THE GOULSTONIAN LECTURES

ON

THE ORIGIN AND RELATIONS OF NEW GROWTHS.

Delivered at the Royal College of Physicians.

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LECTURE I.

MR. PRESIDENT,—The title of the course of lectures which I shall have the honour of delivering before you is one so wide and comprehensive, that I must endeavour to define somewhat more precisely the limits of the subject.

The term tumour, which was, I suppose, the one first applied to the structures which I have called new growths, had once, it is needless to say, a very wide range of meaning, and even in modern times has been used with considerable laxity. With the ancients, for instance, before inflammation had been conceived of as an abstract process, the phlegmon or inflammatory swelling was put in the same category as what we should now call a cancer; nor was it then possible to separate from this class swellings produced by any cause whatever. So wide a conception would, of course, at the present day be practically useless, and is accepted by no one. But even in the most important work yet devoted to this subject, Virchow's great treatise on tumours, the corresponding German term is taken in a very comprehensive sense. Virchow includes in his work, for instance, all kinds of cysts, even hydrocele, as well as the products of tubercular and syphilitic diseases. Without any intention of fully discussing the proper definition of the word tumour or new growth, I still feel it necessary to mark out clearly the subject of the following lectures, and will therefore just say, by way of preliminary, that my remarks will be confined to those tumours which may be fairly described as new growths, omitting mere enlargements of parts already existing, and the products of inflammation, whether acute or chronic, and omitting also the consideration of syphilitic and tubercular products, as being more nearly allied to inflammation. What we include, then, are nearly what Virchow distinguishes as pseudo-plasmen or true growths (*Gewächse*).

The group thus limited includes all new formations, in the form of a more or less circumscribed mass, of substance resembling the simple tissues of the body, or immature stages of them; it includes also those productions known as cancers, and various growths nearly allied to these, known as sarcomatous tumours.

Among the simple tissue-tumours, I recognise fibrous (fibroma), mucous (myxoma), fatty (lipoma), cartilaginous (enchondroma), osseous (osteoma), vascular (angioma), muscular (myoma), nervous (neuroma), glandular (adenoma), and lymphatic (lymphoma and lymphangioma). Under cancers, I include epithelial cancer or epithelioma; and, under sarcomatous tumours, several forms which approximate to simple growths. Finally, there are combinations of the forms just mentioned. I shall not attempt to define the class thus made up, except by simple enumeration. The characters of the smaller groups are tolerably well marked, and no practical difficulty need arise in knowing what kind of objects it is intended to discuss.

The chief fact which all these structures have in common is the fact of growth or increase, and, moreover, of a growth which appears to be, in a certain sense, independent of that of the body, as if the tumour had some separate life of its own. So strongly did this impress the older observers, that for a long time tumours were regarded as something parasitic, or foreign to the organism.

Harvey has expressed this conception very distinctly. After showing that embryos, once fecundated, are inspired with a soul, or *anima vegetiva* of their own [and this may be taken to mean, in Harvey's philosophical language, what we should now call a separate life], "which," he says, "when they have received, they order themselves and grow, living at their own, not their parents' command". . . . "And in this manner," he goes on, "doe mushrooms and plants growing to trees live. We discover likewise in our own bodies, that cancers, fleshy and also phlegmatical tumours and such like swellings, are supplied and fed as it were with their own proper vegetative souls, while in the interim the live and genuine parts of the body do extenuate and wither, and that because these tumours do seduce all the aliment to themselves; and so defraud

the rest of the body of its fostering juice (as of its genius) wherefore they are called phagedanæ and lupi, devouring cankers and wolves." (*Anatomical Examinations concerning Generation*, p. 153. London, 1653.)

The idea of a separate life is of course now untenable, and no one can doubt that a tumour is essentially a part of the body; but, nevertheless, there are certain respects, both morphological and dynamical, in which tumours do separate themselves from the general unity of forces displayed in the organism. Dynamically or physiologically speaking, we may say that this departure consists in a preponderance of the vegetative, and an almost entire absence of the animal, life. No tumour or new growth exercises any specially animal functions. Their life is simply nutritive; and, if we may adopt the distinction of Mr. Herbert Spencer between the function of accumulation and that of expenditure of force, then we may say, though it seems a paradox, that tumours are like plants, in being almost wholly accumulators. This difference, also, is not without its bearings on morphology; for if expenditure or liberation of energy, which is the characteristic dynamical feature of animals, be scarcely exhibited in new growths, we may see in this fact partly the cause of their unrestrained increase in size. It has been shown by Mr. H. Spencer to be a general and almost self-evident law of organic nature, that the amount of growth depends upon the surplus of nutrition over expenditure. Growth will, then, the nutrition being equal, vary inversely as the amount of force liberated. When the expenditure is nothing, the whole of the nutrition will be applied to growth. If the expenditure of energy be very great, growth will be strictly limited.

A simple illustration may make this distinction plain. The antagonism between increase of bulk and the quantity of force evolved in different organisms is seen in the contrast between birds and mammals, or between birds and reptiles. The former, compelled by their aerial life to exert a relatively much greater amount of energy in motion, will have the less material remaining for nutrition; and the only members of the class which approach in bulk the larger mammalia and reptiles are those which, living on land, use far less energy in locomotion. Comparing birds and reptiles alone, as being the most nearly allied, we see another broad contrast in the greater amount of heat liberated in the small bodies of birds than in the comparatively bulky reptiles, as well as in the more rapid and varied motions of the former.

Applying these principles to the growth of tumours, we have, of course, to compare structures which are alike in all other respects except those points under consideration. For instance, we may contrast physiological and pathological productions of simple tissues. In the former case, the newly formed structure has what we call a function; in the latter, none. Function is, of course, not always associated with liberation of force. These are simply passive functions, like those of the fibrous tissues and the skeleton in preserving mechanical equilibrium, or that of the fatty subcutaneous tissue in preserving the equilibrium of temperature; in these cases, there is evidently no considerable liberation of energy. Again, the precise dynamical relations of the functions of the organs of assimilation and of those of secretion are still doubtful. But in the case of muscular tissue, and in some parts, at all events, of the nervous system, liberation of energy is inseparable from the functional activity of the organ. Hence, it is only from the latter class of tissues that our illustrations can be drawn.

To illustrate our present point, we may compare, for instance, the physiological growth of muscular tissue in the uterus, during pregnancy, with the pathological production of the same tissue in the form of tumours. In early stages, we know that the process of growth is essentially the same in both cases. There is, in both, a new production of muscular fibre-cells, and the histological development appears to be identical.* The production of new tissue in the simple physiological hypertrophy of the gravid uterus, is as abundant as that in many tumours; it must, also, be equally rapid; but it reaches a certain limit, and conforms to a certain type; while the tumour, on the other hand, has no very definite limit, and shows no conformity to rule in its shape. How are these differences to be explained? Certainly not by a difference in the amount of nutriment supplied. The pregnant uterus is a structure extremely rich in vessels, and most abundantly nourished; uterine tumours, on the other hand, contain so few vessels, that the existence of the latter has been even denied altogether. The chief point of contrast seems to be that the uterus, however large, is still capable of exercising normal functions, and there will thus always be a certain liberation of force, proportional to the pressure which the organ has to sustain, even independently of the immense efforts of parturition. The muscular tissue contained in a tumour, on the other hand, although also capable of liberation of energy by contraction (for spontaneous contraction has been observed in such tumours), does not, in fact, exercise

* The identity of the processes was indeed observed directly by Dr. Bristowe in the tumours of the pregnant uterus. (*Path. Trans.*, iv, 218.)

any force; its situation and relations make this impossible. Whatever nutriment, then, it receives, will all be applied to the accumulation of tissue—that is, to growth. The surplus of nutrition over expenditure will, in fact, be nearly the whole of the nutrition. What wonder, then, that such structures, once commenced, show such monstrous exaggeration of growth? Dr. Bristowe has remarked, that “such tumours not only do, but must, grow during pregnancy, and must, at least, attain a bulk, the ratio of which, to the former bulk, is that of the gravid to the unimpregnated uterus.” If our principle is correct, they must grow in an even higher ratio, since they lose nothing by functional activity.

An obvious test of the truth of this principle is the relative frequency of new growth in passive or actively functioning tissues respectively; and we do find, as a matter of fact, that they are incomparably more frequent in the former. Fatty tissues, bone tissues, and all the varieties of growth which originate in fibrous tissue, are instances of the connection between mechanical passivity and excessive growth. On the other hand, voluntary muscle, the dynamical tissue *κατ' ἐξοχήν*, never gives rise to tumours, or forms a part of any, except of certain perfectly abnormal mixed growths, which more nearly resemble an abortive foetal development. We have here, perhaps, the secret of the extraordinary rarity of tumours composed of striped muscle.

This argument might obviously be pressed too far. If taken without qualification, it would go to prove that there could be no limit to the growth of a tumour. In fact, we know, of course, that tumours do not unfrequently cease to grow, though their growth is much less clearly circumscribed than that of the normal parts of the body. They must, indeed, obey the general laws of limitation of organic growth, which laws are very clearly stated by Mr. Herbert Spencer somewhat as follows. “Growth,” he says, “is unlimited, or has a definite limit, according as the surplus of nutrition over expenditure does, or does not, progressively decrease.”

In the case of organisms, Mr. Spencer shows that there are certain relations which necessarily cause this surplus to decrease. That which is most applicable to the case of tumours is the following.

“Since, in similar bodies, the areas vary as the squares of the dimensions and the masses vary as the cubes, it follows that the absorbing surface will increase in a smaller ratio than the mass. If a growth like an organism increase, so that its dimensions are doubled, the absorbing surface will be only four times what it was, while the mass has become eight times as great. It follows, then, the ratio of nutriment absorbed to mass will become less and less, while, if there be any expenditure of force whatever in the mass, this will come, in the end, to more than balance the nutrition. The supply of nutrition over expenditure will at least become zero, and growth will be arrested.”

Now, in tumours, the absorbing surface is, of course, represented by the inner surface of the blood-vessels, and this would, of itself, be sufficient to show that the growth of tumours cannot be really unlimited. In special cases, too, particular causes, such as the condition of the vessels, the relation to other parts, will have their effect; but, notwithstanding all this, the broad distinction will remain that, while organs of the body reach only a definite size, and then remain stationary, the growth of tumours is limited by no rigid law; their growth being like the growth of a tree, rather than like the growth of an animal. In fact, if we may, for the moment, speak of a morbid growth as an organism, the following statement of the law of limitation, in Mr. Spencer's words, will be strictly true.

“In the same organism, the surplus of nutrition over expenditure is a variable quantity, and growth is unlimited, or has a definite limit, according as the surface does, or does not, progressively decrease. This proportion is exemplified, on the one hand, by the increasing growth of organisms that do not expend force, by the growth, slowly diminishing, but never completely ceasing, of organisms that expend comparatively little force, and by the definitely limited growth of organisms that expend much force. On the other hand, this law follows from a certain relative increase of expenditure that necessarily accompanies increase of bulk, and is, therefore, an indirect corollary from the persistence of force.”

The aspect of new growth just considered has perhaps been too much neglected, but greater importance will always attach to the morphological aspect, and that I now propose to consider.

For the formation of tumours or new growths, I have been able to arrive at no better definition than this: the addition to an organism, which is in its general outlines already completed, of new parts without any definite function. Such a process must be—in the case of highly organised animals, at all events—one extremely abnormal. To explain it all, we must have recourse to the method of a comparison, and endeavour to find out what better known processes it most resembles, and what, on comparing it with each of these successively, are the points of likeness and the points of contrast.

It appears that there are three processes much more commonly met with in living bodies with which the production of tumours may advantageously be compared. These are the formation of parts in the incomplete embryonic organism; the reproduction of parts worn out or lost in the complete organism; and, finally, the enlargement of parts already existing. Of these three processes—embryonic development, repair, and hypertrophy—each possesses some points of contact with the processes of which we are to speak; in fact, so gradual is the transition in some cases from each of them to tumour-formation, that it may be difficult to know what term we ought to apply. The transition from embryonic development to tumour-formation is seen, for instance, in the occurrence of congenital tumours. Sometimes, as in the peculiar congenital tumours from the sacral region, a continuous series may be traced from a comparatively simple cystic structure through teratoid forms, gradually increasing in complexity up to a complete twin foetus, or “pygodidymus.”

The transition from repair to tumour-formation is also quite gradual. It is seen, on the one hand, in such structures as granulations, which would be called new growths, had they a more permanent existence; and in such growths as cicatricial keloid of the skin, which, though ultimately tumours, start from a scar.

Finally, that there are numerous transitions from hypertrophy to tumour-formation is a fact so generally recognised, that it need hardly be insisted upon as a general principle, though certain special cases will afterwards be discussed. It seems, then, worth while to follow out the three lines of comparison here suggested, and to see how far the formation of tumours agrees with or differs from each of these processes. In making these comparisons, I shall, in the first place, confine myself chiefly to the consideration of tumours which resemble the simple tissues of the body, since the formation of each of these must of course be more nearly paralleled by physiological formations than the malignant heterologous growths, such as cancer and sarcoma; but it is not always possible to draw the line, and I hope to show in subsequent lectures that the same principles which apply to the one class of tumours apply also to the other.

Comparison of Tumour-Growth with Embryonic Growth.

The most striking features of embryonic growth may perhaps be set down as follows. There is, according to the great law of Von Baer, progress from the general to the special, with ever increasing differentiation of parts—so that it is, in fact, development or increase of structure, not merely growth or increase of size. The amount of growth is limited by some general law of the organism, and we can predict beforehand with tolerable certainty what size will be ultimately attained. The form of growth is also limited, or, so to speak, predetermined in the same way, so as to be susceptible of prediction in most cases, if we know the circumstances. These three features, which may be called the general laws—namely, progressive development, limitation of size and of form by some inherent but not apparent law—are true of the parts of organisms as well as of the whole. Minute investigation reveals part of the machinery by which these results are produced; viz., in the growth and multiplication of cells. The primordial cell divides and divides again, till the whole has become converted, by the process of segmentation, into a mass of nucleated cells. These embryonic cells become transformed into tissues by further division and proliferation—a process which may be termed histogenesis.

There are, then, two chief stages or periods: the first, cell-multiplication without differentiation; the second, differentiation with development. In the formation of limbs, the same laws generally prevail [as was first clearly laid down by John Goodsir]. Just as the germinal spot of the ovum is that from which the whole organism derives its origin, so each part, or even each limb, he supposed to have its subsidiary germinal spot or centre of nutrition. Though further observation has shown that this is not strictly true—at least of the higher animals—still each embryonic cell, as it multiplies, bears of course the same relation to its progeny as was borne to it by the germinal spot of the ovum.

The causes of differentiation, like those which regulate size and form, remain obscure. What we know is, that the embryonic cells arrange themselves into certain layers, from which the subsequent development of organs and tissues takes place.

The whole process of development, then, whether of organisms or of parts, may be summed up as being histogenesis by cell-proliferation and multiplication; the development controlled by certain obscure laws of size and form, and involving constant progression from the general to the special.

On comparing with this process the process of tumour-development, it is impossible to deny the close analogy of the early stages in both, and of the results up to a certain point. In both cases, cell-proliferation and multiplication are the starting-point of growth. Whether, in-

deed, a tumour starts from a single cell, like the ovum, or from a single germinal centre, as, according to Goodsir, do the limbs and other parts of the body, is uncertain, for the actual beginning of all tumours is concealed from us. When we are able to examine the process, we find germination taking place from several points, but it may, of course, have originated in the first place at one.

The analogy between these processes is, as is well known, the basis of the Cellular Pathology of Virchow. Confining ourselves to the subject of new growths, we find Virchow laying down the general principle that they all pass through a stage comparable to the undifferentiated cellular stage of the embryo. This is the stage of "indifferent cell-proliferation", in which all the elements are alike, whatever they may be destined ultimately to become. A mass of these indifferent corpuscles he supposes to have a latent possibility of differentiation and development like that of the cells of the embryo; so that of these elements, which appear quite like one another, some may become epithelium, some cartilage, some bone, and so on.

Indifferent cell-proliferation is an undoubted fact; we may see it at the margin of almost every growing tumour. Sometimes, considerable masses of a tumour are made up of this, while other portions are more specialised. Nor need we hesitate to allow that, as the earlier stages of all animals have a considerable resemblance in structure, so have the early stages of all tissues. For instance, the Malpighian layer, or rete mucosum of the skin, from which the epidermis is formed, has a structure as "indifferent" as that of granulations or connective hypertrophy, which give rise to vessels and fibrous tissue.

The difficulty is to allow as great a faculty of differentiation to the granulation material as to true embryonic tissue. Is there any distinct evidence that the former ever does give rise, by progressive differentiation, to several kinds of tissue, or that a new growth, composed of several kinds of elements, had its origin in a simple mass of indifferent corpuscles, formed when the organism was already complete? One line of specialisation can, doubtless, be often traced—are there several? Virchow has given a categorical answer to this question, and states positively that, in certain tumours, a part of the original elements become converted into connective tissue, another part into epithelium, till a complex structure is produced like that of an organ of the body, i.e., a pathological organ or an organoid tumour, which usually, he says, imitates a gland. Further, he describes a class of "teratoid" or monstrous tumours which represent, not an organ only, but a system of the body, and in which, for instance, there may be skin with both its connective tissue and its epidermis, its sweat-glands and hairs. Such a development is, as he says, not more difficult to conceive than that of simple tissue tumours or organoid tumours; for, "if there be, in fact, a stage in which there are indifferent elements capable of development in various directions, then it is just as conceivable that they should sometimes develop in one direction, another time in two, as a third time in five or six directions." (*Die Krankhaften Geschwülste*, i, 95.)

And, if these relations were as easy to see in reality as they are to conceive in thought, the case would be clear enough, and we should have no difficulty in recognising the precise analogy between embryonic development and new growth. But, differing with all respect from the great authority of Professor Virchow, we must say that the case is not so clear, for it is doubtful whether either the organoid or the teratoid tumours can be shown to originate in a stage of indifferent granulation-cells. By organoid tumours are chiefly to be understood adenoid or glandular tumours and papillomata, with some cysts. Now, glandular tumours appear to be, in almost every case, outgrowths of existing glands, the few exceptions being certain detached masses of glandular substance near a normal gland, which there is generally much reason to regard as congenital structures; so that, at least, no clear instance can be quoted where the histogenesis of such a tumour from indifferent cell-proliferation has actually been observed. (*Lücke, Geschwülste*, p. 281.) The same may be said of papillomata or their analogues, the polypi of mucous surfaces, which always appear to be either enlargements of pre-existing structures, or else composed of two tissues, namely, vessels and an epithelial covering, which are evidently of different origin, and not differentiated from a common basis. With regard to the only forms of cyst which can be called organoid, those, namely, which contain proliferating structures, these appear to be always either enlargements of pre-existing structures, or else it appears that their epithelial element is really of different origin from the other tissues which they contain.

Finally, the extremely rare structures described as teratoid tumours, in which, for instance, skin, hair, sweat-gland, teeth, or bone, are all found together, appear to be always instances of inclusion of part of the integument at an early period of foetal life, or else to be comparable to an imperfectly formed fetus. They are apparently always congenital, with the exception, perhaps, of some growths in the ovaries. When a growth of this kind, originally small, increases rapidly, and is found to

contain various tissues, some imperfectly formed and in various degrees of evolution, we cannot doubt that the process of tissue-formation has been actually going on; and, since a considerable proportion of such a tumour always consists of immature or indifferent tissue, it is reasonable to assume that histogenesis has gone on at the expense of this tissue. But in such a case the embryonic mass was formed before, not after, the completion of the organism; so that it must be regarded as part of the produce of the original conjugation by which the organism was produced.

Such growths are singularly suggestive of the process of budding and agamic reproduction in the lower animals, which are, as Quatrefages (*Metamorphoses of Man and Animals*, translated by Lawson, 1864, p. 238) has pointed out, essentially processes of growth. Waldeyer, indeed, goes so far as to speak of these growths in the ovary as a parthenogenetic development from an ovarian epithelial cell turned into an ovum-cell; and similar productions in the testis have been explained by the presence of ovarian elements, or part of the germinal epithelium in that gland. But tumours quite as complicated occur in distant parts of the body, as the mediastinum (Virchow, *Archiv*, vol. liii, p. 444; Lang, *ibid.*, p. 128).

Other forms of tumour remain to be spoken of, which might be supposed to bear the same interpretation; namely, mixed tumours, such as those composed of partly cartilage, partly fibrous tissue, or partly sarcoma. These undoubtedly pass through a stage of indifferent cell-formation, indifferent tissue being found passing by insensible gradations into each of these forms. Now, in these, all the tissues belong to what is termed the connective-tissue series, or, to use the expression of Virchow, are physiologically interchangeable. We know that one may, under certain circumstances, pass into the other; so that the plurality of tissue-forms need not be taken absolutely as showing plurality of lines of development, or at least the degree of difference is far less significant than in the cases which we have been considering.

One great class of tumours—the true cancers—remains to be considered. Here we find in general two types of elements—the stroma, which is a connective-tissue structure; and the cells, which are usually thought to have more or less an epithelial character. If both parts of the structure arise from an indifferent cell-formation, then of course there is a differentiation, or progress from the general to the special, quite comparable to that of embryonic development. Whether it is really so, will be discussed hereafter. At present, we may take it provisionally as not proved, and conclude that indifferent cell-formation does occur in the early stages of cancer, but that it is not certain whether that does or does not produce the epithelial elements.

From all this we must conclude that the process of tumour-formation is strictly analogous to that of embryonic development up to a certain point—namely, so far as both processes result in the formation of a mass of indifferent or similar cells, such as the mulberry-mass of the embryo, or the indifferent granulation-material of new growths. Beyond this, the parallel is less exact, and the progressive differentiation which is characteristic of embryonic development is less clearly traceable in tumours. The indifferent granulation-material, which is analogous to the undifferentiated embryonic structure, is capable of producing structures which vary within certain limits, such as the group of connective tissues, or, on the other hand, of producing epithelial elements; but it is uncertain whether the same group of cells can produce both.

One very striking coincidence may be noticed with regard to the point at which the resemblance ceases to be exact; viz., that the early stage of development of the ovum—that which is imitated by new growth—is possible, and perhaps even in some animals the rule, without impregnation. This amount of development is possible to elements derived from one organism alone, though conjugation with elements derived from another is necessary to establish the progressive differentiation which results in the development of a complex structure. We may, therefore, say that what amount of development an unimpregnated ovum is capable of, that, at least, is possible to new growths, which may imitate on the one hand the incomplete process of development of such ova in the higher animals, and on the other hand, in rare cases, make some approach to repeating the agamic reproduction of the lower animals.

Comparison of Tumour-Growth with Repair and Reproduction of Lost Parts and with Inflammation.

It is well known that the capacity for reproducing lost parts differs very greatly in the animal kingdom; and, while it is generally greater in the lower than the higher animals, the differences are not entirely to be so explained. The most general law which seems to have been arrived at is this, that the capability of repair is inversely as the amount of metamorphosis or change through which the animal has gone. Insects, for instance, have no power of restoring lost parts; batrachia have a great deal. In the mammalia, at all events, this power is extremely limited. An organ

once lost is lost irretrievably; and even the more specialised tissues, as muscle and ganglionic nervous matter, are usually replaced by other tissue, not actually restored. These very tissues, it is worth notice, rarely or never appear in new growths. New growth, taken as a whole, has, perhaps, greater possibilities than has the process which constitutes repair—giving rise to more various and more specialised products. On the other hand, the latter process is far more completely subject to the general law of evolution of the whole organism, for the parts reproduced always conform to the size and shape of the whole body; while it is, of course, the most remarkable feature of new growths, that they are so entirely unlimited in these respects. In other respects, the reproduction of lost limbs in some of the lower animals, has a decided analogy to the production of a tumour. Harry Goodsir (*Anatomical and Physiological Observations*, 1845) described, for instance, long ago, the reproduction of a claw in the crustacea, as starting from one nucleated cell, which multiplies and gives rise to other centres of growth. In fact, there is a true cell-proliferation.

With regard to the minute processes of repair, they differ from the corresponding processes in new growth very greatly, in the degree to which the vessels and the blood with its formed elements participate therein. The share taken by vascular changes in ordinary repair is known to be very great; so much so, that it has been the great question with surgeons, whether the healing of wounds is possible without inflammation. In new growth, vascular phenomena seem to play a subordinate part, though perhaps their importance has been underrated. At all events, in order to compare the one with the other, we must leave out of account the vascular changes; and then we find that the residue, or changes in the fixed tissues in repair, bear the closest analogy to new growth, being really, in the early stages, processes of germination and proliferation. These, of course, are also the tissue changes in early stages of inflammation, with which repair is so intimately connected. In describing one, we are, therefore, describing the other. Of course, the extent of these germinative changes is a matter of much controversy; and I am, therefore, glad to be able to show you the results of some direct observations.

As an instance, we may take the changes produced in an extremely simple structure, such as the omentum, by inflammation and by new growth respectively.

It is well known that mechanical injury, heat, and the action of various irritating substances, all give rise to the same series of changes called inflammatory. We may, then, take any one of these as a type of the rest. I have accordingly represented on the diagram the appearance of a human omentum inflamed in consequence of perforation of the bowel. The endothelial cells covering the fibrous trabeculae are seen in several places to give evidence of proliferation; that is to say, one sees divided cells, cells with divided nuclei, groups of cells showing by their shape that they have been formed under mutual pressure, and, therefore, probably from one original mass; and also what look like compound, or mother cells.

These are the evidences of tissue-germination, and agree with the observations of Stricker, Burdon Sanderson, and others, on the cornea. They also resemble the phenomena brought to light by the comprehensive researches of Dr. Klein on the serous cavities of animals in which he has found germinating endothelium. Now, in the early stages of three different new growths—namely, cancer, sarcoma, and tubercle—we see the same or similar proliferative changes, sometimes affecting the endothelium, sometimes the connective tissue. Without now dwelling on other peculiarities of these minute changes, it will be enough to have shown that in the early stages of all these growths there is actual germination of the tissues, and that the same is to be seen in inflammation. The appearances of inflammation in connective tissue are still more like those of certain stages of new growth. The diagram, for instance, representing indifferent cell-proliferation, might equally well stand for one of inflammation. At the same time, I must venture again to lay stress upon the immense preponderance, in the latter process, of phenomena connected with the vessels and blood-corpuscles, which are only subsidiary in the case of new growths. We know, moreover, that even the resemblances are only like the resemblance between all embryonic tissues, for instance; it is a resemblance involving great latent possibilities of difference.

Products of the Reparative Process.—If we pass to the more definite structures produced by the process of repair, we still see a considerable analogy between them and new growths. The repair of many tissues passes through a stage very fairly comparable to what we called the indifferent cell-proliferation of new growths. Granulations are tumours in everything but in permanence. It is unnecessary to describe their structure minutely. Essentially outgrowths of vessels, they possess a framework or stroma which, except in its extreme vascularity, is not unlike that of a lymphatic gland, and to which histologists have not

always done justice; and, beside, we have a large number of lymphoid corpuscles. The structure has been compared to that of a round-celled sarcoma, but in reality it is only the cells that are alike; the architecture of the growth is very different. It might rather be called, in the nomenclature of new growths, a highly vascular fibroma, with very numerous migratory cells. But, as we know, this condition is far from permanent. Granulations either die away or else they lose their abundance of lymphoid cells; the fibrous element increases; and they become organised, as it is said, into fibrous connective tissue and similar tissues. Do they also become organised into epidermis? We know that some epidermis commonly covers them; and, according to the more generally accepted view, this is produced by metamorphoses of some of the lymphoid or indifferent cells. Some authorities, again, regard the epidermis as of different origin; and the question is so undecided, that we must hesitate to pronounce an opinion. The only point on which we must insist is that, both positively and negatively, these results agree perfectly with what we said just now about the indifferent cell-proliferation. The question of the origin of all epithelium produced for purposes of repair is one which I prefer to consider in the next lecture.

So far, then, as we are able to compare the phenomena of repair and inflammation with those of new growth, there are important analogies; but a large part of the phenomena of the two former processes—those, namely, connected with the vessels, exudation and cell-migration—have not, so far as is yet known, their parallel in the development of tumours, except as simply subsidiary to the germinative changes.

[To be continued.]

LETTSONIAN LECTURES ON SYPHILIS AS A CAUSE OF DISEASE OF THE NERVOUS SYSTEM.

Delivered before the Medical Society of London.

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LECTURE III.—Concluded.

Syphilitic Disease of the Cerebral Arteries.—Varied and important as are the effects of syphilitic disease in the membranes and substance of the cerebrum, not less so are the results of syphilitic disease of the cerebral arteries. Here, again, as in every part of my subject, I have to acknowledge my indebtedness to Dr. Hughlings Jackson, who has led the way in this as in many other investigations, and has repeatedly insisted on the importance of recognising the effects of syphilitic disease of the arteries. The arteries of the brain in syphilis are frequently attacked by inflammation, usually beginning in the outer coat. This may lead to thrombosis, which cuts off the supply of blood, and produces the result now known to follow this event. The effects are first an accumulation and stagnation of blood in the capillaries in the area of distribution of the vessel blocked, and, unless collateral circulation can be established, there will subsequently be softening. The symptoms will depend upon the part fed by the artery which is obstructed. I am disposed to think they are more varied than those produced by embolism, since a fragment carried from the valves of the heart, or from the aorta, appears to find its way into certain vessels (notably the left Sylvian artery) in preference to others, while syphilitic thrombosis may occur anywhere. Identical situations, the effects of thrombosis and embolism would, of course, be identical.

Syphilitic thrombosis must be of very frequent occurrence, judging from my own experience and from the number of cases collected by Zambaco, Gros, and Lancereaux, but set down as examples of inflammatory softening.

CASE 1. *Left Hemiplegia, affecting chiefly Face and Upper Extremity; Convulsive Attack followed by Mania; Peculiar Loss of Intelligent Use of Hands, without Loss of Power; Syphilitic Disease of Arteries; Thrombosis of Right Middle Cerebral; Softening of Convolutions near the end of Fissure of Sylvius, etc.*—Emma C., aged 30, dressmaker, was admitted into St. Mary's Hospital, under my care, on March 28th, 1873, suffering from partial left hemiplegia. She had been married four years, and, during that time, had had four miscarriages before the completion of the sixth month of pregnancy. Her husband was found to be suffering from ulcers on the tongue and plantar psoriasis from syphilis contracted eighteen months before marriage. Her health had not been affected till two days before her admission, when she suddenly lost the use of the left arm. There was first twitching in the fingers for about