REMARKS ON NUTRITION AND GROWTH.

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WHAT is meant by the terms "nutrition and growth?" How are we to define them in strictly scientific language, and what is the relationship of the one to the other? Such are questions which have often puzzled the biologist, and have led some (Sachs, *Text-Book of Botany*, translated by Bennett and Dyer, p. 693) to suppose that it is impossible to define the meaning of growth in strict terms, which will be applicable to all cases. I am far from taking this view of the matter, and would look upon the growth of an animal or vegetable organism as a definite process, limited in extent by certain recognizable laws, and due to specific properties inherent in the tissues.

In this paper I have endeavoured to trace the processes of growth and nutrition as far back as it seems to me our present knowledge will permit of. In doing so I have been chiefly actuated by a desire to form some sort of a basis for the rational definition of the conditions of hypertrophy or atrophy. Properly speaking, these ought to be considered along with any work on growth; but, as this method of treatment might, in the present instance, complicate matters, I have considered it better to limit the scope of the paper to the subjects of nutrition and growth alone.

Healthy Nutrition.—The requirements for the maintenance of a healthy state of nutrition, I hold, are twofold: 1. essential, 2. accessory.

1. Essentials of Nutrition.—Man, and the higher vertebrates, are far too complex organisms to study the essentials of nutrition in. In order to understand what the bare necessities for the proper nourishment of an animal or vegetable are, we must go much lower in the scale. It is in the lowest members of each kingdom that we can best perceive what the rudiments of a nutritive apparatus are. In the animal kingdom the protozoa, and more especially the class of naked rhizopoda, are specially suited for this purpose. The most of these are simple masses of protoplasm, sometimes surrounded by a slightly differentiated covering, sometimes not. The amoeba is one of the best examples. So far as we know, this organism possesses neither formed channels for the conveyance of nutrition, nor anything comparable to even the most elementary nervous system. Yet its nourishment seems to proceed with perfect regularity. The nutritive pabulum is simply brought in contact with its protoplasm as minute particles of organic matter. These are taken into its substance by a process of invagination, and the materials suited for the nourishment of the animal are extracted from them, the refuse non-assimilable substances being rejected by a reversal of the process by which they were absorbed.

The same primitive means of obtaining nourishment prevail in the lowest members of the vegetable kingdom. Like the protozoa, they are essentially masses of protoplasm, and they obtain their food in the same way, namely, by the ingestion of organic fragments of various bodies which may lie in their neighbourhood. These are digested and assimilated, and the refuse material rejected. It is hardly necessary to say that, like the amoeba, they do not possess any definite channels for the conveyance of nutrition, nor is there anything to represent a nervous system.

Some of the best examples of these low vegetable organisms are to be found in the myxomycetes. They consist, in a certain stage of development, of an amoeba-like mass of protoplasm or plasmodium, which has the power of locomotion by alternately shooting outwards and retracting lobes of its protoplasmic substance. These masses of vegetable protoplasm nourish themselves in the same manner as the protamoeba. According to De Bary (*"Morphologie und Physiologie der Pilze,"* in Hofmeister's *Physiologische Botanik*; and *"Die Myxomycetes,"* Leipzig, 1874), one often observes foreign bodies in the interior of the plasmodia, consisting of fragments of dead plant-cells, spores of fungi or of myxomycetes, granular matter, or particles of coloured substance, when such have been placed near them.¹ These fragments of foreign matter are laid hold of by quite a well-defined movement. The surface of the plasmodium raises itself upwards into a little tumour-like mass beneath the body which is resting upon it. The edges of this tumour-like projec-

tion then gradually flow over, and finally enclose, the little nutritious particle. It is not to be supposed, however, that the foreign bodies lie naked and simply imbedded in the plasmodium. Around them there forms a little vacuole or cavity similar to that which surrounds the ingesta of infusoria—the so-called "stomach-vesicle." The materials, if of the proper composition, are gradually dissolved, and the indigestible refuse is thrown out of the plasmodium by a reversal of the means by which the particles were absorbed. The organism contains, according to Kühne, a powerful pepsin-like ferment, by means of which the particles are dissolved, and rendered capable of being assimilated.

These two groups of organisms—the amoebæ and the myxomycetes—may be looked upon as among the lowest members of their respective kingdoms. Their means of nourishment are alike, namely, that the organic material is brought in contact with them, they surround it, and bring it into a state of solution. The higher, or, as we may call them, the compound organisms, I look upon, like the original propounders of the cellular theory of the tissues, as aggregations or colonies of such simple structures. The primitive vertebrate, in the first part of its embryonic existence, consists essentially of a mass of nucleated cells. There is no differentiation of these as yet into tissues. They all closely resemble each other. Soon, however, the specific properties inherent in each begin to assert themselves. They begin to undergo certain transformations. From those which are destined to form fibrous tissue, a substance is thrown out which in course of time becomes fibrillated, and converted into a bundle of fibrous tissue. The original cell is flatly applied to this bundle, and continues during its lifetime to throw out this same substance, and so to retain the integrity of the fibre. In bone, a similar fibrous basis is produced from the bone-corpuscle, between the fibrils of which calcareous salts are deposited. The bone-corpuscles meanwhile remain in the same relationship to the bone-matrix as the connective tissue-corpuscle bears to the bundle of fibrous tissue. In cartilage, there is the same arrangement; a series of lamellæ, consisting in reality of fibrous bundles, are closely applied to each other (Thin, *Quarterly Journal of Medical Science*, vol. xvi.), while the so-called cartilage-corpuscle is nothing more than the protoplasmic centre from which this fibrous matrix, infiltrated with chondrigen, is derived. The very essence of the cartilage-cell is, that it has the power of producing this peculiar matrix. Similarly, muscle is formed in the embryo from certain cells, which at first are rounded nucleated masses of protoplasm. From these, there is thrown out (Zielonk, *Virch. Archiv*, Band lxii, s. 29) a quantity of granular substance, which is soon prolonged at each end into a tapering extremity forming a spindle. This spindle becomes striated, and constitutes a muscular fibril, the original cell remaining flatly applied to the fibril, in the same manner as a connective-tissue-corpuscle remains adherent to the bundle of fibrous tissue. (Thin, *Proceedings of the Royal Society*, No. 155, and *Edinburgh Medical Journal*, September, 1874.)

In all these tissues, there is a community of design. The origin of them all is a mass of nucleated protoplasm. Each of them is to be regarded as a product or secretion manufactured, so to speak, by the machinery of the respective protoplasmic centres of the various tissues. Certain nutritive elements are supplied to these different protoplasmic factories, if we may so represent it, and out of the raw material there is produced a manufactured article corresponding to the special molecular machinery contained in each. This substance gives to the parts in which the protoplasmic units are contained the particular character by which the tissue as a whole is known. Thus, when myosin is the substance formed, we call that muscle; when a calcified fibrous matrix, the fabric is known as bone, and so on.¹

It is therefore clear that the formed material is a product of the nucleated protoplasm in its neighbourhood. It does not arise independently, but has its *raison d'être* in the amoeba-like protoplasmic colonies of the part. The formed tissues of the higher animals, in fact, are to be regarded in the same light as the slightly organised exterior of some of the rhizopoda, such as the test-like covering surround-

¹ Goodsir, in his paper on "Centres of Nutrition" (*Anatomical Memoirs*, edited by Turner, vol. ii, p. 389), regarded the nuclei, or, as he then called them, the germinal spots, of the tissues, as acting individually as a means by which nutriment could be extracted from the capillary vessels or from other sources. In the development of a tissue or organ, he looked upon the primitive cells out of which it grew as the rudiments of a colony, which colony, in course of time, would evolve itself into a special organ or tissue. He, therefore, named these primitive cells centres of germination. "As the entire organism," he writes, "is formed at first, not by simultaneous formation of its parts, but by the successive development of these from one centre, so the various parts arise each from its own centre, this being the original source of all the centres with which the part is ultimately supplied."

ing the protoplasm of the foraminifera. The compound organism is, in reality, an aggregation of colonies of amoeboid structures, each leading an existence of its own, and each throwing out a special secretion.

We can even go so far as to separate some of the individuals of such a colony, and, by supplying the necessary nourishment artificially, can keep them alive quite apart from any influence exerted upon them by the nervous system or circulating blood. A leucocyte, if removed, and kept in a proper nutritive medium at a body-temperature, will live for several days, and will show active movements. Other cells, such as those derived from the endothelium in peritonitis, will also live under the same conditions, and, in some cases, become partially organised. The embryonic mulberry-mass of cells nourishes itself quite irrespective of any differentiated mechanism for this purpose, each cell assimilating, by contact, the substances which are necessary for the maintenance of its integrity and growth.

The pabulum which is essential for the support of a simple organism is similar to that which is requisite for one much more complicated. It contains the elements carbon, hydrogen, oxygen, and nitrogen, with various salts.

So long as the animal or vegetable is a simple organism, its nourishment can reach it by mere contact or by imbibition. Indeed, there are certain compound animals, such as the flat entozoa, in which imbibition is the only means of conveying nourishment to central parts. They are immersed in the materials which serve as their food, and they simply absorb these, being in this way enabled to live and grow rapidly without the intervention of any accessory in the shape of a nervous system, and without any special blood-vessels for conveying nourishment to, and refuse material from, their central parts.

All, therefore, which can be said to be essential for the nourishment of an organism is, that it should be composed of what we know as living, and usually, if not invariably, nucleated, protoplasm, and that it should be placed in contact with a suitable pabulum.

II. *Accessories to Nutrition:* (a.) *Digestive System.*—It can easily be understood, however, that the system of nourishment by simple imbibition must always be confined to such animals as live under circumstances where their food is specially prepared for assimilation.

The cestoid worms before mentioned are, perhaps, the best examples of nutrition carried on in this way. Being destined to have their *habitat* in the intestine of other animals, the digestion of their food is done by the stomach and intestine of the host, and hence any such arrangement for preparing the food in the tenant would be superfluous and useless.

The greater number of compound animals, however, are not placed in circumstances so favourable for obtaining a specially selected and prepared food-supply at first hand, and hence one of the accessories most commonly found in compound animals is a digestive apparatus. This, in different classes, is more or less complicated according to the amount of transformation which the ingesta have to undergo.

(b.) *Blood-Vascular Apparatus.*—The food, having been thus prepared, requires to be circulated through the body by special channels, because it is evident that, in an animal of large bulk, mere imbibition would be totally inefficient for this purpose. The means by which this is accomplished is, of course, by a blood-vascular system. The food, in a state of solution or minute subdivision, is absorbed by a special set of vessels which carry it into the blood-channels, to be distributed by them throughout the body. In plants, the spiral vessels perform the same function in distributing nourishment among their dense cellular parts.

Such blood-channels are, however, mere accessories to nutrition. They are not, strictly speaking, essential. A mass of protoplasm could be nourished by mere contact of the nutritive fluid in other ways, quite irrespective of the blood-vessels, provided that the materials, which it assimilates, could reach it readily by other paths. In the human body, we have actual evidence that the blood-vessels are not essential, in the fact of their being absent from such parts as the cornea, cartilage, and the inner coat of the arteries. In the first two of these their presence would be inconvenient, while in the last, the immediate contact of the membrane with the circulating blood, obviates the necessity for any further means of transmitting nourishment. In all these tissues, the method of nourishing the protoplasmic units of the colony closely approaches that of the lowest organisms. It is a system by which the nutritious substances are imbibed by them, each selecting the necessary constituents to nourish itself, and to elaborate its particular secretion.

Although, however, blood-vessels may be mere accessories to nutrition, yet their presence in all parts which have to withstand much tear and wear, or in which metabolic changes are particularly active, is absolutely necessary. There must be a full supply of organic substances in order to afford such a part the means of deriving energy. Parts which perform a mere passive action, such as bone or cartilage, are meagrely provided with nourishing channels, while in those, such as muscle or brain, in which the transformation of energy into work done is much greater, the supply of nourishment is commensurately larger.

(c.) *An Influence of the Nervous System.*—It may be asked, however, whether an influence of the nervous system is not an essential for nutrition. There is still considerable doubt as to whether it is. The lower classes of animals seem to nourish themselves quite independently of such; and, in the vegetable kingdom, if anything of the kind does exist, it is of the most rudimentary nature. The experiment which seems to support the idea, that the nerves exert a direct trophic influence upon the tissues, is that of division of the trigeminus (Magendie, 1824). If this nerve be divided in a rabbit, the nutrition of the eye and face is seriously interfered with. There is at first loss of sensibility on the corresponding side of the face. Within twenty-four hours, the cornea looks cloudy. The whole eye then becomes inflamed, and this is followed by total disintegration of the eyeball.

It has been asserted, however, that these effects are not due to loss of the supposed trophic action of the nerves, but are mechanically produced by the irritation caused by foreign bodies, which, on account of the loss of sensibility, readily impinge upon the conjunctiva without being perceived. The evidence in regard to this assertion is somewhat contradictory. Snellen (*De invloed der Zenuwen op de Ontsteking*, Utrecht, 1857. Paget's *Surgical Pathology*), for instance, states that, if the eyeball be protected from external injuries, as by tying a pad of cotton over it, the destructive phenomena are not induced, or are rendered feebler. Sennleben (*Virchow's Archiv*, Band. lxxv, s. 69, 1875) has arrived at much the same conclusions—namely:

1. That the cornea-affection, after division of the trigeminus, is independent of any trophic action possessed by the nerve.
2. That it is a necrosis, brought about by the traumatic operations which follow on its anaesthesia.
3. That the circumscribed necrosis acts as an inflammatory irritation, and calls forth a secondary inflammation, spreading from the periphery of the cornea.

Other experimenters have not been so successful in preventing the destruction of the eyeball by protecting it from external agencies; and hence, as yet, it may be said that the matter of the trophic action of the fifth nerve upon the eyeball and tissues of the face is undecided.

Another instance, often quoted, of the supposed trophic influence of nerves upon tissues, is the fact of bedsores following paralysis of the lower extremities. These are more liable to occur in paralysis due to disease of the spinal cord than in that which owes its origin to cerebral causes. It seems, however, that the occurrence of bedsores on such paralysed parts may also be explained on the supposition of vaso-motor nervous disturbance interfering with the circulation, and not on the ground of a direct trophic action of the nerves upon the tissues themselves. This appears to be the more likely explanation, because it is on those parts which are subjected to pressure—the buttocks, heels, or shoulders—that the slough takes place. If such bedsores be due to a vaso-motor nerve-disturbance, it can easily be seen how pressure would act injuriously. The arteries having lost their means of regulating the amount of blood passing through them, or this action having become enfeebled, congestions of such parts, with all their accompanying evils, would be very liable to occur. Were the sloughs caused, on the other hand, by the loss of a direct trophic action of the nerves upon the tissues, there is not any reason why they should not occur upon the parts which are free from pressure, as well as those which are subject to it.

Another cause which may predispose to such sloughs, especially in paralysis of the lower extremities, is that there is frequently loss of sensation, as well as motion, particularly in such cases as owe their origin to spinal lesions. In such circumstances, the patient does not experience any discomfort from lying constantly in the one position. Hence pressure may be exerted continuously, for hours or days, on one spot, and may consequently induce a slough. We all know that, in such cases, the formation of bedsores may often be postponed temporarily or indefinitely by frequently changing the position of the patient. Continuous pressure on a part, even in a healthy subject, will cause sloughing in a very short time. The pressure of a splint will, in a few days, induce a slough of the skin.

Cellular tissue sloughs, again, take place in persons lying in bed for a lengthened period, if they are in a weakly state of body, even although they are not the subject of a paralysis. This tends to support the simple malnutrition theory, independent of any direct trophic action of the nervous system, by showing that similar effects may supervene, even where there is not any paralysis, simply from continuous pressure on a part in a weakly subject.

The wasting of the paralysed muscles in persons suffering from hemi-, or para-plegia is often quoted as additional evidence of a direct trophic action. The mere disuse of the muscles, however, would bring about the same effect. Faradic excitation, to a certain extent, prevents it. Besides, if the vaso-motor nerve-action is impaired, it is possible that the nutrition of these muscles would also suffer indirectly through the deleterious action on the blood-vessels. Cerebral paralysis of the lower extremities is not nearly so liable to induce bed-sores as a paralysis due to destruction of the nerve-cells of the spinal cord. On the supposition of a loss of the regulating action, exerted by the vaso-motor nerves on the vessels, being the indirect cause of the bed-sores, this might be explained by the injury which the branches of the sympathetic issuing from the cord would receive in primary disease of that organ, and the comparative immunity that they would preserve, were the lesion situated, for instance, in the cerebral cortex.

It is only right to mention, however, that many cases have been recorded which, apparently, seem to point to a direct trophic action of nerves upon the tissues. Sir James Paget (*Surgical Pathology*) states the case of a man who had fractured the lower end of the radius. The amount of callus which was thrown out was so great that the median nerve was compressed. Apparently, as a consequence of this, ulceration of the thumb, fore, and middle fingers ensued. The ulceration was stopped by so binding the wrist as to relieve the pressure upon the nerve. When this treatment ceased, the ulceration returned. It is also a well known fact that fractured bones in paralysed parts do not tend to unite, and that wounds of paralysed limbs have little inclination to heal. Mr. Travers (*Further Inquiry Concerning Constitutional Irritation*, p. 436) mentions the case of a man who fractured his humerus and tibia, and who at the same time was rendered paraplegic by a fracture of his lumbar vertebra. The fracture of the humerus united in the course of time, while that of the tibia remain ununited.

Whether cases such as these are to be explained on the theory of a deprivation of a direct trophic action of the nervous system upon the tissues is doubtful. For so long as we know comparatively little about the effect of vaso-motor nerves on nutrition, indirectly, through the blood-supply, it would be unwise to come to any definite conclusions. In locomotor ataxia, not only muscles, but bones degenerate, yet we cannot say what the agent is which directly brings this about. It may also here be simply a vaso-motor disturbance. There is, therefore, not any conclusive proof, as yet, that nerves are actually necessary for the nutrition of other tissues in compound animals. They may be essential for regulating the machinery for transmission of nourishment, but there is doubt whether they actually control its assimilation.

There is not, however, any doubt that nerve-fibres are subject to the trophic influence of the nerve-cells with which they are connected. Waller's experiments (*Philosophical Transactions*, 1850, Part II, p. 423) have demonstrated this beyond doubt. If a nerve-fibre be divided at a certain spot, the peripheral portion degenerates, even although its blood-supply continues as before, while the proximal portion remains unaltered. That this should be so is easily enough comprehended when we take into consideration the intimate connection between the axis-cylinder and nerve-cell. The axis-cylinder may be looked upon simply as a process of the nerve-cell from which it arises. It is, in all likelihood, possessed of protoplasmic properties, much greater than is generally supposed, and hence the nucleus of the cell is probably necessary for its vitality. When, therefore, we divide an axis-cylinder, we in reality are separating a portion of the protoplasm of the cell from its nucleus, and thus it is only to be expected that the separated portion would die.

Some very curious and, if trustworthy, valuable experiments, referred to by Dr. James (*Edinburgh Medical Journal*, August, 1883) in his paper on nutrition, have been made of late by Rumpf (Pflüger's *Archiv*, 1881, p. 415), tending to show that not only is there a trophic influence propagated from the nerve-centres to peripheral parts, but that a similar trophic action, or, as he calls it, a "retrotonus," is exerted from peripheral parts upon the spinal cord. If the spinal cord, in a frog, be transversely divided in the cervical and lumbar enlargements, and if the intervening portion

of the cord be separated from all its attachments by cutting through the anterior and posterior nerve-roots, the portion of cord so isolated undergoes absorption in from five to eight days. This does not follow, however, unless the nerve-roots are also divided. The result is not due, he states, to interference with the blood-supply, on account of injury to vessels entering the cord through the intervertebral foramina; but, apparently, is owing to what the author and Kühne formerly described (*Arch. f. Anat. u. Phys. v. Reichert und Du Bois-Reymond*, 1860) as a trophic action propagated from the end organs in the tissues in a centripetal direction. Both roots of the nerves seem to convey such centripetal trophic influences, but chiefly the motor branches. If one doubly divide the cord as above, then cut across the motor roots, leaving the sensitive untouched, degeneration and absorption follow as before, but not so completely, strands of the cord being still retained. Whether there be not some influence at work in these experiments, other than that referred to, is hard to say. It certainly seems somewhat curious that peripheral parts of nerves themselves should degenerate when the nerve-trunk is divided, and yet the cord, if similarly divided, retains its integrity if this retro-trophic action is propagated from the end organs in the tissues.

Growth.—By growth of a living organism I understand the following: *The increase in bulk of a tissue or organ by addition to the number of its cellular elements without the production of structural abnormality or differentiation into unlike tissues.* The process, therefore, is quite a different thing from mere increase in size. Increase in size may be brought about by many different agents. Thus an organ or tissue may become loaded with a foreign substance, and increase even symmetrically in bulk. The liver may become infiltrated with the "wax-like" substance, and its proportions may be increased equally in all directions. The form of the liver is thus kept up, the bulk it occupies apparently is greater than natural; and yet, when we come to examine it minutely, hardly a vestige of true liver-tissue may be found. The liver-parenchyma has been supplanted by a new and foreign substance. The organ has not grown; it has, in reality, suffered extreme atrophy.

Again, the same organ may have the protoplasm of its cells distended with oil; and likewise in this case may increase in bulk equally all over. The cause of the increase here, as in the former case, is the loading of the organ with a foreign substance. This produces, certainly, increase of size; but the process is not that of growth. A muscle, similarly, may increase in bulk from the interposition of fat and fibrous tissue between its bundles. This, however, as in the waxy liver, may bring about absolute atrophy of the muscular fibre, although apparently the bulk of the muscle has been augmented.

Nor is development to be placed in the same category with growth. The matured ovum, when fertilised, divides, and very soon numbers of new cells result. These cells, however, in course of time begin to differentiate into unlike tissues, that is to say, they develop into muscle, bone, epidermis, fibrous tissue, liver-tissue, and so on, these tissues being unlike the original cells from which they have arisen. This is progressive increase, or the increase of a tissue accompanied by its evolution into one of a higher standard of organisation. It is, in a word, development, not growth. In a part which is veritably growing, each cell produces its like. There is no differentiation of one cell or tissue of low organisation into that of a higher. Muscle-cell remains as muscle-cell, liver-cell as liver-cell, without these undergoing any further evolution. Growth, in fact, commences when development is complete. If, in the increase of bulk of a tissue, there is any differentiation of a lowly organised tissue into a higher, then that tissue is still developing; growth has not yet commenced. The rudiments of all the organs and tissues are first laid down before the latter commence to grow.²

What, therefore, are the characteristics of a growing part in a living organism? How is it that the increase of bulk is brought about?

When we examine a piece of growing epidermis, the one feature which immediately arrests the attention is the active division of the cells composing it. In a young salamander, for instance, the nuclei of the cells are all very large. The majority of them are in the resting condition; but, in a great number, the nucleus is beset with an intranuclear plexus. Transformation of this is actively taking place, the nucleus divides, and a division of the cell-protoplasm follows. The large proportional size of the nucleus, and its rapid

² Paget evidently held a somewhat similar view when he wrote (*Surgical Pathology*, p. 2): "We must carefully distinguish development from mere increase; it is the acquiring, not of greater bulk, but of new forms and structure which are adapted to higher conditions of existence."

division, are two of the most characteristic features of this growing epidermis. There is no loading of the cells with a foreign substance. The whole of their energy seems to be occupied in multiplying by segmentation.

Muscle, according to Zielenko (Virchow's *Archiv*, Band lxii, s. 29), grows in the same way. Numbers of oval or round cells are always to be seen among the fully-formed muscular fibres. These, by a process of division, give rise to a new progeny of cells, which, in course of time, are converted into spindle-shaped bodies, showing transverse striation, subsequently culminating in the production of complete striated muscular fibre.

The endothelium covering a serous membrane in a young animal always shows certain of its cells to be germinating and dividing, so as to produce new cells. The single layer of epithelium covering the air-vesicles in the lung of a growing animal similarly shows the most distinct evidence of germination and division. Young fibrous tissue, young liver-cells—all show, when they are growing, active and unequivocal signs of nuclear multiplication and cell-division.

In growing plants, the great characteristic feature is the division of their cells. This, in thalloids, is particularly evident; and at the parts of phanerogams where growth is proceeding the cells are highly protoplasmic, and are all engaged more or less actively in dividing. A mushroom may in a single night grow truly enormously by a process of cellular increase.

Viewing this matter from a different stand-point, the disparity in growth of two such animals as a mouse and a whale, it may be noticed, is owing to a numerical superiority of the cells of the one over the other, not to an increase in the size of each cell. Certain of the cells in the tissues of the whale are absolutely smaller than those of some of the most insignificant vertebrates. Further, as a rule, it may be said that the foetal cells are larger than those of the adult. We have, on these various grounds, conclusive evidence showing that, in a growing part, the most characteristic phenomenon is numerical increase of its tissue-units by a process of cell-division.

A tissue sometimes gains bulk, however, by the increase in the size of its constituent elements, one of the best examples of this being muscular tissue. Is not this also true growth? According to Zielenko (*loc. cit.*), the muscular fibres of the foetus not only increase in number with age, but at seven months are smaller in bulk than those of the foetus at eight. They are larger in the child of one year than in the foetus, and very considerably larger in the adult than in the child. The increase in bulk here, however, is owing to the greater quantity of the sarcois substance, or myosin. A striated muscular fibre, as Thin (*loc. cit.*) has shown, is composed of a series of flat endothelium-like corpuscles lying on the side or within a mass of striated sarcois substance, just as the connective tissue-corpuscle lies upon a bundle of white fibrous tissue. Similarly, cartilage is made up of laminated sets of bundles of fibres formed from the cartilage-corpuscles. They constitute what is called the hyaline matrix. The cornea also is a laminated fibrous tissue produced from the connective tissue-corpuscles lying upon its bundles. The matrix of bone is a calcified fibrous tissue thrown out from the bone-corpuscles. In each of these cases—and the same may be said of all other formed tissues throughout the body—the special substance thrown out by the particular corpuscle is a secretion from it. The muscle-cell secretes myosin; the connective tissue-corpuscle, collagen; the cartilage-corpuscle, chondrigen; the bone-cell, calcified fibrous tissue. The quantity of these respective secretions varies with circumstances, just as the secretion from the liver, salivary, or peptic cells does. Thus, in a cartilage-tumour, small masses of matrix may be seen round each cartilage-cell, or a group of these; in a myeloid tumour, little abortive portions of bone-matrix are also formed; while in a young growing muscle there are many cells around which the sarcois substance is in very small quantity. On the other hand, in articular cartilage, the matrix is abundant; in an ordinary bone, the bulk is chiefly made up of this; while in the muscle of a well-nourished individual the sarcois substance is more abundant than in one poorly nourished. (Auerbach, Virchow's *Archiv*, Band liii, s. 234.) The amount of these secretions comes and goes according to different conditions of nutrition; it is no constant quantity. Either the amount of pabulum going to the part is decreased, or the corpuscles of the tissue have lost their power of readily assimilating and of converting it into their respective peculiar products. In plants, similarly, increase in bulk may be caused by the varying amount of cellulose secreted by the plant-cells, or by the quantity of starch they accumulate. As a rule, it may be said that, where cell-division is active, the amount of these various formed substances

either in an animal or plant is small. Thus, in a truly growing part, in the "punctum vegetationis" of a plant, for instance, or in growing muscle, the cellulose and sarcois substance respectively are much less than in parts of the plant or animal where cellular increase is not so rapidly progressing.

Granted, therefore, that the substances referred to above as constituting part of animal and vegetable tissues are to be looked upon as secretions from animal and plant-cells, can we, with any show of argument, call the increase in their amounts growth? Can we include the process of their elaboration along with that which is a characteristic of all truly growing tissues—namely, numerical increase of cells? To me, the two things seem utterly incongruous; and I believe we shall never arrive at any correct idea of what growth and hypertrophy mean until we distinguish between them. If we are to call an exalted secretion of a connective tissue muscle or bone-cell growth, then there is just as good reason for calling the hypersecretion of bile, saliva, or pancreatic juice, by the same designation. The muscle may store up myosin, and increase in bulk; but this is quite a different attribute from that of giving birth to a new progeny. In fact, the two things—growth and the secretion of a matrix—are, to a certain extent, in an inverse ratio; for it is not in the actively growing part that the latter is abundant, but rather in that in which a period of comparative quiescence, or state of equilibrium, has been reached. Any tissue, when it has reached this state of equilibrium, may increase in size by the accumulation of a matrix. It has not, however, necessarily grown.

Both methods of increase in the bulk of an organ or tissue, that is to say, by multiplication of its fibres or cells, or by increase in the size of these, however, sometimes go on together. In the growth of muscle this is probably the case, the number of muscle-fibres increasing *pari passu* with their bulk. Whatever the manner, however, in which the growth takes place, there is always this to be said, that the newly formed tissue is similar in its nature to that which preceded it. There is no differentiation into a tissue of a higher standard. Each cell has the power of selecting certain constituents of the blood, and of elaborating these into its own particular texture. Muscle selects those which will form muscle, white fibrous tissue those which can be transformed into its fabric, and bone-cells calcareous salts.

It is, therefore, evident that mere increase in size is not growth. Increase in size is one of the attributes of a growing part. There are others which must be taken into account in its definition, and it seems to me that the more one comes to think on the matter, the only definition which, strictly speaking, will include all cases, is that of numerical increase of the tissue-units, with the restrictions which I have previously given.

On the Limits of Growth.—In discussing the subject of the cause of the limits of growth, there are two divisions under which it must be considered. First, the cause of the limitation of growth to a certain time in the existence of the animal or plant; and secondly, the cause of the limitation of growth to a certain bulk.

Growth commences, as before mentioned, with the completion of development, and ceases in all the metazoa at a certain period. The time of this cessation varies in different animals, and generally is proportional to the whole average length of existence. In plants the same holds good, although not so markedly as in animals. What is the cause of this limitation in time?

Mr. Spencer (*Principles of Biology*) explains it in the following manner. He takes it for granted, to begin with, that in the infant the nourishment absorbed is much in excess of the requirements of the system. It is also to be inferred from his argument that he holds the cause of growth to be excessive nutrition. Starting with these two data as a hypothesis, he maintains that the animal ceases to grow when the requirements of the tissues and the amount of nourishment supplied are exactly balanced. The surplus nourishment, which he holds there is in the infant, is neutralised; he says as the animal gets older, in the following ways.

In similarly shaped bodies their bulk increases as the cube of their dimensions, while their surfaces only as the square of the same. In childhood, he says, the amount of nourishment capable of being absorbed by the gastro-intestinal tract is greatly in excess of that required by the tissues for their maintenance. In youth, as the bulk of the organism has increased more than the absorbing surface, the excess diminishes, and when the ultimatum of growth is reached the amount absorbed is just sufficient for the wants of the system. Now, in order to employ this argument, we must be perfectly certain of two points. In the first place, that the absorbing power of the gastro-intestinal tract is the same in childhood and in

adult life. In the second place, that the ratio of the nutritious quality of the food consumed and absorbed at each period of life is alike. Before we have settled these premisses, it is of no use arguing the matter. Were the living organism like a crystal, around which there is precipitated so much new matter in a given time with perfect regularity, there might be some sort of solid basis to found an argument of this kind upon, but seeing that the conditions are so entirely different in the case of the growth of an animal or plant, any conclusions founded on the supposition that they are similar must necessarily be fallacious. In the economy of the living organism, there are so many side-issues that have to be taken into account, so many modifying circumstances to be allowed for, and which as yet we cannot calculate with accuracy, that it seems to me the whole system of the argument, as employed by Mr. Spencer to the explanation of the limitation of growth, is premature, and the problem is so complicated that it is questionable whether we shall ever be able to reduce it to a mathematical formula. Were the conditions constant, there might be some hope of success, but seeing that the slightest alteration in the external surroundings, the circulation, nervous system, etc., may be reflected upon and influence the absorbing power and general nutrition of the organism, it seems an almost Herculean labour to attempt to allow for all these.

Quite apart from this, however, I hold that we have direct evidence that the limitation of growth is not regulated by the balance of expenditure over demand. Growing animals do not fatten. It is when growth ceases that an animal puts on flesh. The areolar fibrous tissues then become loaded with fat, the muscles increase in bulk, and an augmentation in the weight of the animal follows. This excess of energy-evolving material might have been utilised in growth, but apparently has not been required. It has nevertheless been absorbed, has been offered to the cells of the tissues; they have assimilated it, and have had the opportunity of growing from it, yet it has been rejected by them for growing purposes, and has been stored up in various parts of the body, as utilisable but unused nourishment. There is, therefore, when growth ceases, no lack of nutritious pabulum, but rather an excess. In fact, what has occurred is that the absorbing surface has taken up actually more nutriment than can be consumed, and the excess of this is deposited in certain tissues until required by the system. I cannot, therefore, see that the view taken by Mr. Spencer, in regard to the period of growth being limited by the amount of pabulum sent to the tissues, is actually supported by fact. I am inclined to question the whole theory of growth advanced by him, when he looks upon it as a mere accretion of particles, and compares it to the accumulation of carbon on the wick of a burning candle, or the crystallisation of a saturated solution of a salt. No physiologist at the present day would for a moment think of comparing the formation of a crystal with the process of growth of a living tissue. The one is an accumulation of like particles round a centre in a definite order; the other the calling into existence of a new life from the old, the formation of a new progeny, consisting of cells possessing certain hereditary impressions, and capable of giving birth to an offspring. Mere accretion of particles, as in the carbon resulting from the burning of the wick of a candle, may be due to agencies quite apart from the internal economy of the particles, while growth of an organism represents work done by the particles themselves.

Animals differ in size. In the mammalia, the greatest variation in bulk occurs; yet all arise from an ovum, a single nucleated cell, which does not present any difference in size at all commensurate with the bulk of the future beings into which such ova ultimately become evolved. Not only this, but different species of the same genus, both in plants and animals, arrive at different degrees of bulk and stature. And even when we come to a single species of a certain genus, variation in bulk and stature is a well-marked feature. How is this to be accounted for? What is it that causes the animal, as a whole, and its individual organs and tissues as parts, to grow to a certain size during the early period of its extrauterine existence, and afterwards to retain this bulk, with little alteration, until the time of death?

Mr. Spencer again (*loc. cit.*) explains this by a calculation based upon the difference in the initial amount of tissue with which each individual begins life. For example, he says, a mouse at the time of birth has much less initial tissue-capital, as it were, than an elephant or a whale. Consequently, as the parts of the tissue grow in the same ratio, and as nourishment is proportional in each, the one reaches a much larger bulk than the other. This, to some extent, certainly holds good. Given, to start with, say five thousand cells in the liver of one animal, and five hundred in the other, the

first will, *ceteris paribus*, continue to exceed the bulk of the second. It, however, does not explain all cases. How, in view of this, are we to account for two infants, equal in bulk and weight at time of birth, reaching respectively four feet ten inches and eight feet? Giants are not always remarkably large infants. In fact, nothing remarkable is noticed in their bulk and stature until some time after growth has commenced. Two embryos of equal size of the same genus of a plant, but different species, do not necessarily grow to the same size; nor do the embryos of the same species always reach to like dimensions.

All vertebrates arise from a single cell, the ovum; yet the foetus, in one case, may reach a ton in weight, while that of another may be reckoned in grains. The fact that the ovum, from which all animals spring, may, practically speaking, be said to be of the same size, is an additional argument against Mr. Spencer's initial tissue-capital theory. There is evidently, in the one ovum, some property inherent, in virtue of which the tendency to division is vastly greater than in the other. Both begin to divide in the same way, and there is evidence to show that in each a single spermatozoid is sufficient for fructification. Very soon, however, the cells which form the rudiments of the organs and tissues in the one become much more numerous than in the other. They are not necessarily larger, but the ovum of the progeny resulting from division in the first case, very soon overreaches that of the second.

Growth proceeds actively during the youth of the animal, and the period at which it ceases does not culminate abruptly, but by almost imperceptible degrees. During the remainder of the life of the organism, division of its cells is not entirely abolished, but takes place to such an extent that the newly-formed units are just sufficient to repair waste. Finally, in old age, even although expenditure may be less than in youth, the number of new cells generated in the organs and tissues is absolutely smaller than is required, and some amount of shrinking occurs. It seems to me that the disparity in bulk arrived at in various animals and plants can be explained only by the molecular differences existing primarily or after impregnation in the ovum. It might be argued that the difference in bulk of one animal or plant over another is a question of the amount of nourishment supplied. Does not an animal when fully fed gain a greater bulk than one which is underfed? Does not the cock's spur, when transplanted to the neighbourhood of the cock's comb, grow inordinately, from the extra quantity of nourishment supplied to it by the increased vascularity of the part? Does not a grain of wheat, when placed in particularly rich soil, grow to a greater height than one placed in poor soil? True, that is so, but no amount of extra nourishment would enable the tissues of a mouse to grow even to the size of those of a rat, nor would any amount of richness of soil ensure that a plant of wheat would grow beyond a particular limit. Even the growth of the cock's spur has its limit when placed under peculiarly favourable conditions for growing. The bulk gained by an animal or plant, when it is nourished as highly as possible, has a definite terminus, and no amount of increased pabulum would enable it to grow beyond this. That is to say, over and above the minor differences which may be caused by the amount or qualities of the nutrition supplied, there is something inherent in the cells of the one animal or plant which enables them to multiply out of all proportion to those of another. It may happen that the cells of a part do not multiply as much as they are capable of, owing to insufficient food-supply, and were the food-supply increased, growth would proceed to its full extent. That, no doubt, frequently takes place both in the animal and vegetable kingdom, and hence the disparity in the size of beings of the same species of a particular genus. Yet, quite irrespective of this, each individual has its limits of growth, and nourish that individual as much as we choose, it will never grow beyond it. There is an ultimatum of growth attainable by all organisms; it is not always attained, but cannot be surpassed.

There seems little doubt that the coalescence of the male and female pronuclei in the ovum has the power of causing great molecular disturbance in its protoplasm. The natural equilibrium of the cell is upset. It is possible that the peculiar radiating arrangement of the granules of the protoplasm, known as a "sun," around the pronuclei and permanent conjoined nucleus is evidence of this increased molecular disturbance. The result apparently is, that there is a tendency to cleavage. The particles of the protoplasm tend to accumulate at the poles of the cell. There is, evidently, some sort of repulsion between the molecules of the one half of the cell and those of the other, or an undue attraction towards either pole.

Now we can easily conceive that in ova there may be varying degrees of this molecular instability, just as the molecules of two gases may be vibrating with different velocities, producing different

degrees of tension. The tendency to split in the one ovum, we may say, might thus be a thousandfold greater than in the other. And not only in the ovum, but in the cells which result from it, there would be imparted the same ratio of cleavage-capability. The daughter-cells would divide in very much the same manner as the parent. The tendency to cleavage would thus be propagated from progeny to progeny; with this difference, however, that, apparently, the disruptive capabilities of the cell become less and less powerful in each successive generation. Thus, when the animal is young, there would be a much greater liability to reparative reaction in its tissues than when it grew older. We all know that this is the case. We know that the tissues of a young animal, if stimulated, react, by division and multiplication, more readily than when the animal is older; the reason being, of course, that they are still possessed of a greater residuum of that instability derived from the original ovular cell.

We can in this way, I think, account for the difference in the limits of growth in time and bulk. Ovular cells are possessed of unequal degrees of instability. Thus the impregnated ovum of a mouse would be the subject of much less disturbance in its molecular economy than that of a dog; and the latter, again, much less than that of a whale or elephant. The one ovum, if I may so express it, is wound up to go on dividing, say fifty-fold, the other five thousand-fold, and the third to the five millionth degree. They resemble, in fact, so many charged electric receivers. To outward appearance they are alike, but the one may be possessed of an amount of potentiality far exceeding that of the other. In virtue of this unequal potentiality each ovum would be calculated to produce so much of a progeny before its germinal activity became exhausted, but the extent of this would vary in different cases. The resulting difference in bulk of the animal that each ovum is destined to evolve itself into, would thus be accounted for. It is very much as when we dilute equal quantities of, say, three solutions of a colouring matter of different strengths with successive equal quantities of water. There comes a time when the colour of the weakest solution may be almost imperceptible, while that of the medium and strongest are still distinctly visible. On continuing the dilution, the medium solution will next become imperceptible, while the third may yet be evident. Continue it still further, and the coloration of the whole three may become so weak as to be invisible. So it is, I hold, with different ovular cells. The divisional energy of the one progeny becomes exhausted long before this happens in another, and hence there ensues as a consequence an animal of greater or less bulk. We may, by supplying abundant reparative pabulum, carry the proliferative powers of each to the uttermost multiple, and by undernourishing we may render this abortive, but we cannot by any known means cause individual ova to proliferate beyond a certain predestined limit. The organism resulting from each ovum resembles a tree. The stem is represented by the ovum, the branches by the progeny of cells set free from it, and the greater or less bulk of the animal corresponds to the number of branches and their subdivisions. The exhaustion which takes place in the power of proliferating resembles similarly the decreasing thickness of the branches and twigs.

When we consider what has been the original cause of this difference in the amount of disturbed equilibrium in the ovular cells in different animals, it surely is quite in keeping with what we at the present day regard as the origin of all peculiarities in animated nature to suppose that the laws of variation and heredity might account for it. Given a primitive ovum capable of dividing up to a certain extent, it is quite likely that, out of a great number of instances, some variation in this limit would take place. This, on recognised grounds, becoming hereditary, would be propagated to future generations, and so a peculiarity at first accidental may become a permanent feature in course of time, giving rise to certain characteristics in the being the ovum is destined to form. And if we further consider how it is that such peculiarities are impressed upon the ovum, it surely is not unreasonable to seek an explanation in the arrangement of its molecules. It is possible that although two ova may contain the same number of molecules, the arrangement of these, or of the constituent atoms of these, may be such as to endow each with different physical properties. We could even imagine, were the constituent molecules so arranged that they were more easily set into vibration by heat-radiations, that this might have something to do with the great instability in certain instances, the less in others; and seeing that all cells are in reality derivatives of segments of the original ovum, there is no reason why the same arrangement should not prevail in the segments as primarily existed in the ovum itself, but less marked. We call the

ovum a small body, little thinking that, molecularly considered, it is truly enormous. Sir W. Thomson gives this graphic illustration of what is meant by the size of a molecule. "Imagine," he says, "a drop of rain, or a glass sphere, the size of a pea, magnified the size of the earth, the molecules in it being increased in the same proportion. The structure of the mass would then be coarser than that of a heap of fine shot, but probably not so coarse as that of a heap of cricket-balls." Surely, if this be the case, there is plenty of room in a vertebrate ovum for variations in the arrangement of its molecules of an inexhaustible character. By such variations we can imagine how hereditary peculiarities are transmitted. A very slight deviation from the usual molecular grouping of the ovular cell would, in course of time, produce the most marked effect in the resulting individual.

Turning now to the subject of neoplasms, how is it that they are to be accounted for on the theory just stated? How is it that a tissue, at an advanced period of life, should commence growing to a degree quite incompatible with that of the other tissues of the body? It seems to me that these abnormalities in growth can be explained only on one of two possible conditions; first, that, as Cohnheim supposes, they are derived from embryonic remnants; or, secondly, that some condition of the part locally, or of the system generally, is capable of generating in the tissues new embryonic energy and instability. Cohnheim (*Allgemeine Pathologie*, Band I, s. 623), argues thus:—We have evidence that, in the normal growth of the body, there are periods in which tissues remain in a latent condition, and others at which they suddenly take on excessive growing activity. Before puberty, the generative organs, mammae, and hair of various parts of the body are ill developed, but when the age of puberty is reached, these suddenly begin to enlarge, to grow more rapidly than they did in previous years. In the same manner, he says, it is quite possible that there may be parts of certain tissues whose cells remain latent for a certain number of years, but which burst into embryonic activity as soon as proper physiological conditions are established. Such tissues growing more actively than their surroundings would constitute neoplasms. There is transmitted, from intrauterine life to adult age, the capability of growing to an excessive degree; it only requires the advent of certain circumstances to render this potentiality kinetic. This certainly seems a very feasible view when we come to think on it with due attention, and is quite in keeping with the general theory of growth I have discussed. That is to say, every embryonic cell has the power of dividing up to a given multiple. It is possible, however, that its power of dividing may have been arrested or suspended at a certain stage, and that it may lie imbedded in the other tissues for a length of time before completing its full compass of divisibility. I do not believe, and Cohnheim confirms this, that cells or tissues possessed of this peculiarity would have anything in their external histological characters by which they could be distinguished. We cannot tell, on looking at an epidermic cell, how far it is removed in genealogy from the original cells of the epiblast. So far, this theory of Cohnheim is comprehensible, but it must not be supposed that there are no facts which militate against it. When we examine the state of the epidermis in a commencing epithelioma, it is not a few cells of the rete Malpighii which are affected; but, for a considerable distance all round, the epidermis is pushing columns of epithelial cells into the underlying connective tissue, and, as this goes on, other parts of the epidermis assume the same germinal activity as that of the original site of the tumour. Indeed, the original tumour may slough or ulcerate out, leaving a large granulating surface, while the epidermis at the edge of the tumour shows the same tendency as the original piece of germinating epidermis to push long columns of actively growing cells down into the adjacent subcutaneous parts. Hence the induration of the edge of such a cancerous ulcer. A young growing sarcoma shows the same property of contagion, if I may so express it. A sarcoma originates, say, out of a small piece of fibrous tissue by the enlargement and germination of its connective tissue-corpuses. As the tumour grows, I have frequently seen the fibrous tissues of parts, which are being encroached upon by it, take on the same action as the tumour-tissue itself. Their corpuses begin to enlarge and to germinate, and, in course of time, they contribute their quota to the general bulk of the growth. In fact, Virchow holds that the primary focus of the tumour becomes exhausted in its activity, and that new foci of germination arise in the neighbourhood, which keep adding to the growth. Examine any sarcoma or cancer we choose, there are always parts of it in which growth is progressing more actively than in others, those parts whose activity has ceased being frequently discovered to be in a state of fatty

degeneration. In this way, if new accessions of germinating foci are added to the tumour, we can understand how it continues to grow even when the energy of its original cells is exhausted.

Now, if this be true, I think Cohnheim's theory will not bear criticism; for, if we hold by it, the tumour ought not to influence the parts which are not the subject of this embryonal peculiarity. We should expect that the embryonic tissue would exhaust itself in time, and that a period of quiescence would at last be reached. This, although true of some tumours, does certainly not hold good of all. There are certain sarcomata and cancers whose virulence seems even to increase as they get older.

The other theory on which the neoplasms might be accounted for is that of a local or general stimulant, acting on the cells of a particular part, and causing them to germinate. We have a parallel to this in the evolution of the uterus and mamma in pregnancy. Both of these organs are evidently in a more unstable condition than the other tissues of the body, from the frequency with which tumours of their respective tissues form. The myoma of the uterus, occurring in one of every ten women, clearly shows that there is a tendency to undue proliferation of the muscular tissue of that organ, and the frequency of cancer of the mamma shows that the epithelium of that gland is also in a similarly unstable state. The stimulation of pregnancy, whatever that may be, is sufficient to cause the increased activity of each. Causes other than pregnancy have a similar, although minor, effect. Cohnheim's theory will not explain this. There is evidently something influencing the uterus or mamma, respectively or collectively, which acts as a stimulant. Whether this be chemical or not, we do not know.

On the whole, although it may be said that the matter is as yet almost purely theoretical, I would be inclined to believe that the tissues generally are capable, under certain circumstances, of deriving new embryonic activity, and that some local influence is the cause of this; that, in some cases, this influence is withdrawn after a time, and that then the tumour becomes benign, but that, in others, it is continuous, and is capable of being propagated to adjacent parts; that, in this way, new germinal material is added to the tumour-mass, and so its growth is progressive in some parts, stable or retrogressive in others. I believe that more experimental evidence is required before the pathogeny of the neoplasmata can be settled.

THE RELATIONS OF PHTHISIS AND ALBUMINURIA.

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(Concluded from page 1228.)

CASE XII.—Catherine T., aged 38, mother of eleven children, a laundry-maid, was admitted March 6th, 1879. Her mother died of bronchitis. She stated that she had suffered from cough for two years, and that nine months ago she was attacked with shivering and fever, and confined to bed for three weeks; since that date she had been unable to follow her occupation. Cough had persisted and gradually increased. She had had hæmoptysis to a pint and a half two weeks ago, and a week later the expectoration was streaked. She had been steadily losing flesh for the last six weeks. On admission, her cough was hard, expectoration moderate; the catamenia had been absent four months, and irregular before that date. She complained of interscapular pain.

Physical Signs.—Cracked-pot sound was heard as far as the fourth rib on the left side. Cavernal croak was audible from the first to the third rib. The line of resonance of the right lung extended across the sternum to the left sternal margin. The heart's apex was raised; the impulse was between the fourth and fifth ribs. Posteriorly, cavernous sounds were audible above the right scapula; crepitation was heard at lower left base; the respiration was very harsh on the right side. Her weight was 6 stone 2 lbs.; urine normal. The patient suffered from night-sweats, and the temperature rose, in the afternoon, to 100° Fahr. on March 27th. In the beginning of April she complained of great thirst, and on the 16th albumen was detected in the urine, which was of specific gravity 1012. The temperature was then taken five times daily, and the averages were, at 8 A.M., 97.7°; at 11 A.M., 98.3°; at 2 P.M., 98.8°; at 5 P.M., 99.5°; at 8 P.M., 100.9°; maximum, 102.4°; minimum, 96.4°.

April 21st. Albumen had been detected in the urine every day, and the patient was rapidly becoming worse. There was now, in addition to the above physical signs, crepitation over the whole left posterior chest; also crepitation over the whole right lung.

April 22nd. Pulse, 120, small; respirations, 30. The patient was

wandering in her mind. The pupils were unequal, the right one being the larger. The tongue was protruded straight. She complained of dizziness and drowsiness, and died at 10.30 P.M.

The *necropsy* showed the right lung adherent at the apex and base, especially so to the diaphragm. The lung contained large pigmented patches, two inches in diameter, of transparent tubercle, with caseating centres. The patches were peripheral in the upper and lower axilla. The left lung was adherent at the apex and base; the upper lobe contained several communicating cavities; the lower, some pigmented tubercle. The spleen weighed 11 ozs., and was lardaceous. The liver weighed 5 lbs.; it was not lardaceous. The kidneys weighed 14 ozs., and were rather large. The capsules were adherent; the cortex was not diminished; the right kidney had a cyst of the size of a walnut on its convex surface. The kidneys gave no reaction with iodine, and presented the appearance of interstitial disease with nephritis.

REMARKS.—This case is given more fully, because it was evidently not one of lardaceous disease of the kidneys, though the spleen was lardaceous, a by no means rare occurrence. The history showed phthisis of old standing, manifesting a fresh tubercular outbreak in the opposite lung. The albuminuria seems to have been noted first in the hospital, but probably existed, in some degree, at an earlier date; and the renal lesions, which evidently terminated life by uræmic poisoning, were very acute.

CASE XIII.—Eliza Ann T., aged 46, married, had lost seven children from various chest-complaints. She had pleurisy and congestion of the lungs seven years before admission, and thirteen months ago cough, a sharp pain in the left side, with shortness of breath, and streaked expectoration, which had continued up to the time of admission, and were accompanied by night-sweats, and great loss of flesh. Lately, diarrhoea had come on. On admission, cough was troublesome. She could not sleep at night. She complained of dyspnoea and night-sweats. The urine was of specific gravity 1016, clear, containing one-twentieth of albumen. Crepitation was audible over both lungs, most marked and coarsest over the upper left part of the chest.

The patient remained about the same till April 7th, when the temperature-observations were commenced, and carried on till April 26th inclusive, a period of twenty days. The urine varied in amount from 46 ounces to 52 ounces; the specific gravity from 1008 to 1012; the albumen from one-twelfth to one-sixth of the test-tube. She had some phlebitis of the veins of the left upper extremity, and on April 9th complained of intense pain in the abdomen, of a dragging character; a swelling was discovered to the right of the umbilicus, which was tender and dull on percussion. Vomiting followed, and persisted for some days. She grew rapidly worse; the extremities became anasarcaous; the physical signs showed evidence of cavities having formed in both lungs, with extensive consolidations at the bases. She sank and died April 21st.

The temperature-averages for twenty days, *i.e.*, till five days before death, were as follows: At 8 A.M., 98.4°; at 11 A.M., 99.2°; at 2 P.M., 99.7°; at 5 P.M., 100°; at 8 P.M., 100°; maximum 102.4°; minimum, 95°.

The *necropsy* showed a curious hæmatoma or blood-cyst, of the size of a small orange, in the transverse meso-colon, but the source of the blood was not traced. The liver weighed 2 lbs. 10 ozs.; it was nutmeggy, and soft. The spleen had hæmorrhagic patches. The kidneys weighed 8½ ozs.; they were pale and granular, the appearance being due to interstitial disease, with chronic superadded tubal inflammation. The lungs had both pleuræ loosely adherent by oedematous areolar tissue. The lungs themselves were very oedematous, and contained patches of broncho-pneumonia, with emphysema at their borders. The right lung contained a large tuberculated cavity at the apex, and the left, three small ones in the upper lobe, surrounded by a deeply pigmented zone. The intestines were healthy.

REMARKS.—This is another instance of granular disease of the kidneys, supervening on old phthisis, as shown by the character of the cavities, and inducing pulmonary oedema. The thermic chart was, on the whole, low. The complication of hæmatoma was a curious one.

CASE XIV.—Mary P., aged 18, was admitted November 25th, 1879. She had cough, expectoration, and night-sweats, two years. During the last two months she had had diarrhoea, and was greatly wasted. In December, the ankles were noted to be puffy. Diarrhoea ceased after admission, but recurred in January 1880. The urine was found to be of specific gravity 1025, containing one-twentieth albumen.

Physical Signs.—On the right side there was crepitation to the third rib. On the left, distant cavernous sounds were heard from