THE BRADSHAW LECTURE ON THE UNION OF WOUNDS.

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MR. PRESIDENT AND GENTLEMEN,—It appears to me that there is considerable difference of opinion amongst surgeons and pathologists as to the way in which simple wounds unite, especially as to whether the process of healing is an inflammatory one or not. In selecting a subject for the Bradshaw Lecture this year I thought that I could not do better than discuss this question, and see whether, by a consideration of the subject, we can arrive at some distinct conclusion. I have formed a very definite opinion myself and it remains to be seen whether I shall succeed in winning you round to the same view that I hold.

Many surgeons and pathologists, and amongst them some of the most eminent in this country and on the Continent, believe that the union of wounds takes place without inflammation, and indeed assert that "repair in all its forms is effected without inflammation." These pathologists teach that "repair and inflammation are not only not identical, but that they are incompatible. That repair is a constructive physiological process and resembles closely that of development and growth; but that inflammation is a destructive pathological process, brought about entirely by micro-organisms introduced from without, and that when it attacks a wound in the process of repair, it at first checks repair, and later on brings about disorganising changes, and when a part repairs after it has been the seat of inflammation, it does so only when the inflammatory process has been arrested."

Other pathologists, again, hold the opinion that all wounds unite by a process which they regard as inflammation. And while admitting that inflammation is a destructive pathological process, they believe, nevertheless, that the union of wounds takes place by it, and that there is a decrease in the vital activity of the affected tissues, and, as a result, a lower vitality in the product of this inflammatory process; I mean in the scar, or connecting medium, which binds the severed parts together.

There can, I think, be little doubt that John Hunter believed that wounds may heal without inflammation. In fact, in one place he distinctly states in his lectures "that primary healing takes its course without inflammation, and is painless." He did not, however, greatly emphasise the fact, and appears to have believed that the bond of union in these cases was extravasated blood. He thus describes the process: "The blood"—that is the blood extravasated into the wound—"being alive, this uniting medium becomes immediately a part of ourselves, and the parts not being offended by it, no irritation is produced. The red particles are absorbed, and nothing but the coagulating lymph is retained, which, being the true living bond of union, afterwards becomes vascular." But John Hunter certainly did not believe that "repair in all its forms is effected without inflammation," for he states that "in many diseases it is the first step towards a cure."

I do not propose, however, to weary you further with the opinion of the older pathologists. I prefer rather to limit myself to a consideration of the question, as it exists at the present time, as to whether wounds heal without inflammation; and I take as my text on which to base our discussion the words of Karl Roser, of Marburg, a German pathologist of great repute. He says: "The clean, non-infected wound heals without inflammation by first intention; the infected wound, on the contrary, heals by second intention with the appearances of inflammation. In the first case healing follows immediately after the injury. In the other case inflammation intervenes between injury and healing as a disturbing complication."

Clearly the first point in considering this question is to

have a clear and definite understanding of what inflammation is. As you are all aware, Burdon Sanderson has defined inflammation as the "succession of changes which occurs in a living tissue when it is injured, provided that the injury is not of such a degree as at once to destroy its structure and vitality." Or, more briefly and succinctly, that inflammation is the "response of living tissues to injury." Now, if we accept this definition, the whole question falls to the ground at once. Clearly, if this is true, no wound can unite without inflammation; a wound is an injury; therefore a response must take place, a succession of changes must occur which constitutes inflammation. Those, however, who believe that wounds heal by a strictly physiological and constructive process clearly do not accept this definition of the word, and regard inflammation as something else.

The older definition of inflammation was that it was that condition which was attended by certain, so-called, cardinal signs—pain, heat, redness, and swelling, and that we must regard these signs, again to quote the words of Dr. Burdon Sanderson, "as the characteristics of the thing of which the word 'inflammation' is the name." There is no question that these signs do attend or follow a wound, and so again, we must admit that if the aggregate of these signs constitutes inflammation, then that there is inflammation during the process of healing of a wound.

The opponents of the theory that wounds heal by inflammation admit that the four cardinal signs of inflammation are present, but they do not admit that therefore there is inflammation. Let me quote to you what Mr. Bryant says in his *Practice of Surgery* on this point. Speaking of wounds he says, "Within an hour or an hour and a-half the edges of the wound will be seen to be swollen, and slightly red, from increased vascularity, and if the connective tissue of the wounded part is loose, as in the eyelid or male genital organs, it will be puffed up and cedematous. To the patient the part will feel hot and stiff, and it will be the seat of a dull, aching, or burning pain. The edges of the wound will also probably be more sensitive, the amount of pain depending much upon the tension of the parts and upon the treatment to which they have been subjected. If the edges of the wound have been stitched together, and the parts are much swollen and cedematous, there will be tension upon the wound and a disposition to separate and gape. In a healthy subject however, where repair goes on well, all these local phenomena will subside and disappear in the course of two, three, or four days, according to the rapidity and perfection of the healing process and a cure will then take place. But should the local phenomena above described be more persistent, increase in severity, spread beyond the margins of the wound and surrounding parts, or alter in character for the worse, what has been a physiological reparative process will pass into a pathological or diseased one, and the parts will then be said to be inflamed."

The opponents of the doctrine of the healing of wounds by inflammation do not, therefore, hold that the presence of these four signs necessarily constitute inflammation; and no doubt this, in fact, is quite true. They are present in that condition which indeed is the first stage of the inflammatory state, but which may also occur quite independently of it; a condition to which we apply the term "determination," and which is undoubtedly a physiological process, and is an element in thousands of actions of daily life, and occurs in those conditions where a sudden increase of blood is required for some physiological purpose. Thus, a morsel of food is introduced into the mouth, requiring an increased quantity of saliva for its salivation; immediately a determination of blood to the salivary glands takes place, causing a more active secretion and an increased flow of saliva.

The first use of the word "determination" has been attributed to Paré. John Hunter called it the "incipient enlargement of the vessels," and in no part of his treatise on inflammation does he use the word "determination." He says: "The very first act of the vessels when the stimulus which excites inflammation is applied is, I believe, exactly similar to a blush. It is, I believe, simply an increase of distension beyond their natural size. This effect, we see, takes place upon many occasions; gentle friction of the skin produces it; gentle stimulating medicines have the same effect."

As a German equivalent to the word "determination" Virchow introduced the term "Wallung" (surging), which has been constantly used by his successors.

This determination, which we admit is a physiological process, is attended with a sudden afflux of blood to a part, and is characterised in consequence by certainly, at least, three of the four cardinal signs of inflammation: heat, redness, and swelling; and, possibly, also, in many cases, by the fourth also; for, at all events, if there is not actual pain, there is an uneasy or abnormal sensation, such as a sensation of fulness about the part. It is evident, therefore, that we are not in a position to say that a part is inflamed because of the presence of these four symptoms.

I have alluded somewhat at length to this question of determination, because I think it is important, with a view to accuracy of statement, that the employment of the word "determination" should be strictly limited, when used in connection with the inflammatory process, to the primary acceleration of the blood stream in and about an injured part, and should not be so extended as to comprise the subsequent stages of retardation resulting in stasis and exudation.

We have not yet arrived at our definition of inflammation; and, indeed, the difficulty is great in giving a clear and logical definition to this form of disease, although we easily recognise the condition, and understand the combination of processes which are taking place in the tissues.

I should regard inflammation as a modification of the normal physiological processes in the various tissues of the body, resulting from the application of some irritant to the part. This process being attended or followed in most cases by the formation of a new material of a less highly organised nature than the original tissue in which the inflammation has taken place.

And here I would draw your attention to a very important point, and one which it is very desirable that we should keep strictly in our minds, and that is, that these cases of what we may call "traumatic inflammation"—that is to say, inflammation produced by a wound in which no foreign body is allowed to remain—and which inflammation is, as I hold, necessary for the healing of the wound, are very different from those inflammatory processes which are due to the admission of septic organisms. And they differ especially in this marked peculiarity—that the irritation in the tissue does not extend beyond the immediate neighbourhood of the injury. The irritant which has produced the inflammation has been momentarily applied, and therefore the inflammation which results has a tendency speedily to resolve itself as soon as it has brought about those changes which are necessary for repair. This is very different from those cases where a prolonged irritant is applied to a part; then the process of inflammation is also prolonged, and when this irritant is some septic organism which has the power of multiplying in the tissues and of producing ptomaines which poison the tissues, the inflammation is not only prolonged but has a tendency to spread and diffuse itself rapidly by continuity of tissue.

It must be admitted on all hands, I think, that in the process of union of wounds there is the formation of a new tissue which forms the bond of union, and the point which we have to discuss is whether this new tissue is the result of inflammation or whether it is merely a physiological process, a condition of ordinary development or growth which is constantly taking place in the body. If we regard the subject from a clinical aspect, I admit that there is considerable difficulty in making any distinction between these two conditions. For, as I have endeavoured to show, we may have all, or almost all, the signs of inflammation as the direct outcome of a physiological process, and, on the other hand, we often meet with cases of wounds which heal without any of the four cardinal signs being present in any marked degree at the margins of the wound, though I believe they are always present to a certain extent, though it may be this extent is not appreciable to the ordinary observation. And it must be borne in mind that the difference between slight redness, swelling, and heat of the edges of a wound and the most intense form of these conditions is only one of degree, the latter being patent at the merest glance to the most

superficial observer, whilst the former is so slight as to be scarcely distinguishable to the most careful investigator. When, however, we come to consider the question from an histological standpoint, it seems to me that we cannot separate it from an inflammatory process, however slight its extent and intensity may occasionally be.

Let us then examine the subject from an histological point of view, and let us first consider the manner in which adhesion of the edges of a wound takes place, whether this process is regarded as inflammatory or not, and this we will do in the briefest possible manner by simply stating the most salient points which have been observed, so that we may clearly carry them in our minds. And in order to do this we will take an example of the simplest kind of tissue, in which an incision has been made, and which unites by what is called adhesive union, or the "first intention" of John Hunter. For I do not propose at present to say anything about the so-called "immediate union of wounds," which was first described by Macartney, as I do not believe that such a condition exists. I shall have something to say, however, about this at a later period of my lecture.

Suppose, then, we make an incision through the skin into the subcutaneous tissue beneath. What happens? First it bleeds; then the bleeding ceases, and finally union takes place. The wound first bleeds because the capillaries contained in the tissue are divided; the bleeding stops because the blood coagulates in the capillaries as far as the nearest anastomosis, that is to say, to the next point of intersection of the capillary network. So that the first change is that all the cut vessels become filled with clots up to their first collateral branch, and this is undoubtedly simply a physiological process; the clotting being the result of the physiological conditions which bring about the formation of fibrin.

Secondly, the capillary vessels in the neighbourhood, that is to say, beyond the point of clotting, will be noticed to be dilated. By some this would also be regarded as a physiological process, and to arise merely from mechanical causes, from the increase of pressure to which the capillaries have been subjected in consequence of the coagulation which has taken place in their several extremities. About this I shall have to say a word or two in a moment, but let me first glance at the other changes which are to be observed in a wound before the process of union is effected.

The third change to be noted is in the connective tissue in which the vessels ramify. This becomes infiltrated with cells, and these cells multiply, so that we have the tissues at the edges of the wound infiltrated with a vast accumulation of cells, which are for the most part simple, nucleated cells, resembling leucocytes. After a time other larger cells appear, and some of these find their way to the surface of the wound, and are to be seen covering it.

Fourthly, the cells which cover the surface of the wound undergo a developmental process, and first becoming spindle-shaped and then fibre cells, are eventually converted into fibrous or scar tissue, which forms the cicatrix or bond of union.

Finally, and lastly, the capillary network at the margins of the wound prolongs itself in the form of loops into this new tissue, and becomes continuous with similar loops on the opposite side, and thus the new tissue becomes an organised structure, and unites the edges of the wound together.

These, very briefly, are the changes which can be observed with the microscope as taking place in the edges of a wound, whereby union is effected; and the question we have to consider is whether these changes are strictly physiological and akin to those of development or growth, or whether they are the result of that pathological process which we know as inflammation. Whether, in fact, these cells which are the essential elements in the process of union find their way between the edges of the wound in conformity with known physiological laws, and, having found their way there, undergo changes similar to those which are witnessed in the embryo, when the blastodermic cells of the ovum grow, develop, and differentiate into the various structures of the human being, or whether these changes take place as the result of a pathological process, altogether different and distinguishable from normal physiological action.

In discussing this point, we shall have to consider four

questions: (1) Is the dilatation of the blood vessels, which we described as the second change in our process of union, simply a mechanical one, and due to the increased pressure exerted on the capillaries of the part? (2) Is this vast accumulation of cells in and around the wound the simple outcome of a physiological process? (3) Are the changes which take place in the cells exactly identical with the mode of growth and development in embryonic cells? (4) And, lastly, What is the nature of the newly formed tissue?

The first point, then, which we have to consider is whether the dilatation of the blood vessels, which undoubtedly occurs, is simply due to mechanical causes. We have seen that when a wound is made the blood vessels at its margins become blocked, and it is perfectly clear that the blood will have to accommodate itself to this, and find another channel by the existing and patent by-paths around the blocked vessels. The result of this is increased pressure in these parts, and, as a consequence, distension and dilatation of the vessels. So there can be no question that in this simple mechanical explanation there is a way in which we may account for the dilatation of the blood vessels, but unfortunately this mechanical explanation does not fully account for the subsequent changes which take place. It fully explains the first step in the process—the determination with increased motion—but it does not explain the determination with diminished motion, in which the circulation becomes slower and slower until the retardation results in stasis, with consequent diapedesis. For this we must look to some other cause than a mechanical one, and hence, as it is certain that this slowing of the blood current does take place, we cannot accept the theory that the dilatation of the blood vessels in inflammation is entirely due to a simple mechanical cause. To what, then, must we attribute this dilatation and this increased flow of blood? Numerous hypotheses have been advanced at different times as to the cause, and it cannot be said that even at the present time any one of these hypotheses gives a really complete and absolute explanation of the phenomenon. In considering the question I would strongly emphasise and ask you to bear in mind the words of Sir John Simon, who says that “a part does not inflame because it receives more blood; it receives more blood because it is inflamed.” For if we do not admit this, the whole argument falls to the ground.

It is self-evident that the proximate cause of the dilatation must be change in the tonicity of the muscular coat of the vessels, and the question we have to determine is how this change of tonicity is brought about. It at once suggests itself that this may be due to some irritation which disturbs the function of the nerves of the vessels. And this may to a certain extent be so, especially as it has been proved by direct experiment that irritation of a sensory nerve causes dilatation of the arteries in the whole area to which the nerve is distributed. Why this irritation of a nerve should produce this active, directly paralyzing effect is not quite so clear, though I think it may be very fairly explained in the following way. We know that the vagus nerve possesses an inhibitory action upon the heart, and that irritation of this nerve produces a diminution or obstruction in the action of this organ. We therefore assume that there is an inhibitory nervous system which arrests the contraction of muscles. And if this is true of the heart, why should it not also be true of the blood vessels; and why should we not assume that the muscular elements of the blood vessels, like the heart, are under the control of both the sympathetic and the cerebro-spinal system; the former of which causes the rhythmical contraction of the vessels, and the latter regulates and obstructs their contraction?

If this is so, it would explain the reason why irritation of the cerebro-spinal nerves would exert an inhibitory effect upon the muscular coat of the vessel, and as a consequence vascular dilatation. But it is quite clear that this explanation of the cause of the dilatation of the blood vessel is not sufficient to explain the phenomenon. It is true that part of the dilatation may be due to this cause, but I am inclined to think it is only a very small part; for it is clear that if this was the cause, and the sole cause, the dilatation would not be confined to the injured area, but would embrace all those parts supplied by the nerve irritated. Moreover, experiment and clinical experience negative this view. The experiments are

those of Cohnheim, who has shown that in the tongue of a frog, after its nerves have been severed, the process of inflammation can be excited by almost any irritant, and, indeed, that where the tongue has been severed from all its connections, so long as the arteries and veins are allowed to remain intact an inflammation can be excited by similar causes. It is certain here that the dilatation is not dependent on any influence conveyed to the blood vessels from the cerebro-spinal centre.

Clinical experience also points in the same direction. I need only allude, in illustration, to the fact that it is a matter of every-day experience to see inflammation set up in paralysed parts, where the nerves clearly can have nothing to do with the primary condition of dilatation. We must look, therefore, to another cause to explain the dilatation which takes place in the inflamed area. I think it may be briefly stated to be due to the direct effect produced upon the vessels of the part by the injury that has caused the disturbance, or, in other words, that the irritation disturbs directly the function of the muscular coat of the arteries and veins and the living cell substance of the capillary walls. This is in strict accord with Cohnheim's so-called “alteration” theory of inflammation, namely, that the “alteration of the physiological condition of the walls of the vessels is the cause of those phenomena and processes the sum of which is designated by the term inflammation.”

The grounds on which Cohnheim based this proposition was by cutting off the circulation from a part for a certain length of time, say twenty-four hours, by encircling it with a ligature, and then at the expiration of this time loosening the ligature and restoring the circulation. By this means he produced as typical and intense an inflammation as by subjecting the part to the direct action of an irritant. By thus depriving a part of blood he unquestionably altered the physiological conditions of the blood vessels and other tissues, and this changed or abnormal condition was the proximate cause of the dilatation of the blood vessels, as well as the other phenomena of the inflammation. If, then, this undoubted alteration in the walls of the blood vessels—the part with which the blood first comes into contact in these experiments—causes them to act as if they were inflamed, may we not assume that a similar change takes place in the vessels when inflammation is set up by other causes, and induces a similar result?

If we accept this as true we have a strong argument in support of the view that inflammation is necessary for the repair of tissue, and therefore for the union of wounds. For we have here in the vessels a deterioration of tissue, a retrograde metamorphosis, which certainly cannot be regarded as a healthy physiological action; a something which is quite different from the *affluxus sanguinis*, the active congestion or determination of blood which is due entirely to nerve influence.

We pass on now to consider the second question which I set myself—namely, is the vast accumulation of cells in and around a wound during the process of healing the simple outcome of a physiological process? In order to answer this question, we have to ask ourselves another: Whence do they come? I suppose there is no one here present who would hesitate in answering that, at all events to a very considerable extent, they are emigrated leucocytes. And this is undoubtedly one source from which they are derived, though I think there is very little doubt that they are also in part derived from a second source. Into this point, however, it is foreign to my purpose at present to enter; and it is sufficient that we believe that the myriads of rounds cells which we see in and around a wound during the early stage of the healing process were originally derived in part from the leucocytes which have passed out of the circulation through the walls of the capillaries. We then ask ourselves another question, Why has this emigration taken place? It is a condition very different from what we observe in health. For though it cannot be denied that exudation of the plasma of the blood takes place as a physiological process, and emigration of the leucocytes very probably does so, still it is a very different condition to what we see in a wounded part, and we never find in healthy tissues the whole of the structure infiltrated with leucocytes to such an extent as almost, if not quite, to obscure the natural structure of the part. There is no doubt that the answer to this second question is that the emigration is due to stasis, or that condition of arrested circulation which

we know speedily follows the dilatation of the blood vessels in an inflamed part. And then we ask ourselves a third and final question, What is the cause of this stasis?

Many theories have at different times been put forward to explain this phenomenon. It has been attributed to the dilatation of the blood vessels, to changes in the corpuscles, and to changes in the tissues, especially the lining membrane of the walls of the vessels. It cannot be due to the dilatation of the walls of the vessels, because we do not find a similar phenomenon attending the dilatation of vessels from other causes. Division of the sympathetic in the neck of an animal causes dilatation of all the vessels of the head and face, from paralysis of the muscular coat of the blood vessels, but there is no tendency to stasis or arrest of the circulation. Then, again, it cannot be due to changes in the corpuscles; for if we examine under the microscope the mesentery of a frog in which inflammation is slowly set up from exposure to air, we may watch a leucocyte showing a tendency to stick to the wall of the vessel so long as it is contained in the inflamed area; it partially adheres, oscillates to and fro, but gradually makes progress onwards till it reaches the extreme limit of the inflamed area, when it at once loses this tendency to adhere, and flows on rapidly in the normal course of the circulation.

Another reason why it cannot be due to changes in the corpuscles is because if it were we must assume that not only the corpuscles in the inflamed area are changed, but all the corpuscles throughout the body, and therefore this same adhesiveness must be observable in every vessel in the body, for only one small portion of the blood was acted upon by the irritant which set up the inflammation, and the blood in the area of stasis cannot be that which was thus acted upon.

Stasis must therefore be due to changes in the walls of the vessels, or the tissue with which the blood comes in contact, so that the corpuscles when they pass into the injured area acquire a tendency to adhere. The lining membrane of healthy vessels differs from every other solid in the fact that the corpuscles have no tendency to adhere to them, and therefore no coagulation of the blood takes place; but when the corpuscles, and especially the leucocytes, come in contact with any foreign body, that is to say, anything else except the healthy wall of the vessel, they show an immediate tendency to adhere to it, to disintegrate and set free their fibrin ferment, and coagulation is the natural result. The same thing holds good if the lining membrane becomes altered in structure or diseased. It no longer possesses the power of repelling the corpuscles, but, on the other hand, attracts them and causes them to adhere. It acts as a foreign body. Look, for example, at many cases of thrombosis, where the coagulation is due to an altered state of the vessel wall, which causes the leucocytes to adhere to it, and as a consequence the vessel becomes occluded with clot. Or, again, look at the natural process of cure in an aneurysm. The lining membrane of the sac is an altered tissue from the ordinary lining membrane of an artery; it is a foreign body—a something other than the wall of a healthy vessel. In consequence of this, the leucocytes adhere to it; they disintegrate, they set free their fibrin ferment, and thus fibrin, the active clot of Broca, is formed on the interior of the sac.

In the fact, then, that in the union of wounds we have the tissues in and around the wound infiltrated with cells, we have another strong argument in favour of the theory that the union of wounds is an inflammatory process. This infiltration with cells is the direct outcome of stasis in the vessels, and this stasis is a necessary result of their deterioration or retrograde metamorphosis which can scarcely be regarded as a physiological process.

In connection with the third question which we set ourselves to consider, whether the changes which take place in the cells, which are now believed to be in a great measure large mobile cells formed by proliferation of the original cells of the part, which have replaced the emigrated leucocytes, are exactly identical in their mode of growth and development with embryonic cells, I am bound to say that I know no difference. It seems to me that we must acknowledge that these cells of granulation tissue are exactly identical with embryonic cells, and behave in the same manner, undergoing the same form of development into higher tissues. It would appear that the recognition of this fact has caused objections to be raised against designating as inflammatory the purely regenerative

processes which take place in the healing of a wound. But I would contend that it in no wise invalidates my argument that the new formation of tissue which leads to the adhesion of wounds is inflammatory. My contention is that this newly-formed tissue, which is by a process of development eventually to form scar tissue, or the bond of union between the severed tissues, is the result of an inflammatory process; though the subsequent steps by which it undergoes development into scar tissue may be distinctly physiological, or at all events identical with processes which take place in the blastodermic membrane of the embryo, where the primary nucleated masses of protoplasm of which it is composed undergo changes of growth, multiplication, and differentiation until they become converted into complete animal cells of many different types. It is the mode of origin of the cells, and not their subsequent changes which marks off the process of union of wounds as an inflammatory one.

Leaving this point we pass on to consider the fourth and last question which I stated it was my intention to bring under your notice in elucidating the point which we have under consideration. The question is as follows: What is the nature of the newly-formed tissue which acts as a bond of union, and joins the two severed surfaces together? And in the answer to this question I think we shall find one of the strongest arguments in favour of the view for which I am contending—namely, that wounds always unite by a pathological process which we term inflammation.

The elucidation of this point will require a little careful consideration. So long as tissue elements retain their vitality they possess the power of undergoing nutritive and formative changes on the application of a physical or chemical stimulus. Up to comparatively recent times the knowledge of this fact caused pathologists to regard inflammation as a condition of increased, though perhaps perverted, activity of the process of nutrition. The converse of this is, however, the fact. Lord Lister was the first to initiate the doctrine that "inflammation consists not in increased, but in diminished vitality of the tissues affected." The process of inflammation, whether showing itself by enlargement, multiplication, or formation of cells is always a sign of lower vitality, and results, as Dr. Burdon Sanderson expresses it, in "tissue spoiling and not in tissue stimulation." And the more rapid the rate of reproduction, the less is the stability of the newly-formed tissue, and those tissues which are the result of the inflammatory process are always more lowly organised and of a lower vitality than the original tissue of the part before the process of inflammation took place. Inflammation must therefore be regarded as a destructive process. If we admit this—and who will gainsay it?—we have an extremely strong and potent argument in favour of the fact that the scar tissue or bond of union in a wound is a product of inflammation, and not a new formation the result of a physiological process.

Let us briefly consider what scar tissue is. It is composed of dense white fibrous tissue, which differs from the normal tissue which it has replaced in many important particulars. And, as Rindfleisch says, "Cicatricial tissue is far from being a connective tissue of ideally high quality." It is more dense than ordinary areolar tissue, and contains no yellow elastic fibres. It is smooth on the surface, and presents no papillæ. It is devoid of sweat glands, sebaceous glands, or hair follicles. It contains no lymph spaces or lymphatics, and nerve fibres are very few in number or altogether wanting. When first formed it is vascular, but its vessels soon disappear, and it becomes dry, hard, and white, and of lower organisation than the natural parts. Moreover, scar tissue is exceedingly prone to diseases of degeneration. How common a thing it is to find a scar breaking down and ulcerating, and how slow these ulcers are to heal, and how liable to recur. And, again, how frequently we find scar tissue becoming the seat of epithelioma; constituting what was first described by Mr. Cæsar Hawkins as the "wartlike tumour of cicatrices."

And even keloid must be regarded as a disease of degeneration; for though there is an excess of growth, this growth consists of a lowly organised fibrous tissue, intermingled with cells, which are arrested in their progress of development, and degenerate in their incomplete forms. If, then, this is the character of scar tissue, it can scarcely be regarded as the product of a healthy physiological process, and it becomes a powerful argument of the view that union of wounds is an

inflammatory, and therefore a pathological process, and not a physiological one.

This, then, is the evidence which I have to bring forward in favour of the view I am upholding, and it only remains now for me to endeavour to reconcile this view to the doctrine of the different forms of union of wounds.

In our textbooks on surgery it is customary to describe five classical ways in which wounds unite: (1) by immediate union, primary adhesion, or direct growing together of the severed surfaces; (2) by first intention; (3) by scabbing; (4) by second intention; and (5) by secondary adhesion or growing of two granulating surfaces together. To these I think we ought to add another—namely, healing by blood clot. It will be my endeavour to show that there are only two ways in which union of wounds takes place—namely, without suppuration and with suppuration; and, moreover, that the difference between these two conditions is very slight, being one more of degree than of kind, and that they are both the result of the same morbid process going on in the part—that is, inflammation.

Let us consider these different modes of union a little more in detail. It is the first of these that I most desire to consider, because it is a mode of union in which the essential principle was laid down by Macartney, of Dublin, who first described it, that there was no inflammation. He says: "Union takes place without any intervening substance, such as blood or lymph." We are told that when the surfaces of a clean-cut wound are carefully adapted and supported they will probably be found to present no signs of inflammation appreciable to the senses, and in the course of from twenty-four to forty-eight hours the wound will be so soundly united as to require no further attention, nothing being left except a linear mark, which at first looks more or less red, but gradually fades away, and in the case of small cuts disappears altogether.

This is hardly an intelligible account of what takes place. In what does the process of union consist? There must be some process by which the severed surfaces are caused to adhere together, and to become united in such a way as to present no trace hereafter of where the union has taken place. And, again, what is the nature of this linear mark, which at first looks red and then gradually fades away? And, finally, must we assume that there is no inflammation because there are no signs appreciable to the senses present? I confess that this theory of immediate union is beyond my comprehension, and I have searched for an intelligible account of what takes place without being able to find it.

Hear what another author says!

"When wounds unite by immediate union no other changes than these"—namely, coagulation in the vessels up to the nearest anastomosis and dilatation of the capillaries in the neighbourhood—"take place beyond the gradual restoration of the capillary circulation through the parts that have been divided, and under such somewhat rare circumstances no scar or cicatrix is left. The soft parts at first simply adhere together, and subsequently become continuous."

But why do they adhere? How do they become continuous? What becomes of the clots in the vessels, and why do the neighbouring capillaries dilate?

Another author says:

"The divided blood vessels and nerves are brought into perfect contact, and reunion ensues by the opposed surfaces simply growing together." Very simple! but I confess that I should like to be told how they grow together. Does the author mean that when the parts are replaced each minute filament of nerve and the open orifice of each capillary vessel is brought into "perfect contact" with its corresponding and severed half on the opposite side of the wound? The idea is of course absurd.

It seems to me that we must acknowledge the presence of some connecting material which shall first cause the cut surfaces to stick together, and through which they shall become continuous, just as much as in the case of two pieces of wood, which we cannot make stick together without the intervention of some adhesive material.

I for one, therefore, must discard the doctrine of the first mode of union of wounds as untenable. I explain those cases in which it is said to occur, and I must confess that I have

never been so fortunate as to observe the process in my own experience, as cases where the inflammatory process is reduced to a minimum, and where therefore the adhesive material is correspondingly small.

Direct experiment negatives the proposition. If a wound, however small and however carefully adapted immediately after its infliction, be made, it will be found upon killing the animal and making sections of the injured part that there is a greater or less amount of connecting substance between the edges of the wound. Even if a very small incision be made through the cornea of a rabbit with the sharpest knife, and be prevented from gaping by at once closing the eye, the resulting cicatrix will be invisible to the naked eye, but nevertheless the intermediary substance may be demonstrated on microscopic examination. It seems clear to me therefore that we must exclude this fancied method from our category of modes of union of wounds, and arrive at the conclusion that, where union takes place very rapidly and without the ordinary signs of inflammation being appreciable to the senses, the difference is merely due to degree, and that the same changes take place here as in the so-called union by the first intention, though to a less extent. For who shall say how much hyperæmia, how much exudation, what amount of new formation of tissue is necessary to agglutinate and unite the edges of a wound together.

We proceed, secondly, to allude to the second mode of union of wounds, viz., union by first intention or by, as I believe, adhesive inflammation. I shall not say more about this mode of union than to mention that this would correspond to my suggested first division, that is to say union without suppuration. I have already discussed this process very fully and the changes which take place in the part up to the conditions of complete union and which changes are admitted by all whether they are believed to be due to an inflammatory process or not. We pass on therefore to union by scabbing. This I believe to be merely a modification of the process of union by first intention and not to be worthy of being placed in a distinct class by itself. When a wound heals by scabbing the separative material which is poured out undergoes similar changes to those which take place in the same material when the wound heals by first intention, the scab merely forming a protective film over the wound and preventing decomposition or putrefaction. Union by blood clot is another mode of union, which can only occur in an aseptic wound and has only recently been described. It is merely another modification of union by first intention or by adhesive inflammation when the edges of the wound are not in contact, but are separated by blood clot, which acts as a mould or framework into which the leucocytes and the plasma cells, the result of the inflammatory process, penetrate and where identically the same changes go on as in those cases where the edges of the wound are in close contact and where there is nothing between them but inflammatory exudation.

It is obvious that all these modes of union are merely modifications of one process and are identical as far as regards the changes which take place. They may therefore, I think, with propriety be classed together as modes of union of wounds without suppuration.

It remains for us now finally to consider the two other processes or modes of union of wounds, namely, union by second intention and union by secondary adhesion, or as it is sometimes called "third intention"—two modes of union which I would venture to class together in one group as cases of union with suppuration.

With regard to this mode of union it will be seen, I think that it is merely a modification of the mode of union we have already described; that in both the essential features are identical, and that the difference in the two is one rather of degree than of kind. The difference in the two would appear to be due to some circumstance which produces a prolonged irritation, and therefore the resulting inflammation is prolonged, and the amount of inflammatory exudation is increased. If we examine the changes which take place in this mode of union, we find that we have the same initial changes; the same blocking of the severed vessels; the same hyperæmia around, and the subsequent stasis, and the same exudation of what Hunter termed "plastic lymph." But instead of this exudation being slight in amount, and speedily ceasing, it goes on and on until the surface of the wound becomes

covered with a considerable layer, too thick to be nourished by the vessels in the underlying tissues. From malnutrition, therefore, the cells in the superficial layers undergo degeneration, and are converted into pus cells, and thus suppuration takes place. At the same time the deeper layers become vascular and converted into granulations, which undergo cicatrization, and so the wound is healed. There can be no question, I think, that the cause of the prolonged irritation is the presence of septic micro-organisms in the wound.

Time will not permit me to describe the process in detail, but sufficient has been said for my purpose, which is to point out the close analogy between the process of union by first intention, and union by second intention. In both there is inflammation; in both this is attended with exudation, though varying in amount; and in both this exuded material forms the bond of union.

In union by secondary adhesion or "third" intention we have the same exudation of inflammatory material acting as the bond of union. We have inflammation, exudation, and the conversion of the exudation into granulations. If these granulations are now brought in contact they coalesce together, just in the same way as the exudation does in union by first intention. The vessels grow through this coalesced material from side to side of the wound, the cells of which it is composed undergo developmental processes, and are converted into scar tissue and the union is complete.

Such, then, Mr. President and Gentlemen, are briefly my views with regard to this important question of inflammation in connection with the union of wounds. The whole subject hinges on the one point of what we mean by inflammation. If we agree with Hueter and Kocher that no injury alone is competent to produce inflammation without the intervention of micro-organisms, then my whole argument falls to the ground. But if we believe, as I do believe, that inflammation may be induced without the concurrence of organisms—an inflammation, I admit, different from that excited by these bodies, for it neither tends to spread to contiguous parts beyond the area of injury, nor to infect distant parts through the blood stream or otherwise—then I say I have brought forward conclusive evidence to prove that the union of wounds is an inflammatory process. At least, if it is not, I know not what it is.

REFERENCE.

- ¹ Hunterian Oration, 1893, Bryant.

ABSTRACT OF THE HARVEIAN LECTURES.

ON

DISEASE AND ITS TREATMENT, AND THE PROFESSION OF MEDICINE IN THE YEAR 1899.

Delivered before the Harveian Society of London, December 1898.

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LECTURE I.

THE PRESENT ASPECTS OF DISEASE.

THE NINETEENTH CENTURY.

FROM the year 1899 we shall soon be looking back upon the greatest century medicine has ever known, a century of labour and of results. But our recent vicissitudes, our changes, and our prospects will be sufficiently illustrated by a review of a shorter period, that which is included within the memory of our own generation.

Gradually the class distinctions have become less marked, and now, in the closing years of this century, the physician is only distinguished from his fellow workers in more general subjects in that he is credited with a more ample knowledge of the matters to which he restricts his attention; while the humble apothecary of the early days of the century, who was not paid for his professional advice but solely for the medicines which he supplied, has given place to the highly accomplished practitioner of medicine and of surgery.

He is to be found everywhere through the land, well taught, with a great knowledge of his profession, careful and judicial, wanting but little outside assistance in his work, and then only to help to solve some of the difficult or insolvable problems that present themselves in the practice of the profession. "*Fin de siècle*" is not an idle term. The whole world is conscious of changes, profound and rapid, and to these none are more keenly alive than ourselves who stand by and watch.

THE CONTRACTION OF THE FIELD OF MEDICAL PRACTICE.

Another great fact around which my remarks will centre is the increasing limitation of disease and the contraction of the field of medical practice. It will be seen that in many cases ailments which hitherto had belonged to the exclusive care of the general practitioner have had a tendency to escape from his undivided control. The causes of this change are various, its ultimate consequences of considerable importance, and to them some attention will be devoted in due course. Other changes no less remarkable have occurred, influencing the status, the practice, and the prospects of the profession.

THE GRADUAL DIMINUTION IN THE PREVALENCE OF DISEASE, AND ITS CAUSES.

The prevalence of disease has considerably diminished within the memory of the present generation, and, if its characters have altered in any degree, the change has been rather in the direction of attenuation. The notion of the parasitic origin of disease dates back to a remote antiquity; but the full proof of its correctness has been delayed until our own times, and with it the idea that their spread can be controlled and even arrested.

Etiology loses its use unless disease be recognised. In diagnosis also the most brilliant advances have been worked out in the laboratory. Bacteriology has given us tests for some of the most virulent affections, and the other sciences have been drawn into the service of the physician. Diagnosis must always be an art, but it is becoming more and more a science, needing technical knowledge and skill and an increasing supply of instruments of precision. One of our most striking innovations is the employment of scientific aid by the practitioner, and the adequate means which have come into existence to supply his requirements. At hospitals all this is provided by the clinical laboratory, which is therefore an essential part of their equipment, irrespective of any educational object.

It is to Jenner we owe the great idea that a disease may be practically stamped out by a thorough application of some universal protection. I need not weary you with figures, but you are aware that wheresoever efficient vaccination and revaccination are performed the mortality from small-pox is almost *nil*, and its incidence is restricted both in numbers and degree. In our own country it survives only by the will of the people.

THE SHARE OF HYGIENE IN THE PREVENTION OF DISEASE.

To hygiene, inspired of bacteriology, are due most of our practical measures of prevention. The suppression of cholera, of relapsing fever, and of typhus, the limitation in the spread of the common exanthems, our successful though still fractional results in the limitation of phthisis, and, not least, the improved health and strength of the rising generation; all this has been the direct fruit of a faithful application of its principles.

Again, we are indebted to it for the suppression of the epidemics of puerperal fever and septic peritonitis. This great progress was initiated by Semmelweis, but the modern life-saving reforms did not become part of practical gynaecology until Lister's great work had shown us how the previously unchecked spread of septic infection could be absolutely prevented. Pyæmia and septicæmia, which claimed so many victims, are now almost unheard of. Moreover, suppuration itself, with its long delays, its risks and sequelæ, has now ceased to be regarded as part of the process of healing.

Bacteriology has in some instances supplied us both with the prevention and the cure. The treatment of diphtheria is the most brilliant example of the curative value of the serum of immune animals. Less successful, but not wanting in promise, are other forms of serum treatment. The strepto-