THE GOULSTONIAN LECTURES ON THE ORIGIN AND RELATIONS OF NEW GROWTHS.

Delivered at the Royal College of Physicians.

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LECTURE I.—*Concluded.*

BEFORE leaving the subject of hypertrophy, it will be desirable to inquire what are the minute changes by which the increase of parts is effected, and whether these are comparable to those which are concerned in embryonic development, and in the production of tumours. Enlargement of organs appears to be partly effected by increase in size of the elementary parts, and partly by multiplication of these parts. The latter, or hyperplasia, is no doubt the more important process when the overgrowth is considerable.

It is a little difficult to get direct evidence of the minute changes; but in one of the commonest instances, hyperplasia of connective tissue, or fibrous induration, it is quite evident that the first step is the multiplication of nuclei; and the proliferation of connective tissue thus resulting is an important factor in many diseases.

In order to exhibit a very similar process in another part of the body, I will recur to the point which was touched upon just now, the structure of the omentum. The human omentum is a structure which undergoes considerable, though very gradual, changes as life goes on. As is well known, we comparatively rarely find, in elderly persons, an omentum as thin and pellucid as that of children. It becomes thicker, shorter, and often adherent to neighbouring parts, while adhesions are also formed between the parts of the membrane itself. When minutely examined, it is found that these changes are twofold. On the one hand, the amount of homogeneous intercellular substance contained in this membrane in early life becomes diminished, the fibrous element increases, and fibrous outgrowths are formed which effect adhesions and contractions of distant parts. It therefore becomes completely fenestrated as life advances, while, at the same time, the fibrous bundles are actually stronger and thicker. Minute examination reveals, even in perfectly normal structures, some of the ultimate changes connected with these transformations. We see what I have represented in the diagram (Fig. 1). Here may be noticed a comparatively large amount

Fig. 1.—Apparently healthy Human Omentum, shewing elongated connective-tissue cells, and masses of germinating endothelium; groups of three, four, or more nuclei, surrounded by some protoplasm. Magnified about 250 diameters.

of intercellular substance, a few connective tissue corpuscles, and besides, many cells and groups of cells attached to the outside of the fibrous bundles. These represent the endothelium or serous epithelium of the surface, but of course only in part. The conditions under which these structures are examined in the human body prevent us from getting these structures, so liable to decay, in a perfect

state, and from applying the most satisfactory process for their demonstration, viz., nitrate of silver, since this only acts properly on quite fresh tissues. But what can be seen is enough to show in the normal structure phenomena of germination quite comparable to those involved in the processes of inflammation, tubercle, and new growth. Dr. Klein has shown the same thing much more completely in the serous membranes of animals, and regards the process as one strictly normal.

Compare with this the appearances shown in the diagram (Fig. 2) representing the early stage in a minute secondary sarcomatous growth

Fig. 2.—Portion of Human Omentum, shewing one larger and two smaller sarcomatous tumours in an early stage. Magnified about 80 diameters.

of the omentum of a child. It was a case in which the rupture of a cystic sarcoma into the peritoneum set up a large number of small secondary growths, which appeared superficial and were easily detached. In Fig. 3, one of these is shown more highly magnified, and is seen to

Fig. 3.—Portion of Fig. 2 more highly magnified, shewing a minute sarcomatous tumour arising wholly by multiplication of small cells. Magnified 250 diameters.

be made up merely of a mass of simple elements, cells, or nuclei. Other parts of the same preparation gave more distinct evidence of germination in the elements, connective tissue or endothelial, of the part.

I conclude, then, that a hyperplastic process is one of the chief factors in hypertrophy, in the embryonic development, in repair and inflammation, as it is in the growth of tumours. It would also appear that the element common to all these processes is one which is also a normal one in certain parts at least of the human body, and connected with the chronic processes by which certain fundamental changes are effected in it.

New growth, then, is distinguished from the other processes just referred to—embryonic development, repair, inflammation, and hypertrophy—not by its minute characters, but by what may be called figuratively its direction and end, or by its relation to the rest of the organism; and the physiological factor which is common to all these processes, far from being strange or alien to the soil, is probably even a part of the normal life of the body.

LECTURE II.—Abstract.*

MR. PRESIDENT,—The application of the laws of growth, which were considered in the last lecture, is most obvious in the case of the simple tissue-tumours; in which new growth is obviously a phase of the continuous production of homogeneous tissue. We now reach the point at which we have to consider how far these principles apply to tumours not like normal tissues. Such tumours have been called heterologous, a term referring to structure, or malignant, referring to properties. It is with the former term only that we are now concerned.

The tumours, unlike simple tissues, form two great divisions, the sarcomata and cancers. Both of these are heterologous, but in somewhat different senses.

The sarcomata are essentially embryonic, representing early stages of tissue-formation; and parts of them are not unfrequently found forming a transition to simple tissues, but only to those of the connective tissue group. All varieties of sarcoma arise from some tissue of this group; and hence, though they may be called heterologous, they are so only in a limited degree, since they arise from tissue which, though not identical with their own, represents another phase of the same development. Hence they have been included by Waldeyer, with tumours of the connective tissue class, in one group, the desmoid tumours.

With regard to cancers, the case is somewhat different. They are even more unlike the tissues from which they spring, being, in fact, strictly speaking, unlike anything in the body. Nor can it be said that they are more like embryonic tissue. The only normal structure to which they bear any resemblance being that of glands; and here the resemblance is only partial, the cells being something like epithelial or gland-cells, but the arrangement entirely different. It is an undoubted fact that the majority of such tumours arise in or near glands, or near epithelial surfaces. Hence, some suppose that they grow entirely from such parts, and that their elements are derived from epithelium exclusively. Directly opposed to this is the theory of Virchow, who holds that these cells are not derived from the epithelium, but produced *in loco* from the connective tissue. If the former view be correct, they can hardly be called, strictly speaking, heterologous; but on Virchow's view they are undoubtedly so. The question is important as involving the problem whether there really is or not such a thing as heterologous growth. Virchow's view implies that there is in the body a tissue having a certain embryonic character, and still susceptible of growth and differentiation. It also involves a certain opposition between specialisation and reproductiveness. The opposite theory, with which the name of Waldeyer is now associated, but which was originally suggested by Remak, rests much upon embryology. Remak was led, in his embryological researches, to distinguish in the fowl's embryo, at a certain stage of development, three layers, to which he gave the names of the corneous, the motor-germinative, and the intestino-glandular, respectively. This distinction has been generally accepted; and Huxley has applied the simpler names of epiblast, mesoblast, and hypoblast. From the upper layer are developed, with other parts, the epidermis and its glands; from the lower, the digestive and respiratory mucous surfaces with their glands; and from the middle layer, many other parts, including the connective tissue. There is thus a certain antithesis between the middle layer and the other two. Remak supposed that this distinction was maintained, even in the adult organism; and that elements pertaining to one layer could never be derived from the tissues developed out of the others. The chief criterion would be the production of epithelium; and thus the motto of this school might be the thesis, *omne epithelium ex epithelio*. The evidence for this proposition comes chiefly under two heads; 1. The normal regeneration of epithelium; 2. The origin of morbid growths containing epithelial or quasi-epithelial elements.

Before discussing these lines of evidence, it was pointed out that there is a certain antithesis between the tissues of the different layers in the morbid products other than new growths to which they give rise, and in the diseases to which they are subject. Fibrin seems to be, notwithstanding some apparent exceptions, exclusively produced by tissues of the middle layer; the tissues of the other layers being subject chiefly to catarrhal inflammations.

It is quite clear that epithelial surfaces do not give rise to a new growth of vessels or connective tissue; this is illustrated by the surgical rule, that wounds of the intestine unite not by the mucous, but by the serous surfaces; the latter belonging to tissues of the middle layers.

The question of the origin of epithelium, produced for the purposes of repair, has been much discussed of late years. Surgeons are not yet agreed whether the epidermis which forms on a granulating wound is produced from the granulations or only from the pre-existing epithelium

at the edges. The appearances, seen in sections through granulations, are very ambiguous. Of late years, much importance has been attached to the evidence derived from the process of skin-grafting. In this operation, the transplantation of a portion of skin or epidermis alone to a granulating surface, causes an abundant production of epidermis, which it has been supposed grows only from the graft. The phenomena of the transplantation of a piece of negro's skin to the surface of a white body, seem to show that some multiplication of the graft must take place, since a black patch is formed, much larger than the original piece transplanted. But of all the observers who have examined the question microscopically, one only, Jacenko, has brought any histological evidence to show actual germination of the elements of the graft. Others have referred the origin of the new epidermis either wholly or chiefly to the granulations, stimulated by the presence of the foreign epidermis. Moreover, very similar results have been obtained by the transplantation of periosteum, muscle, or even by adding blister fluid to the granulations. These results cannot, then, be quoted as evidence for the production of all epithelium from epithelium.

Direct observations of the growth of epithelium have been of late years numerous but conflicting; and the subject cannot be regarded as being by any means in a settled state. The phenomena of the repair and regeneration of epithelium do not, then, certainly confirm the law of Remak. Evidence respecting the same law derived from the growth of tumours, especially cancer, will form the subject of the next lecture.

ON HYPEREXCITABILITY AND PARESIS.

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THE conditions of nerve-tissue giving rise to functional disorder are essentially two, viz., hyperexcitability and paresis. The first may be defined as an undue readiness in the tissue-elements to assume the active state on very slight provocation, perhaps, even, without any, except what may be afforded by the circulating blood. The second is an apparently opposite state, the nerve-tissue being less excitable than normally. Feebleness and deficiency of vital action is a necessary part of paresis, but not of hyperexcitability, though it is present in the great majority of instances.

These morbid states may exist in either of the three great departments of the nervous system—the intellectual, sensory, or motor. They may be of various grades, and may occur combined in various proportions. Thus there are produced a multitude of disorders, which we commonly meet with. It would be highly desirable if microscopical or chemical scrutiny could disclose to us the ultimate changes in the nerve-cells and fibres on which the derangement depends, or if it could be shown what alterations (if any) in the circulation, or in the interstitial fluid—as the subarachnoid—coincide constantly with the two states above named. It must be considered, however, extremely doubtful whether it can ever be possible to bring the nerve-elements under the lenses of our microscopes in the same state as when they were actual components of the living organism, or whether chemical analysis will ever be so discriminating as to show a difference in composition between healthy nerve-cells and those which have been hyperexcitable or paretic. And supposing it to be possible, and to be done, it does not at all follow that we should gain thereby any more control over these morbid states than we have at present. It is not our knowledge of the pathology of gout that has given us our best remedies against it. The most hopeful way of attaining to a more complete and more useful knowledge of the morbid states in question seems to be, to study the circumstances which affect their development.

Before commencing, we may remark that both are disorders, deteriorations of the healthy state. This is a truism; yet the point needs to be noted, lest any of the various manifestations of hyperexcitability, under the shelter of the term “increased action”, should be imagined by any to imply a real increase of vital energy.

In studying the nature of hyperexcitability and paresis, we may first remark that the amount of blood-flow to the nerve-centres is certainly an influential cause. Brown-Séquard regards hyperæsthesia as associated almost always with increased temperature, which is itself dependent on hyperæmia. At pages 87 and 88 of my work on *Functional Nerve-Disorders*, I have cited instances where active hyperæmia of the head produced delirium. On the other hand, we know that deprivation of blood, as in syncope, produces a cerebral paresis, which continues until the flow of blood is restored. A middle-aged friend of mine used for years to suffer from indigestion after a late dinner. He had acid-rising and heart-burn, with very great heat and flushing of head and restlessness; was obliged to apply wet cloths to cool his bald head; and was

* As these lectures will be published in a separate form by Messrs. Smith and Elder, they will only be given in abstract.