THE LUMLEIAN LECTURES ON INFLAMMATION.

Delivered before the Royal College of Physicians.

By J. BURDON SANDERSON, M.D., LL.D., F.R.S.,
Professor of Physiology in University College, London.

LECTURE III. PART I.—ETIOLOGY OF INFLAMMATION.

THE most important of the propositions which I submitted to you in the last lecture was this: that the attribute which distinguishes an infective inflammation (*i. e.*, one which is capable of extending and reproducing itself) from a normal one (which tends to discontinuance on the removal of its cause)—in a word, the property of infectiveness—is but the pathological expression of a chemical state of the tissue and exudation-liquids of the inflamed part, for which, in the absence of any reliable chemical characteristics, we gladly accept the microscopical test of the presence of septic organisms. A second proposition, to which I also attach great importance, related to the agency of the floating particles of air and to the viable organisms which we know to be present in ordinary water, and moreover to be capable of exciting putrefaction. I endeavoured to show that there is no scientific reason whatever for attributing to either of these phlogogenic properties. As I am very desirous to present this question from both sides, I will endeavour, by way of sequel to my last lecture, to place before you the argument of one of the most strenuous and efficient supporters of the opposite view that I know, Professor Hueter of Greifswald. Formerly, says Professor Hueter (*Grundriss der Chirurgie*, page 1), it was taught that inflammation was produced by mechanical, chemical, or thermal irritants. We now know that the most severe injuries can be inflicted without producing inflammation. Consequently, when an inflammation takes its origin from a wound, all that the wound does is to play the part of a door of entrance for the real *noxa*—water-germ, air-germ, or germ which sticks to the surface of the weapon or missile which inflicts the injury—as the case may be. When, on the other hand, the injury is not of such a nature as to occasion a breach of surface—as, for example, in the experiments I related in my first lecture, in which heat was employed for the purpose of producing inflammation—the reason why the warmed part becomes inflamed is, according to Hueter, that its vitality being depressed, air or water germs are enabled to penetrate it. Honestly following out the theory to its legitimate issues, Professor Hueter continues: Septic organisms exist everywhere, ready, whenever access is offered to them, to enter the body and fulfil their morbid function. Consequently, inflammation may be defined, with reference to the universality of its cause, as an *epidemic and contagious disease which prevails universally over the whole world*, with the exception of mountainous regions, near and above the line of perpetual snow. Here there are no germs, and, we may presume, no possibility of inflammation.

Such is the theory. Its ostensible foundation is the alleged experimental fact that the most extensive and severe injuries of vascular parts—involving bone, muscle, cellular tissue—may be inflicted under antiseptic precautions without producing any inflammatory effects whatever. To prove this, Professor Hueter has made extensive series of experiments, all of which had this in common, that large portions of deep-seated tissues were destroyed—usually with the aid of Paquelin's cautery—without injury to the skin or superficial textures. As soon as the cautery had done its work, the external wound, which was so directed that it did not coincide with the track of the cautery, was brought together, and of course treated antiseptically. With the exception of a few instances in which these precautions could not be carried out, the wounds not only healed by the first intention, but gave rise to no disturbance of any kind; so that, inasmuch as the operation was itself performed under deep anæsthesia, it may be fairly assumed that, notwithstanding the severity of the operation, there was little or no suffering. The animals were killed at various periods after the injury, varying from a few days to a few months. In the successful cases, the wounded surfaces of muscular tissue were as it were welded together, so completely that, on microscopical section of the

hardened part, the line of junction could only be distinguished by a blackened mark due to the charring action of the cautery.*

Now, *primâ facie*, these facts seem very like establishing Professor Hueter's aphorism; for it is clear that there were here no appearances suggestive of inflammatory exudation. I need scarcely say that there are other facts, both clinical and experimental; though I doubt whether any bear so directly on the point at issue. The most noteworthy are those which relate to the extraordinary results which, thanks to the antiseptic method, have been obtained during the last few years in the transplantation of tissues—such, for example, as the substitution of removed portions of peritoneum, by bits of dead membrane, without producing peritonitis†—a kind of sewing of new cloth on to old garments which a few years ago we should have thought absolutely incredible. All of such cases, which it would be easy to multiply, Hueter would say, are instances of injury without inflammation—proofs that if inflammation is the physiological effect of damage, you may, under aseptic conditions, have the cause without its consequences. But I venture to think that this is not the correct way of putting it. All that is definitely proved is, that in the absence of septic contamination, inflammatory changes are of limited extent and duration, not that they are absent. Surely, this is triumph enough for Lister's great discovery.

There is an experiment which is daily performed in the streets of London, and elsewhere besides, which is very much to the point. Its results constitute a very serious objection to the theory that the presence of "viable inflammation-excitors", as Hueter calls them, is a condition *sine quâ non* of inflammation. That experiment is simple fracture, which affords us an example of a severe but localised injury inflicted on a part to which germs cannot possibly find access. In every fracture a good deal of blood is extravasated, and in many a good deal of vascular tissue is damaged. Does that tissue inflame or not? Hueter says, consistently with his theory, No. We say, as emphatically, Yes; and need not, I think, fear to stake the correctness of our view of the etiology of inflammation on the issue. Now, the progress of the partly pathological, partly physiological changes which take place in a fractured bone, is exceedingly well known. They have been investigated in man and in animals macroscopically and microscopically. The decision of the question has nothing to do with the first stage in the process—that of extravasation, coagulation, and absorption of blood. It has still less to do with the third stage—that of the formation of the callus. All turns on the appearances which the injured part presents during the short period which begins with the absorption of the extravasated blood and precedes the earliest regenerative changes in the periosteum—those which lead to the formation of the provisional callus. At this time the surrounding muscular tissue, and the medullary cavity of the bone, the contents of the Haversian canals, are alike the seat of infiltration with small cells. The periosteum is separated from the bone, near the line of fracture, by a microscopical layer of similar character, through which the periosteal capillaries pierce to the bone—and all this at a time when no calcareous matter has begun to be deposited in the neighbourhood of the periosteal vessels. The example of simple fracture confirms the proposition laid down in last lecture—that every injury which is sufficiently severe, provided that it fall short of directly killing the tissue, produces inflammatory exudation.

Having occupied more time than I originally intended to give to the subject which at the present moment has, perhaps, more interest than any other—that of the cause and origin of inflammation—the time has come for considering how I may best bring my task to a conclusion within due limits; and, with this view, the best course open to me seems to be to select from the many topics which I have not found opportunity to discuss a few of the most important and interesting.

During the ten or twenty years which followed the anatomical and physiological discoveries of the middle of the present century, pathologists looked in two directions for the explanation of the phenomena of inflammation; namely, to the blood-vessels and their recently investigated muscular coats, and to the vital properties of cells. The vascular phenomena, it was hoped, might receive their complete explanation in vaso-motorial action; the textural changes, in the germination of tissues. In my first lecture, I endeavoured to show that neither of these modes of physiological action is directly concerned in the process. I trust that I have already given you sufficient evidence that an acute local process characterised by heat, redness, and swelling, may be induced under conditions which preclude the possibility of textural germination. In any case, I do not propose to try to add to it, but will

* "Experimentalstudien über das Verhalten tiefer Brandwunden" (*Deutsche Zeitschrift für Chirurgie*, vol. ix, page 381), and "Ätiologische Lehre der Entzündung" (same volume, page 401).

† Glück, Ueber Transplantation, Regeneration, und entzündliche Neubildung. *Langenbeck's Archiv*, vol. xxvi, p. 89.

content myself with adverting to one or two considerations which are likely to suggest themselves as tending in the opposite direction. One of these is the supposed fact that the production of heat is greater in inflamed parts than in others; the other, that, in many cases, inflammation appears to lead immediately to new growth. If it could be shown to be the case that a focus of inflammation is also a focus of calorification—that, in an inflamed part, the chemical changes which produce heat are more active than elsewhere—that fact alone would be fatal to the simple conception of inflammation which I have been endeavouring to enforce in these lectures; for, inasmuch as the production of heat is the direct result of normal tissue-activity, a process dependent on diminution or arrest of tissue-activity could not lead to increased thermogenesis. Fortunately, the experimental evidence on the subject is now clear and decided. Twenty years ago, we all thought that John Hunter's sagacious utterance on the subject—that a "local inflammation cannot raise the temperature of an inflamed part above the source of the circulation"—was mistaken; for, by the very remarkable observations of Mr. Simon in this country, and of the late Professor Otto Weber in Germany, it appeared to be shown that the temperature of the blood-stream returning from an inflamed part actually exceeded that of the heart. Notwithstanding the extraordinary care with which these observations were made, they have not been confirmed by those who have repeated them. It has been established by observations relating to all sorts of inflammations, and made at every stage of their progress, that the temperature of the inflamed part never exceeds that of the rectum. Here, as in respect of other matters, we find that the most complete experimental observations are those of Cohnheim, who has shown in the most striking way that the increased temperature of external organs, when inflamed, depends on the activity of the circulation. For this purpose, comparative measurements were made by him of the temperature of the fore-paw of a dog in a state of acute inflammation, and that of the opposite paw after division of the axillary plexus; the conditions compared being hyperæmia from vascular paralysis on the one side, from inflammation on the other. It was always found that the temperature of the paralysed paw was slightly warmer than the inflamed; the difference between them being least when the inflammation was in the initial stage, and consequently the circulation most active. On this subject, therefore, John Hunter turns out to be quite correct, both in fact and theory.

The other question that I suggested may be thus put. On the one hand, we know that the inevitable issue to which every acute inflammation tends is necrosis by arrest of the capillary circulation of the inflamed part; on the other, we observe that it often happens that regeneration of tissue follows so closely on the heels of this essentially destructive process, that we can hardly say where the one ends and the other begins. What is the relation between the processes of inflammation and repair in cases of this kind—as, for example, in simple fracture of the bone, when we see the physiological process of callus-formation preceded by a normal inflammation involving all the vascular tissues injured? The instance of bone, for the very reason that it serves well to illustrate the blending of inflammation with repair, is, of course, not suited for the investigation of the relation between them. For this purpose, I must ask your attention once more to the cornea, where both processes can be studied either together or separately, and under conditions which are so perfectly simple that no question can arise as to the significance of what is observed. When, in the manner described in my first lecture, the central part of the cornea of a rabbit is destroyed by the action of chloride of zinc, the immediate result is, as we then saw, that the tissue dies, and that its structural elements waste and disintegrate. We also saw that, outside of the necrotic area, these elements show themselves in an unaltered condition. But, in a cornea which is removed in an animal killed three or four days after the injury, it is seen that these marginal cornea-corpuscles have begun to extend their branching processes in the direction of the dead area; and, if this be compared with another cornea excised a few days later, appearances present themselves (in sections parallel to the surface) which indicate that, in their further growth, these processes are gradually pervading the whole area. In this way, a new cicatricial tissue is formed, which consists of the same elements as the tissue which it replaces, although it differs from it in the way these elements are arranged. Here there can be no question that the vital endowments of the injured part have nothing whatever to do with the new growth by which its destroyed structures are restored. The regeneration takes place by an exogenous growth from the margin, not interstitially. The cells which take part in it lie outside of and beyond the limit of injury, from the direct effects of which they enjoy complete immunity. As accounting for their behaviour, all that can be said is that, being in the neighbourhood of a defect or gap that requires filling up, they bring about that end by growing into it.

However clear may be the purpose of this regenerative growth of the cornea-cells, I do not think that we are in a position to explain the nature of the conditions which determine it; so that here, as in other cases, we must have recourse to that provisional kind of explanation which consists in placing the particular instance in rank with a number of others with which it corresponds so closely that, whatever the determining conditions may be, they are the same for all. The instances to which I refer are those in which a gap or defect in living tissue is filled, not as in the famous experiment by which Hunter discovered the process of animal grafting, but by a bit of some porous material, such as elder-pith, sponge, or catgut. Thanks to antiseptic surgery, it has of late years been shown that what we should at one time have called the "organisability" of such materials is almost unlimited. Probably everyone here is acquainted with the remarkable success which has been achieved by Dr. Hamilton of Edinburgh ("On Sponge-grafting", *Edinburgh Medical Journal*, November 1881) in what he calls sponge-grafting. Dr. Hamilton has found that, when a granulating wound is filled with purified sponge, the granulation-tissue grows into the interstices of the sponge in such a way that eventually the whole of it disappears, having been incorporated in the cicatrix. Again, if an excised cornea be introduced into the peritoneal cavity of a rabbit, under antiseptic precautions, it occasions no disturbance whatever. It soon becomes enclosed in a vascularised envelope, the capillaries of which are derived from those of the serous membrane to which it adheres, and the same thing happens if you substitute a bit of sponge or catgut. These last cases differ from that of the cornea, in the presence of vessels, as well as in the circumstance that the framework or tissue does not belong to the place it occupies; but all have the same relation, or rather antagonism, which exists between inflammation and new growth. The one condition which is essential to the institution of a reparative or regenerative process, is the existence of a solution of continuity. Whether the defect be occupied by sponge, by tissue derived from another part of the body, or by dead tissue of the same part, the result is the same—namely, that the dead becomes incorporated with—grafted into—the living, by the agency of the normal elements of the uninjured part.

There is one other question which I am desirous to bring before you in these lectures; and it will necessarily be the last. It is that of the influence of the nervous system on the inflammatory process. I have already placed before you, very shortly, the evidence which exists that, in the well known case of inflammation of the cornea after section of the fifth nerve, the origin of the process is not neuroparalytic. On similar grounds, it has been established that the bronchopneumonia, which inevitably follows section of both pneumogastric nerves, is also a traumatic inflammation due to the entrance of portions of food and other foreign bodies into the respiratory passages; and is, therefore, only an indirect consequence of the severance of the nerves.*

When these neuroparalytic phenomena were first known, they served, if not to suggest, at least to strengthen the belief that the action of nerves had a great deal to do with inflammation, either by virtue of a trophic influence exercised through them on the tissues, by the cerebrospinal centres, or by vaso-motor reflex action. Thus, the attempt has been made to show, but with signal failure, that pleurisy could be induced by extirpation of the third cervical and first dorsal ganglia of the sympathetic chain in the neck; that meningitis, in like manner, would result from destruction of the superior cervical ganglion.† With somewhat better success, Dr. Brown-Séquard (*Leçons sur les Nerfs Vasomoteurs*, Paris, 1872, page 44) made certain experiments for the purpose of ascertaining why, in the human subject, severe burns are so frequently followed by inflammatory lesions of the intestinal mucous membrane. What he found was, that such results could be produced in guinea-pigs by similar causes; and, further, that it was essential that the nervous connection between the injured limb and the spinal cord should be intact. He accordingly was led to regard the visceral lesions which occur in burns as examples of "reflex inflammation". We may accept the fact, but scarcely its explanation.

But the point to which I wish more especially to draw your attention is not that of the relation of the nervous system to the causation of certain inflammations, but the part which it may be supposed to play in its initial phenomena. The phenomena I mean are those of determination of blood, or affluxus, or, as Virchow calls it, surging of blood ("Blutwallung", *Handbuch der Speciellen Path.*, vol. i, p. 141) towards an irritated part, of which we have the most familiar example in the congestion of the conjunctiva, which promptly follows the introduction

* A good summary of what is known on this subject will be found in Professor S. Mayer's "Speciellen Nervenphysiologie", published in the second volume of the *Handbuch der Physiologie*. Leipzig. 1879.

† See on this subject Vulpian, *Leçons sur l'Appareil Vasomoteur*, vol. ii, 1875, pp. 570, 571, as to the source of fallacy in these experiments.

of a grain of dust between the eyelid and bulb. In many inflammations, this preliminary rush of blood along the dilated vessels is absent: witness the cases dwelt on in my first lecture, in which the inflammatory state comes into existence *d'emblée*, in consequence of exposure to heat or cold; or the case of mycotic inflammation of the cornea, in which the episcleral vessels do not become affected until the infective material has slowly found its way from the ulcerated surface to the limbus; or in the case of erysipelas, where redness and swelling invade the skin in company, without any antecedent active congestion; whence we conclude that, although determination of blood is a frequent precursor of inflammation, it is not a part of it; and we are confirmed in that opinion by the observation that the "inflammatory blush", as Hunter called it, presents itself as the sole response of the vessels to local irritation; of which fact no better illustration can be given than the famous instance in which he observed it day after day in a patient whose toe he had occasion to cauterise regularly. "After each application", he relates (*Treatise on the Blood and on Inflammation*, 1794, p. 158) "the surrounding parts put on a blush; and all the veins on the top of the foot, as well as up the leg, immediately began to swell, and became large and full."

No experiment can be better adapted to show the complete distinction between determination of blood and inflammatory hyperæmia than that described by Dr. Williams in the Gulstonian Lectures to which I have already referred. Hunter had shown by his experiment that it is possible for the inflammatory blush to subside, leaving no trace, or the injured part to be flooded with blood and then return to its original condition. But Hunter's attention was entirely fixed on the blood-vessels, to the action of which he attributed the whole process. For the purpose of separating Hunter's "incipient enlargement of the vessels upon the first excitement of inflammation", (*Treatise on the Blood, etc.*, p. 279) from the definitive changes which followed it, Dr. Williams most judiciously adopted this method of graduated irritation of the web of the frog's foot, which was at that time the only field of experimental observation. He found that a weak solution of capsicum applied to the web causes dilatation with acceleration of the movement of blood (hyperæmia with increase of motion) in arteries and capillaries; but if the solution were strengthened, or the application several times repeated, the quickening soon gave way to slowing and commencing stagnation. (See *Principles of Medicine*, third edition, pp. 241 and 263.) The effect of the weak excitation was transitory, and the observation could be repeated any number of times on the same web. The stronger solution produced permanent damage of the tissue, resulting in inflammatory congestion, exudation, and stasis. In the mammalian mesentery, the same effect may be produced in a similar way. The substitution of 1.5 per cent. solution of salt for the ordinary .75 per cent. solution which is used as an irrigating fluid, has the effect, as Dr. Thomas has shown,* of fluid at once hurrying on the blood-stream; and if this is done at a time when the mesentery has already undergone inflammatory slowing, and the colourless corpuscles are hugging the walls of the veins, these corpuscles at once resume their place in the axial current; so that, so far from the initial affluxus being itself an inflammatory phenomenon, we can, by inducing it, arrest an inflammatory process when it is in progress.

(To be continued.)

* Thomas, "Ueber Entzündliche Störung des Capillarkreislaufes bei Warmblütern." *Virchow's Archiv*, vol. 74, Sep. abdr., p. 27.

REMOVAL OF PLACENTA IN MISCARRIAGE.—Dr. Crummer gives the following instructions in the *Transactions of the Illinois State Medical Society*, 1881. 1. One index finger introduced into the womb while the organ is depressed well into the pelvis, and steadied by the other hand applied externally. In this way a moderately contracted os may be dilated, a sharp antelexion of the uterus straightened, and, using the finger as a hook, the uterus may commonly be thoroughly emptied. 2. With one or two fingers in the vagina for counter-pressure against the anterior surface of the womb, and the other hand making firm pressure over the fundus and posterior surface of the uterus, the contents of the womb may sometimes be pressed out. These procedures, though somewhat painful, do not require an anæsthetic. But, in a certain proportion of our cases, they do not succeed. Very often the detached after-birth can be just felt at the tip of the finger, or glides from it in any effort at extraction. We may then resort to: 3. The introduction of the hand into the vagina and one or more fingers into the uterus, and this requires an anæsthetic. 4. In some cases where the vagina is small, or an anæsthetic not desirable, I have succeeded admirably with Loomis' placenta-forceps in grasping and removing the offending substance.

CROONIAN LECTURES

ON THE

CLIMATE AND FEVERS OF INDIA.

Delivered before the Royal College of Physicians of London.

By SIR JOSEPH FAYRER, K.C.S.I., M.D., F.R.S.,
Physician to the Secretary of State for India in Council.

LECTURE II.—(Concluded.)

Pernicious Forms.—The conditions to which the term "pernicious" is applied occur as intensifications of any of the stages. The cold stage may be unduly prolonged and occupy the whole paroxysm, the patient either sinking, as in the collapse of cholera, or reaction taking place slowly. The hot stage may be intensified and prolonged, the patient becoming delirious, comatose, convulsed; stupor begins with the commencement of the paroxysm, and gradually deepens into complete coma and death, or the symptoms may gradually disappear as the period of the paroxysm passes away. The sweating stage may be very profuse and prolonged, the pulse sinks, and death may take place from exhaustion, or extreme depression, during which the patient is intelligent but hardly sensible of his own weakness, when any exertion or even the erect posture is attended with danger. These are the principal dangers with which I am acquainted. There are other conditions pointing to the cerebro-spinal centres and abdominal viscera, arising out of the general disturbance produced by the malaria rather than by its direct action. Pernicious symptoms sometimes come on suddenly with little warning, after one or two ordinary paroxysms, probably from the intensity of the poison in those who have been unusually debilitated. In the damp hot months in certain parts of India, the symptoms which indicate cerebral disturbance are most likely to occur.

Masked Malarial Fevers.—To certain conditions the term masked has been given: neuralgia with imperfectly developed fever, hot hands, aching pain extending along the course of the great nerve trunks in the limbs; gastralgia often intense, and various forms of disturbed innervation, functional derangement of the liver and other abdominal viscera, nervous irritability, dyspepsia, asthma, hæmaturia, bronchial irritation, insomnia, and symptoms pointing to the effects of malarial poison on the nervous system. The symptoms may be those of collapse, as in cholera, or apoplexy, epilepsy, cerebral effusion, hæmorrhage from stomach, bladder, bowel, or kidney; but the history and the circumstances under which the symptoms occur, indicate their true nature, and malarial origin. Malarial symptoms, are influenced by the state of the weather, and the natives think by the full or new moon. This subject has been discussed in the *Medical and Physical Transactions of Bombay*, by Mr. Murray and Dr. Peet. Morehead says a familiar fact for the hospital physician in India is to find several of the inmates in his wards affected by febrile disease on the same day, though all were free previously; that these days are coincident with the lunar changes; and that those who have suffered from malarious fever had recurrences on those days. But, as it was generally observed that there were atmospheric changes on those days, the fever was due to them, not to the moon. Such is probably the real explanation of the so-called solilunar influence, advocated by Dr. Balfour, who declared that the meridional periods, diurnal and nocturnal, were distinguished by remarkable changes of the weather, which were most remarkable at the lunar periods.

Malarial Cachexia.—A frequent result of exposure to malarial influences and of repeated attacks of periodic fever is anæmia, or even though there may have been no fever, often a profound state of cachexia, with which is associated structural changes in the abdominal viscera, and notably in the spleen. The sufferer has a puffy blanched face, pearly conjunctivæ and lips, short and hurried respiration, weak cardiac action, hæmic murmurs, and a feeble pulse, a tumid abdomen, not unfrequently dropsy, oedematous lungs and areolar tissue generally, wasted muscles, and a bronzed discoloured skin, with a large spleen extending sometimes as far as the iliac fossa (ague cake). Such is common enough in the notoriously malarial regions of India, where the whole population present more or less of this appearance, and where the physical degeneration is accompanied by an almost equally well-marked mental and physical torpor; depression of energy being characteristic signs of this state. I have known individuals return to this country too late to profit by the change. I have also seen a