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.

unable to apply himself to anything. Here was hyperexcitability from increased blood-flow. On the other hand, Gooch tells us how he himself, an anæmic sufferer, knew well what it was to lay down his head and doze away half the day. Here was paresis from deficient blood-flow. The temporary hemiplegia produced by ligature of the opposite carotid is another and more striking example. The amount of blood coursing through the encephalon is therefore a factor of these two states: if excessive, it causes hyperexcitability; if deficient, paresis. This has, therefore, always to be taken into account. But it is also certain that the blood-supply is not the only condition to be considered; *that the state of the nerve-tissue is also very influential on the result.* I cite the following cases in proof. A patient of my own, aged 63, a wheelwright, had copious hæmatemesis, which deprived him at the time of sight, but not of consciousness. Six days afterwards, having been kept on low diet in the interval, delirium set in, and continued more or less for eleven days, then yielded to bromide of potassium. The diet was materially improved on the third day of the delirium, and the three ounces of brandy he was taking before *per diem* were increased to six ounces. He sank eighteen days after admission. A small ulcer was found in the lesser curvatures. The brain was very pale, rather wet, otherwise healthy. Here the spasmia produced cerebral hyperexcitability, and not paresis; this is no uncommon result. On the other hand, in the *American Journal of Medical Science*, 1870, i, p. 280, there is recorded the case of a young lady, aged 23, very intelligent, who was attacked with hæmatemesis after a hearty meal. She lost 94 oz. of blood in fourteen days, and gradually sank and died twenty-four days after the first attack. A punched out ulcer was found in the stomach. She exhibited remarkable fortitude during her illness, and her mind remained unclouded to the last. Here the anæmia did not disturb the cerebral functions. I have cited an analogous instance in my Lumeian Lectures, where a prodigious accumulation of *ascarides lumbricoides* in the small intestine of a girl, aged 11, produced almost complete extinction of the pulse, and at last death by asthenia. Yet the intellectual and motor powers were apparently intact. In cases of choleraic collapse, the same has often been observed, although the circulation in the encephalon must have been extremely reduced. I had lately a hospital patient who, while moribund and pulseless from peritonitis, was perfectly conscious, and could move all his limbs. His brain must have performed its functions with a very defective supply of blood. On the other hand, we often meet with patients suffering from overwork, whose brains are well supplied with blood, but are yet quite incapable of even moderate exertion. The conclusion to which these and similar cases lead is, that the influence of blood-supply is not so important as that of the vital state of the nerve-tissue, since a defective blood-flow may give rise to hyperexcitability and not paresis, or may not disorder the working of the nerve-centres at all. In fact, in a great many instances, the vital condition of the nerve-centres takes the initiative, and the amount of blood-flow varies accordingly. In common sleep, the brain is pale; but this is surely not because the arteries are primarily contracted, but because the exhausted tissue no longer attracts the blood to itself. During sleep, the brain is simply in the same state as regards blood-flow that all organs are in during their time of repose. When the stomach is empty, its mucous membrane is pale, and contains but little blood. Dr. Maudsley writes, with reference to the point above stated—"The truth is, that the first step in insanity often is, as it is in inflammation, a direct change in the individual elements of tissue, the change in the blood-vessels being secondary." He cites the case of strychnia-poisoning as showing that, with great excitement of nerve-cells, there may be no morbid appearances, and that, when there are any, they are congestion of the spinal cord, aneurismal dilatation of the capillaries, and perhaps small effusions of blood into the grey matter. "The congestion is plainly a secondary result of the intense morbid activity of the directly poisoned nervous element." He believes the very same occurs in attacks of transitory mania, where the face is flushed during the attack, the head is hot, and there is plainly an active determination of blood to the brain. I have taken the same view in commenting on a case of psychical intoxication recorded by Dr. Crichton Browne (see *Functional Nerve-Disorders*, p. 160). Of these two factors, then, of hyperexcitability and paresis, the amount of blood-flow and the vital condition of the tissue, the latter seems to me the more important.

The next point for notice is *the efficacy of states of debility in generating the two disorders in question.* I cite, as instances, overwork, hyperlactation, rickets, the collapse succeeding acute diseases, anæmia, and influenza. *Overwork* often produces insomnia, as in a case recorded by Dr. Hammond, where the patient had not slept a particle for six nights. He committed no excesses, except in the way of mental strain. Moderate brain-work, on the other hand, which causes no excessive fatigue, decidedly tends to induce sleep, though not so much as muscular work in fresh air. Even this, however, if excessive, is apt to cause insomnia.

A person may easily be too fatigued to sleep. It is, therefore, certain that this cause of exhaustion produces hyperexcitability. Dr. Farquharson records an interesting case, in a lad, aged 16, where undue mental and bodily exertion so seriously enfeebled the brain that, after the more urgent symptoms had subsided, the patient was long unable to make any approach to a resumption of head-work. A patient of my own so weakened his brain by hard mental work, that he could not read more than three or four minutes at a time, nor more than fifteen minutes in the twenty-four hours. Such cases of paresis are not rare.

With regard to *hyperlactation*, Dr. Tilt says that he knows no condition "that so speedily drains the ganglionic system of all energy as nursing in some women, even when they can take abundance of food and are surrounded by every comfort. The overpowering debility soon brings on extreme nervousness, and a state of despondency leading up to insanity." Dr. Ashwell mentions headache, insanity, amaurosis, chorea, and even epilepsy, as results of this cause. A patient was lately under my care, who had succumbed, after ten confinements, in the attempt to nurse her last child. She found she was too weak. She did not seem, however, to have suffered from want of food, and her pulse was good and steady. Her nerve-disorders comprehended smart hysterical fits, great nervousness, inability to sleep without sedatives, a feeling of heavy weight on the head, and of excitement, as if she could not refrain from running away, besides a dreadful burning sensation referred either to the abdomen or the limbs, and some vomiting of food. The ward-sister described her mental state as "never satisfied, never contented, a most miserable being", in fact, a melancholic. Under treatment, she improved. Hyperexcitability and paresis are well-marked results in cases of this kind. *Rickets* affords a remarkable instance of the concurrence of hyperæsthesia—sensory hyperexcitability—with a state of marked debility. The child sits or lies unnaturally still, for all movement is painful, and dreads to be touched or handled by those whose caresses used to delight it. It is impossible not to regard this striking derangement of sensibility as the result of the nervous system being involved in the general cachexia.

The *delirium of collapse, succeeding acute diseases*, so well described by Dr. H. Weber, is a very remarkable instance of the generation of hyperexcitability by general exhaustion. This is surely a very instructive occurrence, as it is the apparent contrary of what one would *à priori* have expected, and of what often actually occurs—viz., a condition of paresis. Dr. Buchanan says that, if the head-symptoms in typhus have been prominent, and yet the patient recover, a childishness of intellect is often left for a few weeks. Loss of memory of languages that had been acquired has also occurred under like circumstances. These are evidently pareses.

The influence of anæmia in producing hyperexcitability and paresis has already been illustrated, but I may add two more examples. A military man, who had been loved and esteemed by all, and had an excellent wife, got white flux, and in consequence his temper utterly changed, became infernal, so that his wife used to apprehend personal violence. (Sir R. Martin.) I have recorded (*Functional Nerve-Disorders*, p. 75) a case of extreme anæmia from hæmorrhoidal losses, where the patient for thirty-six hours or more lapsed into a state of rather active delirium, being quite unconscious, but very restless, and struggling a good deal. Under the use of opium he recovered from this state, and regained health completely when the loss of blood was finally arrested. A female, aged 43, marked rather severely by long-past syphilis, extremely anæmic, is now under my care. She suffers from great hyperæsthesia of the legs and feet.

The prostrating effects of influenza are notorious, and one may often observe instances of paresis produced by it. Hyperexcitability is less frequent; but Graves refers to patients who became, after five or six days, excessively nervous, lost all sleep, had continual subsultus and tremors, and talked very incoherently, particularly at night.

I may finally allude to senile and mercurial tremor, and to many instances of paralysis agitans, as affording marked instances of motor hyperexcitability induced by conditions which gravely impair vital energy.

Another important point for notice is, the fact *that hyperexcitability and paresis can be generated by remote irritation.* Brown-Séquard has long held the opinion that many neuroses are produced by a peculiar kind of irritation starting from almost any centripetal part of the nervous system. The reflex paralyses of the same observer are produced quite in the same way. Here is another proof of the great similarity of the two morbid states. The irritation, it is important to observe, may be felt or unfelt, *i.e.*, may not declare itself by any sensory warning. Taking as an example the occurrence of epilepsy from some cause of remote irritation, the idea commonly entertained is, I suppose, that the diseased bone, syphilitic deposit, intestinal worms, etc., provoke the convulsive paroxysm directly, just as when a muscle is made to contract

by pinching its nerve. But there is more in the matter than this, I feel convinced, at least in many instances. In Mr. L. Holden's singular case of anomalous affection of the nervous system in a boy, aged 13, the tetanic seizures were brought on, not only by pressing his "bump", but any spot over the ten upper dorsal vertebrae; moreover, occasionally the "bump" lost, for a time, its peculiar power of producing the phenomena, though this seems to have persisted in the spinal integument. The same, or very similar, effects seem to have been produced by raising him into the upright posture. Again, the periodic quasi-maniacal daily paroxysms occurred without any provocative stimulation. The whole series of nerve-troubles seem to have depended mainly on the bump, since they disappeared as soon as the tumour was removed, and had not recurred four years later, when the last report was made. The only view I can take of such a case as this is, that the terminal extremities of the nerves in the bump, being organised in some peculiar way—say, having their axis-cylinders exposed—kept up a constant state of hyperexcitability or tension in the nervous centres, which was ever ready to display itself demonstratively on slight provocation, or even without any. This peculiar organ of excitement being removed, the nerve-centres reverted to their ordinary condition. A case which I have recorded in *Functional Nerve-Disorders*, p. 570, presented some resemblance to Mr. Holden's. The occurrence of physiological hyperexcitability in the male frog at the copulating season is well known, and is worth referring to in connection with such cases as the foregoing. The thumb of each hand becomes covered with large papillae, and, so long as these are present, the animal is enabled to grasp the abdomen of his mate distended with ova without any exertion, apparently, of volition, or any fatigue, even for weeks. If, however, the papillae be shaved off, the power of grasping in this remarkable way is lost. (Todd and Bowman's *Physiology*, vol. i, p. 315.) They regard the cord of the frog, or, rather, that segment of it with which the nerves of the anterior extremities are connected, as being, during this period, in a state "of exalted polarity".

[To be continued.]

A CONTRIBUTION TO THE PATHOLOGY OF ALBUMINUS EXPECTORATIONIS AFTER THORACENTESIS.

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DURING last summer, a lively discussion took place in Paris on the causes of albuminous expectoration after thoracentesis for pleuritic effusion. A very complete analysis was published in this JOURNAL during October last, reviewing not only M. Terrillon's thesis, which started the discussion, but also the various hypotheses that were advanced in explanation. They were four in number: 1. Perforation of the lung by the trocar (MM. Woillez and Marrotte); 2. Spontaneous rupture of air-vesicles after destruction of pulmonary epithelium (Férol); 3. Resorption of the residual liquid from the pleura after puncture; 4. Transudation of the sero-albuminous liquid through the alveolar walls by means of rapid pulmonary congestion and oedema (Héraud, Moutard-Martin, Béhier, Terrillon, etc.). The reviewer strongly expressed his adhesion to this last hypothesis, which I also believe to be the true one. Neither of the authors named has, however, pushed his theory to its consequences, so as to indicate the mechanism by which the characteristic expectoration may be presumed to be secreted.

Before contributing my quota to this task, I may say a word regarding a fifth hypothesis, which has been suggested by Professor George Johnson (BRITISH MEDICAL JOURNAL, Oct. 25, 1873). "While the lung is compressed by a copious liquid effusion into the pleura, it is probable—nay, it is certain—that, in consequence of the more or less complete blood-stasis within the compressed lung, coagula will form in the minute pulmonary vessels, and especially within the pulmonary veins." After thoracentesis, "it is obvious that the obstruction of the pulmonary veins by coagula would cause a backward passive congestion of the capillaries, and a consequent serous transudation into the air-cells and bronchi." The objections that tell against this view appear to me as follows. 1. Albuminous expectoration has generally been confined to those instances where the amount of pleuritic effusion has been greatest, and the lung consequently most crushed and anemic. 2. Thoracentesis has been performed four times on the same subject, and each time albuminous expectoration has followed (Boule's case, Béhier's lecture, *Union Médicale*, 1875). 3. In the four fatal cases* recorded, no mention is made of coagulation in the pulmonary vessels. The lung was in each

instance choked from top to bottom with the characteristic fluid, so that the coagula would require to be extremely numerous. 4. The phenomenon is itself a very transient one, seldom lasting beyond twenty-four hours, although in that time many pints of fluid may be expectorated. How are the coagula assumed to be subsequently disposed of?

Reverting to the hypothesis of rapid pulmonary congestion and oedema: the authors who uphold this have assumed that it is brought about by the intervention of the pneumogastric nerves, but they fail to inform us by what links of the chain the result is arrived at.

The effects of section of the vagi on the pulmonary circulation have afforded very variable results in the hands of different observers. To obtain any at all, both nerves must be divided. Legallois (*Expériences sur le Principe de la Vie*, 1812), whose experiments were chiefly performed on young rabbits, found section of the pneumogastric in the neck to be almost constantly followed by engorgement of the lung. De Blainville and Provençal (Claude Bernard, *Système Nerveux*, vol. ii, p. 353), on the other hand, missed all trace of pulmonary change. Claude Bernard (*ibid.*, p. 354) admits that death is not necessarily the result of asphyxia at all. He regards the pulmonary lesion, when present, as primarily of traumatic origin, and as induced by the difficulties that arise in the mechanical act of respiration. "The movements gain in amplitude what they lose in frequency; they tend to introduce the same amount of air into the lung." An animal breathing from a bell-jar takes in a notably larger amount of air at each breath after its vagi have been divided than before, and a traumatic emphysema rapidly results (*ibid.*, p. 367).

Dr. John Reid (*Experimental Investigations into the Functions of the Eighth Pair of Nerves*) admits the great frequency of pulmonary congestion and the effusion of frothy serum after section of the vagi; but he has also repeatedly known both to be absent. "The effusion of frothy serum into the bronchial tubes is not a necessary consequence of division of the vagi, even when the lungs were found loaded with blood, and when the respiration before death was very laboured." "I have also satisfied myself that this frothy fluid is not mucus, but is the frothy serum so frequently found in cases where the circulation through the lungs has been impeded for some time before death" (p. 202). He believes that all the morbid changes observed in the lungs may be traced to the diminished frequency of the respiratory muscular movements. Reid also quotes observations on the human subject of death with extremely slow respiration, where the vagi were apparently healthy, but great congestion and oedema of the lungs existed (*ibid.*, pp. 207-209).

It will thus be seen that Bernard and Reid are practically at one in ascribing pulmonary congestion after division of the vagi to interference with the mechanism of respiration; and I may add that, so far at least, Traube is of the same opinion. That we have not the whole truth even here, is rendered very probable by Valentin's observations (quoted by Schiff, *Nerven-Physiologie*, p. 411). He has shown that marmots, in whom the vagi have been cut during hibernation, get pulmonary congestion; although the mechanism of breathing is rarely materially disturbed, the animals do not swallow, and no secretions are formed in the mouth.

Such being the facts in reference to the pneumogastrics, I was led to inquire what evidence there might be of the existence of some vaso-motor tract influencing the pulmonary circulation, and capable of being interfered with by the pressure of an extensive pleuritic effusion.

It seems to me that we have in a limb compressed by Esmarch's bandage and rope a condition closely analogous to that of a lung compressed by an extensive pleurisy. When the apparatus is removed, it is often observed that a blush of redness diffuses itself over the part. Sometimes, but by no means invariably, a troublesome hæmorrhage will then ensue from the cut surfaces. The reason of these I take to be, that the pressure has not only emptied the vessels, but has also compressed the nerves of the limb, and among others the vaso-motor nerves. When the blood returns to the extremity, it finds the small vessels not only empty, but lax, owing to vaso-motor paralysis. A similar condition exists in a lung which has just been relieved from the pressure of a considerable effusion. Its vaso-motor nerves, I take it, are also compressed. As the lung again expands, the tension thrown upon its small vessels is not only sudden, but very great. When the nerves have had a few hours to recover, and blood to revive upon, their controlling action again asserts its influence, and the arterial tension is brought up to the normal. We can thus account for the rapid and violent onset, as well as for the very short duration, of this albuminous expectoration. It has generally been found proportionate to the rapidity and extent to which the lung again expands, and to the amount of pressure previously exercised. In eighteen out of twenty-one of M. Terrillon's cases, from 2000 to 5500 grammes of fluid were evacuated from the pleura, and in all instances rapidly.

Ranvier's researches on the nature of oedema (*Comptes Rendus*, lxi, p. 25) strongly suggest that the vaso-motor nerves of the lung play an

* Two quoted by Terrillon, one by Béhier (*Union Médicale*, June 24th, 1873), one by Dumontpallier (*ibid.*)