eighth day the microscope detects well-marked filaments, like those of the less perfect forms of fibrous tissue. Gradually perfecting itself, but with a rate of progress which becomes gradually less,† the new tissue may become at last, in all appearance, identical with that of the original tendon. So it has happened in these valuable specimens presented to the Museum of the College by Mr. Tamplin.‡

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* See Lecture ii.

† One may remark this as a general fact, that when once the reparative process has commenced, much more appears to be done in it in the first few days than in any equal subsequent period of time. It may be another instance justifying the general expression, that production is easier than developement or improvement, and that the earlier or lower developements require less organizing force than the higher or later.

‡ Nos. 358, 359, 360.

They are the Achilles-tendon, and the tendons of the anterior and posterior tibial muscles of a child nine months old, in whom, when it was five months old, all these tendons were divided for the cure of congenital varus. The child had perfect use of its feet after the operation; and when it died no trace of the division of any of the tendons could be discerned, even with microscopic aid.

Such a perfect repair as this is, however, I believe, exceedingly rare. More commonly the differences between the original tendon and the new substance remain well-marked; the latter does not acquire the uniform arrangement of fibres, or the peculiar glistening thence accruing to the normal tendons: it is harder, and less pliant, though not tougher; its fibres appear irregularly interwoven and entangled, dull-white, like those of a common scar. And these differences, though as time passes they become gradually less, are particularly well seen when a longitudinal section is made from behind through both the ends of the tendon and the new substance that ensheaths and connects them. In such a section, one sees each of the retracted ends of the divided tendon preserving nearly all its peculiar whiteness, only somewhat rounded or mis-shapen and swollen, and imbedded in the end of the new substance, which is always greyer, or less glistening, and looks less compact and regular. In the retracted ends of the tendon, one may discern the new substance mingled with the old, and interposed between its fasciculi, with which one may believe it is connected by the finest dove-tailing.

The strength, both of the new substance itself, and of its connection with the original substance, is worthy of remark. To test it, I removed from a rabbit an Achilles-tendon, which had been divided six days previously, and of which the retracted ends were connected by a bond of the size and texture usual at that period of the reparative process. I suspended from the half-section of this bond gradually increased weights. At length it bore a weight of ten pounds, but presently gave way with it; yet we may suppose the whole thickness of the bond would have borne twenty pounds. In another experiment, I tried the strength of a bond of connection which had been ten days forming: this, after bearing suspended weights of twenty, thirty, forty, and fifty pounds, was torn with fifty-six pounds. But surely the strength it showed was very wonderful, when we remember that it was not more than two lines in its chief diameter; and that it was wholly formed and organized in ten days, in the leg of a rabbit scarcely more than a pound in weight. With its tenacity it had acquired much of the inextensible character of the natural tendon: it was indeed stretched by the heavy weights suspended from it, yet so slightly that I think no exertion of which the rabbit was capable would have sufficed to extend it in any appreciable degree.

The Healing of Muscles subcutaneously divided presents many things exactly similar to those just described as observed in the healing of tendons similarly divided. But in the experiments which I made on the triceps extensor brachii, and the tibialis anticus of rabbits, there was always observed a peculiar inversion, subsidence, or *tucking-in* of the muscular fibres at the divided part, so that nearly all the fasciculi directed their cut ends towards the subjacent bone or fascia. Thus it might, and sometimes appeared to, happen that, though the retracted portions of the muscle were imperfectly united, yet the action of the muscle was not lost, for one or both its ends acquiring new attachments to the subjacent parts would still act, though with diminished range, upon the joint over which the continued fibres of the muscle passed.

In general, it appeared that the reparative material was less quickly produced than after division of the tendons; but this might be because of the greater violence inflicted in the operation, more than because of the structure of the divided parts. The usual method and end of the developement of the reparative material were the same as after division of the tendons; and at length—but always, I think, more slowly than with them—the ends of the retracted portions became inclosed in a tough fibrous bond of union.

After the formation of this bond, the healing of divided muscles is improved, both by the clearing up of the surrounding tissues infiltrated with inflammatory products, and by the contraction of the new bond, which thus draws together the retracted portions of the muscle, so that they may nearly coalesce. Thus, in a man who had cut his throat long before his death, and had divided the left sterno-hyoid, omo-hyoid, and sterno-thyroid muscles, I found that the ends of these muscles, though they must at first have retracted considerably, had all been drawn to attachments on the cricoid cartilage, over which their several portions nearly united.

The *Healing of divided Nerves* presents, in ordinary cases, many features in common with that of divided tendons. A bond of new substance is formed, which connects the retracted portions. In this bond, which has in the first instance only the characters of the material constructed for the repair of all soft parts, there are gradually formed new nerve-fibres, which connect themselves with the old ones in the separated portions of the divided nerve, and thus restore its function. I shall not dwell on this process, for I have made no new observations on it: it is amply treated in several works on physiology;* and it is thoroughly illustrated, so far as the appearances to the naked eye are concerned, by the valuable series of preparations given to the Museum of the College by Mr. Swan,† and by the collection of drawings from Guy's Hospital, which Mr. Hilton has kindly lent for your examination.

Leaving, then, this process, which might be named the *secondary* repair of divided nerves, I will speak of one which, so far as I know, has not been yet described, and which may be justly called the *primary* healing. It may be explained by the h story of a case in which it occurred:—

A boy, eleven years old, was admitted into Saint Bartholomew's Hospital, under Mr. Stanley, with a wound across the wrist. This wound, which had been just previously made with a circular saw, extended from one margin to the other of the fore-arm, about an inch above the wrist-joint. It went through all the flexor tendons of the fingers and thumb, dividing the radial artery and nerve, the median nerve and artery, and extending for a short distance into the radius itself. The ulnar nerve and artery were not injured; the condition of the interosseous artery was uncertain, but the interroseous ligament was exposed at the bottom of the wound. Half an inch of the upper portion of the divided median nerve lay exposed in the wound, and was distinctly observed, and touched by Mr. Stanley, myself, and others. All sensation in the parts supplied from the radial and median nerves below the wound was completely lost directly, and for some days after the injury.

It was decided to try to save the boy's hand. The radial artery was tied, and the edges of the wounded integuments put together. No particular pains were taken to hold the ends of the divided median nerve in contact, but the arm was kept at rest with water-dressing.

After ten days or a fortnight the boy began to observe signs of returning sensation in the parts supplied by the median nerve, and these increasing, I found on the 26th of February, and on many subsequent days, that the nerve had nearly recovered its conducting power. When he was blindfolded, he could distinctly discern the contact of the point of a pencil with his second finger, and the radial side of his third finger; he was less sure when his thumb or his fore-finger was touched, for, though generally right, he sometimes thought one of these was touched when the contact was with the other; and there were a few and distant small portions of the skin supplied by the median nerve from which he still derived no sensation at all.

Now all this proves that the ends of the divided median nerve had coalesced by immediate union, or by primary adhesion with an exceedingly small amount of new substance formed between them. In the ordinary secondary healing of divided human nerves, twelve months generally elapse before, if ever, any restoration of the function is observed; in this case, the nerve could conduct in a fortnight, and perhaps much less, after the wound. The imperfection of its recovery is just what one might expect in such a mode of union. One might anticipate that some of the fibres in one of its portions would fail to be united to any in the other portion: the parts supplied by these filaments would necessarily remain insensible. So, again, one might expect that some of the fibres in one portion would unite with some in the other. with which before they were not continuous, and which supplied parts alien from those to which themselves were destined: in all such dislocations of filaments there would be confused or transferred sensations. But, among all the fibres, some would again combine in the same continuity in which they had naturally existed: and in these cases the function would be at once fully restored.

While this case was under observation, Mr. Gatty, a pupil of the hospital, told me a similar case in which his father had been consulted; and that gentleman kindly sent me, with the permission of Mr. Heygate, in whose practice the case occurred, the following particulars of it:—

A lad, near Market Harborough, thirteen years old, had his hand nearly cut off at the wrist-joint by the knife of a chaff-cutting machine. The knife passed through the joint, separating a small portion of the ends of the radius and of the ulna, and leaving the hand attached to the fore-arm by only a portion of integument about an inch wide; connected with which were the ulnar vessels and nerve, and the flexor carpi ulnaris muscle—all uninjured. The radial artery and some small branches being tied, the hand and arm were brought into apposition, and after removing a small portion of extensor tendon that protruded, were retained firmly with adhesive plaster and a splint of pasteboard. The wound went on very well, and was left undisturbed for a week. The warmth of the hand returned; in ten or twelve days after the injury there was slight sensation in the fingers, but in the thumb

* See especially Müller's Physiology, by Baly, i. 457; Valentin's Physiologie, i. 702.

† Nos. 2169 to 2175. All these specimens, and the interesting appearances of the formation of new nerve-fibres which they display, are described and illustrated by Mr. Swan, in his "Treatise on the Diseases and Injuries of Nerves." In Nos. 2165 to 2168 in the College Museum, Mr. Hunter has shown the formation of the bulb at the ends of divided nerves, and the extension of nerve-fibres into it.

none was discernible till more than a fortnight had elapsed. Finally the sensation of the hand and fingers, and most of their movements, were perfectly restored.

In this case, again, it seems impossible to explain the speedy restoration of the conducting power of the nerve, except on the supposition that its divided fibres had immediately reunited. We have no evidence that new nerve-fibres could in so short a time be formed: all the cases of less favourable healing show that they require a year or more for their formation.

I need hardly add the practical rule we may draw from these cases. It is, briefly, that we may, with good hope of great advantage, always endeavour to bring into contact, and immediately unite, the ends of divided nerves; and that we must not in all such cases anticipate a long-continued suspension of the sensation and other nerve-functions of the part.

Time will not allow me to speak of the healing of injuries of other tissues than these;* for I wish to devote the remainder of the hour to the consideration of some of the relations which the reparative process bears to those of inflammation, and to illustrate, with more pointed instances than I could refer to in the first lecture, the evidences of identity of the power exercised in the repair of injuries and in the developement of the germ.

It is not because we have any well-defined idea of inflammation that it is desirable to refer to it, as if it were a standard with which we might compare other organic processes; but because some idea of inflammation, however vague, mingles itself with nearly every thing that is considered in surgical pathology. Nowhere is this more manifest than in what has been written in surgical works upon the methods of repair; concerning which the general impression seems still to be, that a process of inflammation forms part of the organic acts by which even the smallest instance of repair is accomplished.

Now to judge whether, in any process of repair, an inflammation of the wounded part ensues, we have two kinds of evidence: namely, that which is derived from the presence or absence of the usually admitted signs of inflammation during life, and that which may be found in the presence or absence of inflammatory products, *i. e.* exudation-cells, after death. Each of these has its advantages; but in experimental inquiries the latter is by far the better evidence, and that which I have chiefly sought. Judging, however, as much as possible from both these forms of evidence, the processes we have traced appear to warrant these general conclusions:—

1. That in the healing of a wound by immediate union, inflammation forms no necessary part of the process; rather, that its presence always hinders, and may completely prevent it. The healing by immediate union should be a simple re-joining of the severed parts, without the production of any new material; and in the same proportion as, in any case, inflammatory matter is effused, either in or between the wounded parts, in that proportion does the healing deviate from the true and best process of immediate union.

2. For subcutaneous wounds and injuries, as in divided tendons, simple fractures, and the like, nearly the same may be said. Inflammation is excited by the local injury, but its products form no necessary part of the material of repair; rather, the more abundant they are, the more acute the inflammation is, and the longer it continues, the less speedy and the less perfect is the process of repair. For here the necessary or best reparative material is a substance which, both in its origin and its developement, declares its non-inflammatory nature; a substance which is produced without the signs of co-existent inflammation, and of which the developement is different from that of the true inflammatory products. And this, which is most evident in the case of the healing of subcutaneous injuries by bonds of connection, is probably equally true in the case of subcutaneous granulations.

But 3dly. In the healing of a wound by primary adhesion, or by open granulations, we have evidence of a process of inflammation, not only in the presence of its ordinary signs in a degree generally proportioned to the severity and extent of the injury, but in the character and mode of developement of the new materials that are formed for the repair. For these materials are, in all appearance, identical with those of such effusions of lymph as all are agreed to consider the effects of inflammation.

Still, 4thly, in these cases we have evidences that the inflammatory process is necessary for no more than the production of the organizable matter,—and, in the case of granulations, for the production of only the first portions of it. The right formation of

* The omissions related principally to the disproof of the opinion generally entertained,—that papillæ are not formed on the scars after cutaneous wounds; to the complete formation of the epidermis of the negro on the scars of even deep cutaneous wounds; to the remarkable power of repair shown by the cornea, as illustrated especially by Dr. Bigger, in the Dublin Journal of Medical Science, 1837, and by Donders, in the Nederlandsch Lancet; to the reproduction of the crystalline lens after cataract operations; and to the repair of fractured teeth by the formation of bone, as described by Mr. Tomes in his Dental Surgery.

the cells, and, yet more evidently, their higher organization into cellular tissue and cartilage, ensue only while the signs of inflammation are absent. They are manifestly hindered or prevented when signs of inflammation are distinctly present, or when its existence may be suspected in consequence of the presence of some irritation, as a foreign body, dead bone, or the like. The continuance of suppuration during the process of healing is no proof of the continuance of inflammation, if the account that I have given of pus be true.

In these modes of healing, therefore, we may conclude that inflammation is only partially, and at one period requisite ; and that, in regard to its requisite degree, the least amount with which an effusion of lymph is possible is that which is most favourable to repair.

Lastly, for the process of healing by scabbing, the absence of inflammation appears to be essential: indeed, the liability of our own tissues to the inflammatory process, and to the continued effusion that it produces, appears to be that which prevents their injuries from being healed as easily and surely, by the scabbing process, as nearly all open wounds are in animals.

Such may be regarded as the relations of the reparative process to that of inflammation, as it is commonly understood ; but, I repeat, such a comparison can be made only for the sake of deference to the general state of opinion in matters of surgical pathology. In truth, we know less of inflammation than of the reparative process.

But, admitting the share which inflammation has in the repair of injuries to be such as I have expressed, it appears necessary to consider next how such a process can be made to minister to repair;—what is the power that determines its results to be such, or of such a kind, as are required for the restoration of the perfection of the injured part? The mere act of inflammation in a part would not heal its wounds : it would only produce a material which might be developed into cellular tissue and cuticle, and in which blood-vessels might be formed. Some other power must inform the course of the inflammation, and determine its result towards the healing of the wound. And so with all the other special acts of which each process of repair consists; whether we assume the operation of an assimilative force, or detect germs of tissues, or productive cells, which we may regard as centres of power,—still we must admit, I think, that the reparative process is determined in every act according to the same law, and by the same powers, as those which actuated the developement of the germ. For in the repairs of even the highest animals we may discern all those features which I enumerated as characteristic of the power of the germ, and as distinguishing it from any force of assimilation, or any other force assumed in the explanations of the maintenance of the body by nutrition.

Thus—1st, the material for the repair of an injury is constructed according to no present model, such as is assumed for the hypothesis of assimilative force : it is developed from no tissue-germ left by the damaged part for the construction of its successor.

In the repair of a divided tendon, the whole length of the connecting bond is developed equally ; or, if there be a difference, it is that the mid-space is in advance of the rest. No assimilative force in the ends of the original tendon can be imagined thus equally diffused, nor could germs for the growth of tendon have been strewn along the space left by the retraction. So, in the repair of fractures, the new bone is commonly formed first in contact with the original shaft, as if it were an out-growth from it ; and here the assimilative force may have effect: but it is also often formed in detached parts, even outside the periosteum, at such distance from the old bone, and with such intervening tissue, that no act of an assimilative force can be reasonably imagined sufficient for the result.

What, then, can determine such a reconstruction of parts as this? Surely nothing but such a power as that which determined their original construction from the germ.

The identity of the power is, in the second place, manifested by its mode of operation. Whatever be the structure to be reproduced, it is constructed through the same stages as were traversed in its first developement. Witness the cases that I have referred to: in the two modes of developement of fibro-cellular tissue for repair, both equally imitations of a natural developement,—in the two modes for the production of new bone, both alike repetitions of the natural developement of bone,—in the mode of developement of vascular loops, and of the walls of the blood-vessels. So, that, various as are the conditions in which we watch the process of repair, and various as the degrees of its perfection, yet is there no real variety of plan —no deviation from conformity with the law according to which the new structures are developed in the germ.

Observe, 3rdly, how, as in the germ, many independent developements concur to the attainment of the end. In the several layers of granulation-cells, while one portion are forming themselves to cellular tissue, another are constructing cuticle, and others are permitting and concurring in the progress of new blood-vessels. Or, in a wound involving many different tissues, we may discern the material that unites each of them gradually assuming more of the characters of that which it unites, or that its position needs.

4thly. The limits by which the reparative process is bounded are the same as those to which the developement of the germ was confined. Great as the activity of the process may be in some instances, yet does it never achieve more than the power of the germ did. Trembley's hydra multiplied by mutilation fifty-fold: but the force thus manifested could not have been made to develope that hydra into any higher specific form, nor even, by expenditure in growth, to have formed from it an hydra of fifty times the usual dimensions. And so, in the repair of higher organisms, we find perfect tendon, perfect bone, perfect nerve, and of these just so much as is needed to restore perfection; but, except in disease, the reparative process never, in either the quantity or the quality of that which it produces, goes beyond the point to which the germ-power had developed the same part.

Lastly, the acts of the reparative process are in conformity with the conditions and the gradually-changing modes of action of the germ which we observe in advancing years. A part which is injured in the child is repaired with tissue proper to the childish state; the same part injured in the old man is repaired with some lower tissue, or with tissue like that which is natural to age.

Whether, then, we regard the exact details of the method according to which the reparative process is accomplished, or the end that it achieves, or the limits within which both its methods and its end are confined, we see alike the evidences that the power that actuates it is the same as that which actuated the developement of the germ. In every impregnated germ, we must admit that properties are implanted, which, in favourable conditions, issue in the power to form, of the germ and the materials it appropriates, a being like those from which it sprang. And mysterious as it may seem, yet must we conclude that a measure of those properties is communicated to all the organic materials that come within the influence of the germ; so that they, being previously indifferent, form themselves in accordance with the same specific law as that to which the original materials of the germ are subject. So, through every period of life, the same properties transmitted and diffused through the whole organism, are manifested in the determination of its growth and maintenance, in its natural degeneration, and its repair of every part, in accordance with that type or law which has prevailed in every individual of the species.

Thus the constancy of both the method and the end of the reparative process may confirm us in the belief of the essentiality, we may almost say the immutability, of specific characters. For it shows that with each of all the countless varieties of visible form and structure, which mark the specific characters of living beings, there correspond peculiar internal properties of its constituent matter—properties which are capable of transmission and communication to all that can be incorporated in the living body, and of accumulation in the form of germs; and which, in any way thus transmitted, can manifest themselves in the unchanging power of constructing and composing matter according to the one determined and specific type.

Thus, by watching the life of any being, in all the varieties of external circumstance and accident, and by seeing that, whatever be the deviation from its perfection into which, by the force of these, it is for a time compelled, it yet reverts to the same specific form,—or, if it fall short of it, assumes no lower one: by watching such a life, we discern an image of the constancy of the law of specific characters; we gain an assurance that matter was not, and is not now, cast without design into the world, to be shaped by the force of chance and circumstance, and to be raised or degraded by their various ebb and flow; that the living occupants of the world have been fashioned and adapted for it, not by it; and that each was from the first endowed with properties that might descend unchanged from one generation to another, and in their immutability might be a symbol of Him who at the first created them, and by whose unchanging Will and Power they have been ever since maintained and still subsist.

Wilson and Ogilvy, 57, Skinner Street, Snowhill, London.

42. Schoolhill
Aberdeen, Decr 10th/56.

My dear Dr Bennett;

I give you the loan of my Woodcuts with very great pleasure, on the distinct understanding however that they belong exclusively to me, and that neither the publishers nor proprietors of the Journal have the smallest right to one of them. I forwarded you by Goods train to-day the Woodcuts which you are anxious to print; viz, Figs, 1, 2, 6, 26, 27, 28, 13 & 14, 34 & 35, 45, 51. —

Dr Miller had Fig 10 from me, and it is not named amongst those you got from him. Have you got it? —

Sutherland & Knox have Figs 44, 49, 50, 52, also those printed in my paper in the Journal for Septr /51 – and numbered 3, 4, 7. 8, 9, 10 & 11; – they have likewise my Woodcut of the Ep: & Obturator arteries, and 10 Figs printed in my paper on Tumours in 1850. –

As you speak of having No 50 alone of the last named, will you be good enough to look at what you have to see if you have any of the following: –

- On cartilage Figs 18, 44, 49 & 52.
- In paper of Septr /51 – Figs – 3, 4, 7. 8, 9, 10 & 11 –
- Ob: & Epigastric Arteries –
- In paper on Tumours 1850 – 10 Figures; –

and to write me to say which you have; if not the whole of them, if you know anything of the rest, and I will write Mr Miller

regarding Fig 18 and Sutherland
& Knox regarding all the rest &
for all of which they are responsible
to me. —

When you have printed your Clinical
Medicine, please to forward me
the blocks in your possession. Should
you ever wish for them again
they will be entirely at your
service whenever they will be
useful to you. —

I am very glad to hear
that you at last have a good
Class. — The Town Council have been
very properly rewarded for the way
in which they filled the Chair of
Medicine. —

Very little is doing here regarding
the Union. It may be said to be at
an end, though there is some

tath of a Commission being appointed to inquire &c –

I am perfectly prepared to hear of the demonstration of contractility in any cell wall or other structure whatever. Structure has obviously nothing whatever to do with the originating of the power: it may belong to any form of tissue & to substances possessing no structure at all.

I am sorry that I cannot accept your kind invitation to hear your paper & the debate. We have no Xmas holidays except Xmas day and New Year's day. – I wish you every success. Take care that you not go too far or you will greatly weaken your case. It is a very strong one no doubt but if you push it too far you will not carry the Socy with you & it will do you harm. –

Believe me, My dear Dr Bennett,
Yours very sincerely,
Dr Bennett – P. Redfern –

Saint Bartholomew's Hospital
July 30. 1850.

My dear Sir

I beg you to receive a copy of my Lectures on Inflammation, — but I am quite ashamed to send it, because of my having omitted to put your name with those to whom I acknowledge myself indebted for instruction on the subject. The omission was due to the merest, yet not the less discreditable, forgetfulness: — the postscript was written after the Lecture was printed, & while the printer was waiting that he might 'work-off' — I wrote it therefore in haste, & when I found my mistake it was too late to remedy it — I am extremely sorry that it has happened, — not that it can in any way affect your reputation — but because it will make me seem disrespectful or uncourteous to you. — But I hope and believe that you will excuse my ~~error~~ error, which I will take care to correct if ever the Lectures are published again —

Believe me sincerely yours

James Paget

of your Kingdom has been no more
successful than I was, in obtaining
bats for you — all my endeavours
failed, — it appears really very diffi:
cult to take them except in the
torpid state ——