THE LUMLEIAN LECTURES ON INFLAMMATION.

Delivered before the Royal College of Physicians.

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LECTURE I.—INJURY AND DAMAGE.

I FEEL that I need some apology for coming before the College with a subject which has been frequently discussed already, and about which it may be presumed that I have nothing new to say. I cannot promise that it will not be so; for I have no new doctrine of inflammation to advance, no great discovery to relate.

In what I shall have to say to-day of the nature of the process of inflammation, it will be my purpose to strengthen the position I have taken with reference to the subject on former occasions, and particularly in my essay on Inflammation published in 1870, and in the lectures I gave in the theatre of the University of London seven years ago.* In my second lecture, I intend to enter on a question which, though not new, has attained of late years a significance which it did not before possess—that of the ætiology of inflammation—that is, the discussion of the various agencies which, either as principal or accessory causes, may be concerned in its origin. And, lastly, I desire, in my third lecture, to bring our modern knowledge into comparison and harmony with the teaching of those who have thought and observed best on the subject, from Hunter to our own times.

1. *Inflammation is the Physiological Effect of the Damage done to a Tissue when it is injured.*—The definition which in our epoch has carried more weight and has had more influence than any other, is that given in nearly the same terms, first by Mr. Goodsir (*Anatomical and Pathological Observations*, page 43, Edinburgh, 1845), and subsequently by Mr. Bowman, who, in his well known lectures (*Lectures on the Parts concerned in Operations on the Eye*, London, 1849, page 29), described the effect of an injury of the cornea as “a change wrought in the natural acts of nutrition then existing in the wounded part.” The same conception originated in the mind of these two observers independently, from the study, which the introduction of the microscope and their own anatomical discoveries had rendered for the first time possible, of the textural changes which inflammation leaves behind it. This conception, so thoroughly British in its origin, was soon transplanted into Germany. It was adopted by Virchow with little modification, and became part of that more general doctrine of “cellular pathology” which at one time ruled pathological opinion, and has not even yet lost its influence. The work that Mr. Bowman did about inflammation was, like all the other work he did in those early and fruitful years, complete. The appearances which he described in the cornea as evidence that the “natural action of its nutrition” had undergone a change, are as full of interest to us at the present time as they were to him; and, if we were now to repeat his experiments, we should find the results to be exactly as he said they were. Why, then, should we not content ourselves with the same explanation? Why should we not continue to say with him and with Goodsir, “Inflammation may be described as a modification of existing normal processes”? The answer is that, during the last ten or fifteen years, another step forward has taken place—a step forward in the same direction as the former one, and, as it was, dependent on the acquirement of new methods of observation. These methods may be described as physiological, just as those which led to the brilliant discoveries of the preceding epoch were anatomical. We are now striving to become eyewitnesses of the actual processes of disease at the same time that we continue, with unabated curiosity and vastly improved means, to scrutinise its results. We have thereby learnt that many pathological processes, and particularly the fundamental one which now occupies us, are not quite what, from their anatomical results, they seemed to be. We find, when we actually watch the effects of injury on a living part,

that the old order changes, but does *not* give place to new—that we have before us, not disorder of function, but arrest; not the diversion of the resources of nutrition into new channels of activity, but merely the accumulation of such resources where they are useless, if not destructive, and, consequently, that the restoration of a part to the natural state must be as simple as its departure from it—that the resolution of an inflammation means either that the temporarily arrested processes of normal life simply go on again, or, if the process have proceeded to its ultimate issue—death of the affected part—that what has been destroyed has to be repaired, not (as we used to think) by a continuation of the morbid processes, but simply by the restitution of the normal condition. The principle is the same (if I may be permitted to use so homely an illustration) whether the inflammatory process invade our houses or our bodies. Obviously, no one would think of regarding the destruction of a house by fire as a modification of any normal process, nor would it occur to any one that the damage done would be best repaired by extension of that process, perhaps in a milder form.

I am well aware that this illustration is open to the objection that an inflammation has only the most remote resemblance to a fire; but I use it merely for the purpose of enforcing what I want to say—namely, that, if we confine the word inflammation within the limits of the original definition, and accept as its phenomena those which have been assigned to it by the authority of tradition (which is the only authority that has any claim to be heard in such a question), its essential nature is fully expressed in the word *damage*, and that it has no further relation to the process of repair than that which arises from the universal operation of the physiological law that, whenever part of an organ is destroyed, new growth proceeds from the old, to supply the defect.

2. *Mode of Origin of Inflammation in a Non-Vascular Tissue. Keratitis cannot now be understood as a “perversion of the natural acts of nutrition of the part.”*—Keratitis, as I have already hinted, and will endeavour to show more completely in my third lecture, was the point of departure of the cellular pathology. It is, therefore, with the cornea that we must begin, if we desire to re-examine the grounds of that doctrine by bringing to bear upon it the direct teaching of experiment.

Although in the cornea we have to do with a structure which is devoid of vessels—and therefore, in the sense of the classical definition, incapable of inflammation by itself—yet, inasmuch as, in every keratitis, the adjoining vascular structures sympathise—*i.e.*, are also affected by the injury, it is allowable to include what happens in the vascular border as forming part of the process.

When an incised or punctured wound is made in the cornea of the rabbit, of sufficient depth to penetrate below the superficial epithelium and expose the proper corneal tissue, the reaction is exceedingly slight. All that can be seen by the naked eye is, that the wound is surrounded by a haze of opacity, which rapidly disappears; but there is no congestion of the limbus. As an exciting cause of inflammation, therefore, such a wound is inadequate, for none of the objective signs of inflammation are present. To induce them with as limited an injury as possible, the best way is to insert a silk thread as a seton at the centre of the cornea, withdrawing it as soon as it has accomplished its purpose. After several hours, during which no visible effect follows the injury, the cornea is seen to be surrounded by a red border, which consists of the wreath of dilated capillary loops of the episcleral vessels, from which it, for the most part, derives its nutrition. It often happens that the inflammation which has thus begun proceeds further; that the marginal congestion extends and increases until the cornea is surrounded by a ring of tumid and highly vascular mucous membrane; that the surface of the conjunctiva is bathed with pus; that the cornea becomes more and more opaque; and that eventually pus collects in the anterior chamber.

This effect exceeds what is wanted, as much as the others fall short of. The excess of reaction may be avoided by withdrawing the ligature as soon as the conjunctivitis has begun; in which case it may fortunately happen that the zone of redness is limited to one border only, opposite to which a radial tract of opacity extends towards the middle of the cornea, and becomes continuous with the zone of opacity which surrounds the path of the seton. To understand what this means, it is scarcely necessary to appeal to the microscope. It is plain enough that the central area of opacity is of the same kind as the little cloud which, when the cornea was injured by merely breaking up its surface with the point of the scalpel, as Mr. Bowman did, surrounded the little wound. The other area as evidently comes from the edge, and is a consequence of the surrounding inflammation. Mr. Bowman would have taught us to understand both as results of a “change of the natural acts of nutrition having their seat in the wounded part”; and particularly he would have regarded the central

* The definition which I gave in 1870, in my essay on the Process of Inflammation, published in the *System of Surgery*, was as follows. “1. Inflammation is the succession of changes which occurs in a living tissue when it is injured, provided that the injury is not of such degree as at once to destroy its structure and vitality.”—*System of Surgery*, 1870, page 729. The definition accepts the characteristics of the inflammatory state as they were stated by Celsus, and connects them with each other by their common relation to the cause which produces them—*injury*. The lectures referred to were not reported or published.

cloud—that which immediately surrounds the wound—as directly dependent on nutritive disorder of the corneal tissue irritated by the seton, and the marginal opacity as evidence that similar changes were beginning in the neighbouring vascular parts. Experiment shows that the true explanation is much simpler than this. The reason why the little punctured wound surrounds itself with a cloudy border is, that cells resembling the colourless corpuscles of the blood exist in the conjunctival sac, and find their way by the breach into the little branching tubes which permeate the tissue in every direction; the proof of this being, (1), that, if we place a dead cornea, in which a puncture has been previously made, for a few hours under the same conditions as those to which the living cornea is normally exposed, we find that it remains transparent everywhere excepting in the neighbourhood of the injury; and (2) that we may destroy the tissue of the living cornea by other means, to an extent far exceeding that of either the seton or the puncture, without any such results. We may, indeed, destroy half the organ without producing any opacity whatever, provided the agent is of such a nature as not to disintegrate its protective epithelial covering, and thus open the way for the immigration of cells from the outside. The agent which answers this purpose is chloride of zinc, which, as a caustic, has two invaluable properties. One is, that its action produces very little change in the mechanical properties of the tissue acted on; another is, that it kills up to the limit, without damaging beyond the limit. When it is applied to the cornea over a carefully limited surface, it leaves behind a scarcely visible opalescence; but the tissue is absolutely dead—the necrosis extending in depth, so as to affect two-thirds or more of the corneal tissue. Here, again, the effect, so far as concerns the recognised signs of inflammatory reaction, is usually *nil*. There is no opacity—no surrounding zone of congestion. If you examine the cornea microscopically, what you find is, first, that within the region of necrosis the branched corpuscles which are characteristic of the cornea have become so attenuated as to be indistinguishable; secondly, that, immediately outside of the dead part, these bodies are shrivelled into shapeless masses, like little fresh-water polyps which have drawn in their tentacles; and finally, that, beyond this clump region, the fixed corpuscles present in every way their natural aspect. If the chloride be applied near to the limbus, the case is quite otherwise. Notwithstanding its little tendency to spread, the episcleral blood-vessels are acted on, and fill with blood. The result of this is, that thousands of colourless blood-corpuscles invade the cornea at the congested border, and find their way to the necrotic region, where, from the absence of the normal fixed corpuscles of the cornea, they are the more obvious. In this case, at all events, there can be no question of perverted nutrition; for the tissue which is the seat of the change is as lifeless as a bit of finger-nail. The whole process, indeed, is so self-evident, that neither comment nor explanation is necessary. You have before you a dead tissue, of which all the “natural acts of nutrition” of which Mr. Bowman spoke have ceased; but this dead tissue is as full as it can hold of living cells. If anything is clear, it is surely this—that they were not born there, but were imported from elsewhere; and, if not from the blood-stream, whence?

Let us, before we proceed further, sum up what we have learnt from the cornea. It is the type or representative of those structures which, under the term connective tissue, we recognise as constituting the connecting and supporting parts of our bodies. It consists of a system of branched cells, each of which is united with its neighbours by its branched processes—these being sheathed in a matrix, of a texture identical with that of the non-cellular part of ordinary connective tissue, but possessing those physical properties which fit the organ for its purpose. This matrix is hollowed out into intercommunicating channels, which, in form and branching, are the counterparts of the complicated network of protoplasm they are intended to contain. In every respect therefore, excepting one, the cornea is a complete tissue of its kind; and, if such tissues in general are to be supposed capable of responding to injury in an active way—*i.e.*, by continuing their “natural acts of nutrition in an unnatural, abnormal, or perverted way”—there is no reason whatever why the cornea should not do the same. Trained as we all have been in the “cellular pathology”, we expect this, as it were, instinctively; but what we actually see is quite different. At the border of the faint eschar made by chloride of zinc, we see, on one side, health; on the other, not disease, but death; no reaction—no perverted nutrition—nothing but damage. So far, therefore, as can be learned from a non-vascular structure, the damage done by injury, whether mechanical or chemical, is exclusively negative. It consists in arrest or annihilation of function, not in perversion.

3. *Origin of Inflammation in Vascular parts. In such parts which have been damaged by heat or cold, inflammation comes into existence*

d'emblee.—Let us now see what happens in the more common case in which the injured part is vascular. But, before doing so, let us consider the question which has to be answered. In injuring the cornea, we act directly on cells, fibres, ground-substance, nerves. We have seen what the result is. In acting similarly on a vascular structure, we have the same cells, fibres, ground substance, nerves, but, in addition, blood-vessels. Any signs of damage, therefore, which exist in the latter case that were absent in the former, we have a right to attribute to blood-vessels. To prove this, it is desirable first to select for the purpose agents which, in accomplishing their work, leave nothing behind them excepting the damage they have done; and, secondly, to compare what happens in two cases—one in which the injury is of such a nature as to affect all tissues equally, the other in which its action is specially directed to the vessels.

For the purpose of acting equally on all tissues, there is but one method that can be thought of, namely, the application of cold or heat. It is not necessary to have recourse to a very high temperature. Plunging an organ in water not much warmer than you can easily bear with your hand, is sufficient to accomplish all that is required, provided that, before the immersion, the circulation is arrested by an Esmarch's bandage. The organ used by Cohnheim for the purpose was the ear of the rabbit. The result is in the highest degree worthy of our attention. The immediate effect is, of course, *nil*; but if, after the ear has regained its normal temperature, the ligature be removed and the circulation restored, it is seen that, in a very short time, the signs of inflammation—not merely of active congestion, but of true inflammation—present themselves; and, in an hour or two, the organ is warmer than its fellow by several degrees, full of blood, and swollen to several times its previous thickness. At first, the redness is seen to be due to the dilatation of blood-vessels previously distinguishable, and to the appearance of new ones where none were visible before; afterwards, as the oedema increases, the organ acquires a uniform diffused redness. If, at this stage, the skin be punctured, coagulable liquid, charged with leucocytes (pus-corpuscles), escapes. If the animal be killed, and the swollen ear, after having been suitably hardened, be used for the preparation of microscopical sections, it is found that the subcutaneous tissue exhibits in every respect the character of inflammatory infiltration.

In the experiment I have just described, the part is subjected to two injurious actions simultaneously. It is deprived of blood, and its temperature is raised to about 10° above the normal. It is to the latter of these that the damage is alone attributable; for it is well known that the exclusion of blood from a part, for about six or seven minutes, has no permanent effect. If, however, the state of anæmia be kept up for twenty-four or forty-eight hours, the case is very different. It might be expected, indeed, that so long a starvation of the tissue would definitely destroy its vitality. If the bandage be kept on too long, this anticipation is realised; but in this case the time may be so regulated that the damage, thus slowly inflicted on the starved part, is similar in degree to that which was occasioned in a few minutes by the influence of heat, or it may exceed or fall short of it. In any case, the objective signs of damage are of the same kind. When the ligature is removed, blood finds its way along its accustomed channels, and for a time there is nothing to indicate that the apparent restitution of natural conditions will not be permanent. But, if the ear be examined half an hour afterwards, it is seen that arteries and veins are dilated, and that its temperature is already higher than it should be. I need not repeat here the description of the process, which, although of less rapid development, is identical in its results with that we have already had before us.

Here, again, the lesson to be learnt is so obvious that it scarcely needs indicating. The two experiments prove that an organ which is thoroughly damaged—or, to put it in other language, of which the vitality of every tissue is depressed, but not annulled—is already virtually in a state of inflammation, although, from the absence of the circulation (on the condition of which almost all the visible characteristics of vital changes are dependent) the objective signs of it may be wanting; that, in such an organ, the state of inflammation springs at once into existence, without any antecedent stage of incubation or development; and, particularly, that the formation of pus, which is commonly regarded as rather a consequence of inflammation than as a part of it, begins from the moment that the damaged vessels are distended with blood, and the internal surface of the walls pressed upon by their contents. To those who still find it difficult to realise that pus-corpuscles are not formed by some bioplastic process in the tissues, the experiment may be recommended, as affording one instance, at least, of the formation of pus, to which such an explanation is inapplicable, the rate of production of young cells being far too rapid to be thus accounted for.

(To be continued.)