ADDRESS IN PHYSIOLOGY.

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PROGRESS IN PHYSIOLOGICAL SCIENCE.

MR. PRESIDENT, AND GENTLEMEN OF THE BRITISH MEDICAL ASSOCIATION,—I value very much the honour of having been selected to give the Address on Physiology; and I thank you warmly for the mark of your confidence which it implies.

The great problems of life have in all time had a profound influence upon the heart and mind of man. Whatever concerns the prolongation of life or the increase of the capacity for enjoying it, the prevention or cure of those modified vital actions which we know as disease, has always interested the mass of mankind. Hence the mission of medical men, as extensive as humanity, whatever form it takes; uninfluenced by age, or sex, or country; succouring alike the orphan, the criminal, the virtuous, the poor, and the rich. The medical man is the true friend of all within his reach; he advises, instructs, befriends all alike. There is no one to whom accurate and incessant observation is so essential. His first step is to observe and record all the healthy phenomena of life; it is his constant care to secure the most fitting conditions for their exercise; and his last effort is to note how certainly their continued action brings about their own extinction, and how often they are suddenly arrested in their course by disease.

The delicate adjustments of vital operations, and the unstable physical and chemical equilibrium of living structures, present such difficulties to the physiologist, that thousands of years of the world's history had passed before we had learned a single fundamental doctrine applicable to all life on the globe. Yet I doubt if as great progress has been made in any science as in physiology during the past fifty years, or if such an amount of labour has been expended in the same time on any subject as has been devoted to the study of physiology in the last quarter of a century. Still, all we now know may appear very insignificant in the estimation of our successors of the next generation.

Every step in physiology concerns life and health; therefore, each must be made as secure as possible. I think nothing has given as great confidence and security in the advance of physiology, as the demonstration that all living matter has been derived from previously living matter of its own kind; and that all living beings and living tissues have originated from fragments of previously living beings or tissues, which, when detached, carried the properties of their parents with them.

It is quite true that living bodies are continually influenced and altered by external conditions, but it is also true that conditions at least as potent tend to their return to their original state. The changes which a particular mode of life may effect in the highest type of living beings may be such as to require three generations to make a glass-blower, but it is not probable that his children would care to preserve the advantages which they had derived by inheritance from their parent's father and grandfather.

The formed materials of our tissues differ widely from the original protoplasm to which they owe their origin; but some of that protoplasm remains in each, and still possesses powers of reproduction, which, in many instances, are no less startling because of the character than of the quantity of the tissue produced in a given time. The colossal increase in size, no less than the increase in numbers, of the muscular fibres of the uterus required to raise the standard weight of the adult organ from one and a half ounces to three pounds, is only paralleled by the still more rapid reduction, in two or three weeks, of the same organ from three pounds in weight to three ounces. This happens in an organ which is often more or less dormant for years together; but, in the continually acting diaphragm, the presence of an unusual number of protoplasmic corpuscles in each fibre points to the greater and more persistent activity of the change which takes place there. Observe the vastness, in comparison with its cause, of the change produced in the mode of nutrition of the uterus when an ovum, only $\frac{1}{16}$ th of an inch in size, has come into contact with a still smaller spermatozoon; and the not less remarkable change of a totally different kind when this ovum leaves the uterus. The establishment of different physiological relations has been attended, in the first in-

stance, by deposition and formation of tissue, in the other, by its disintegration and removal.

Changes of external conditions produce as remarkable results. Mr. Ward found ill-fed plants of the common centaury (*Erythraea centaurium*), only half an inch high, with one flower, at no great distance from better-fed ones four or five feet high, covered with hundreds of flowers. Without other difference than greater looseness of the texture of the soil, I had plants of the common rape (*Brassica napus*), between five and six feet high, freely branched everywhere, and, carrying leaves as large as ordinary dishes, as contrasted with others close by only fifteen inches high, but little branched, and having few linear leaves only about an inch long. And everyone is familiar with the marvellous change wrought upon the hive-bee when, from being fed on royal jelly instead of on ordinary bee-bread, it becomes a queen. Yet these naked-eye evidences of the influence upon vital activity of a change in surrounding circumstances are insignificant in importance when compared with those of which the results are witnessed daily in medical practice.

Dr. C. J. B. Williams showed that, when a drop of weak solution of capsicum is applied to the web of a frog's foot, dilatation of the arteries and capillaries takes place, and more blood circulates through the spot in a given time than before, and that from this condition recovery may take place and the experiment be repeated time after time on the same part. But if the solution be stronger, recovery will not occur, and the increased rapidity of circulation will give place to slowing and stagnation. In the first instance, the life of the vessels was affected, and their contractility impaired transitorily, but the stronger solution destroyed their contractility more completely, and produced the phenomena of inflammation, congestion, exudation, and stasis. No matter by what external means the life of the vessel is affected, the same result follows. And if the injury be inflicted from within, by adding some irritant to the circulating fluid, the effect is still the same.

Sir Joseph Lister demonstrated, in a series of beautifully contrived experiments, the delicacy of the relations between the walls of the blood-vessels and the circulating blood; that injury of the wall of a vessel causes arrest of the white corpuscles on the injured part with coagulation of the blood; and if the injury be considerable it will cause complete obstruction to the circulation. Disintegration of the white corpuscles takes place and acts as an efficient cause of the coagulation and stoppage.

On the maintenance of this nice balance of the relations between the blood and the tissue over which it flows, depends the issue whether the blood shall continue to flow or not.

The rupture of the internal coat of a vessel, or the alteration of the lining endothelium by endocarditis, causes arrest and disintegration of white corpuscles at the spot. Consequently, depositions of fibrin, or the formation of thrombi on the valves of the heart, are attendant phenomena on inflammation of the endocardium.

And Cohnheim found that stopping the circulation for from thirty-six to sixty hours through particular vessels in a frog, and then allowing the circulation to go on again, was attended by such exudation as occurs in inflammation. The walls of the vessels had suffered injury from the temporary arrest of the circulation; their elements seemed to have been loosened, and exudation of certain of their contents took place. It is important to note that this is not a mere passive transudation; it is attended with an active movement of living corpuscles through the injured wall—a movement which does not happen in the instance of the mesentery to which solution of sodium-chloride of double the normal strength, which stops amoeboid movements of these corpuscles out of the body, has been applied. An inflammatory exudation is readily distinguishable from the transudation of mere engorgement by being richer in albumen and corpuscles than it, and by coagulating more readily.

Dr. Burdon Sanderson, in his admirable statement of the results of his own observations, and in reviewing our present knowledge of inflammation, has called attention to the great accuracy of Sir William Bowman's early observations on keratitis; and has pointed out that not only do corpuscular elements migrate into injured spots of the cornea, but they accumulate upon and within pieces of dead membrane or other tissue inserted into the peritoneal cavity; and Dr. D. J. Hamilton found that they so completely fill the cavities of pieces of prepared and engrafted sponge, that it soon ceases to be visible. Dr. Sanderson has expressed the difficulty of maintaining the migration of corpuscles in such instances due to an increased attraction between them and the tissues; and he concludes that we are coming back to the notions of John Hunter, who accounted for the inflammatory blush by referring it to the action of the vessels.

On the other hand, it may be suggested that the changed conditions

have diminished the restraining influence of the walls of the vessels, and stimulated the corpuscles to more active migration than ordinary.

The interest and importance of the relations of the circulating fluids to the elements of the animal tissues demand a further consideration of them.

The structure and action of the supply-vessels of any part are doubtless very important, but they can scarcely equal in importance the relations of the tissue and blood-elements, where these lie quietly in contact, and mutually influence each other.

One can scarcely exaggerate the importance of the observation that the pressure impelling the secreted fluid onwards in a salivary duct is twice as great as that propelling the blood in the carotid artery from which that gland is supplied, and that a large amount of secretion is discharged by a salivary gland, on stimulation of its nerve, after the circulation of blood has been altogether cut off from it. In like manner, at the instance of a nervous impulse, a muscle similarly withdrawn from the circulating current, contracts and gives out carbonic acid and sarco-lactic acid, neither of which was free in it before the contraction took place. And in the gastric glands, the pancreas, and possibly in all secreting glands, the constituents of the secretions are slowly abstracted from the blood; and stored in some form of zymogen, until a nervous impulse suddenly causes their transformation into the active principles of the secretion, and its discharge.

Thus we localise the real laboratory of the organism: the place where the work of the body is done, the spot whence nervous impulses emanate, where motion results from chemical and vital changes, where the powers operate which regulate and produce secretions, excretions, nutrition, regeneration, and reproduction. It will be admitted that the simplest mass of protoplasm, whether plant or animal, selects all it needs for the varied purposes of its life from the more or less fluid matters within its reach; and, in exactly the same way, the tissues of our bodies select what they need from the fluid-plasma in which they are continually bathed. The vessels supply a larger or smaller quantity of this fluid, as the demands of the tissues are greater or less at one time than at another; but it is the business of each tissue to select, both as to character and amount, all it requires; and in this selection, no less than in the use it makes of the materials it has selected, the tissue can only be very indirectly aided by the blood-vessels.

The anatomical relations of the tissue-elements to the lymph-spaces, by means of which they are continually bathed in lymph, are very interesting, and have been admirably described and illustrated by Dr. Klein in his *Anatomy of the Lymphatic System* and *Atlas of Histology*. Dr. Curnow has given an excellent account of the history of the acquisition of our knowledge of the lymphatic system in the Gulstonian Lectures for 1879, published in the JOURNAL. Von Recklinghausen led the way, and so many accurate observers, in different countries, have followed him, that we now stand on very safe ground.

The result has shown that the acini, or the tubes of glands, the bundles of fibres of tendons, the layers of the cornea, fasciculi of muscles, and funiculi of nerves, are, in relation with lymph-spaces or vessels, more or less completely lined by endothelial cells, and occupied by lymph containing amœboid corpuscles in variable numbers. These Dr. Klein has shown to belong to the same system as the spaces between the fibres and bundles of fibres of areolar tissue, which contain here and there flattened and branched endothelial or connective tissue cells folded over the bundles which are themselves continually bathed in lymph containing amœboid corpuscles. Similar spaces, under the mucous membrane of the alimentary canal or air-passages, are continuous with the cement-substance between the epithelial cells, where also branched connective tissue cells occur, together with occasional amœboid corpuscles. All such spaces communicate directly with large lymph-canals, immediately succeeded by irregularly dilated lymphatic vessels furnished with valves.

The immediate effect of medicines introduced endermically is abundant proof of the rapid and free communication of the lymph of the spaces of areolar tissue with the current of the blood, whilst if Dr. Creighton's observations on the absorption of fat from the intestines be confirmed, we shall have learned that the emulsified fat of chyle passes through the cement-spaces of the intestinal epithelium into the lacteals and mesenteric glands, the epithelium itself discharging the function of secretion.

But there are much larger reservoirs of lymph than the spaces of connective tissue, tendon, and cornea. The great lymphatic sac of the frog, the serous and synovial cavities, and the sheaths of tendons of mammals and man are similar spaces. Von Recklinghausen was the first to witness the passage of milk and other fluids, containing visible particles, through the stomata of the peritoneum covering the tendon of the diaphragm into the lymphatic vessels, and the dis-

appearance of fluids from the peritoneal sac by this means. You will all call to mind many instances of rapid disappearance of recent pleuritic and peritoneal effusions; others, where such effusions have remained undiminished in amount for weeks and months; and some in which the effused fluid, after a time, assumed all the characters of pus. Coagulated blood does not disappear from the peritoneal cavity, but defibrinated blood is absorbed, and its corpuscles continue to live in the circulating blood.

Ludwig and Schweigger-Seidel have pointed out that the respiratory movements are the chief cause of the entrance of fluids into the lymphatic spaces through the stomata of the peritoneum; that, during the descent of the diaphragm, lymph is drawn into the spaces between the tendon-bundles by their expansion, and pressed on at the same time in the pleural lymphatics furnished with valves; whilst, during the ascent of the diaphragm, exactly the opposite action takes place, the diaphragm thus playing the part of a pump.

The pleura of the intercostal spaces is also provided with stomata, and is similarly related to lymphatic vessels; and as there is an arrangement of a similar kind on the surfaces and in the substance of all fasciæ and tendon-sheaths, it is not improbable that the connection of a large number of muscles with fasciæ rather than bones serves the same purpose. How much of the pleasure derived from muscular exertion depends upon the promotion of the circulation of lymph about all these parts, and upon their consequent invigoration, we may never be able to estimate, but no one can question the importance, even in the limbs, of the free circulation of lymph.

Let us now return to the contents of these spaces. We bear in mind that epithelial cells are masses of protoplasm variously modified for secretion, protection, or for entering into the construction of the terminal organs of the nerves of special sense, and that between epithelial cells, whether on the skin, the cornea, or on mucous membranes, there are spaces occupied by semifluid cement, with branched connective tissue corpuscles and amœboid or white blood-cells. We trace these cement-spaces onwards, and find them continuous with the connective tissue spaces under their respective membranes and with lymphatic vessels. In the different spaces the contained corpuscles vary greatly in number, but a food-supply is always afforded them by blood-vessels in proportion to their numbers.

Under extensive tracts of the mucous membrane of the alimentary canal and respiratory organs, very notably in the substance of villi and around Lieberkühnian follicles in the intestine, the spaces are crowded with amœboid or lymph-corpuscles forming adenoid tissue, or when masses of such tissue accumulate in more or less spherical or pear-shaped blocks, they constitute solitary glands, or the glands of the patches of Peyer. All such parts are supplied very freely with capillary blood-vessels; and, as Brücke demonstrated many years ago, their spaces communicate with unusually large and numerous lymphatic or lacteal vessels. The lacteals become almost immediately connected with the largest group of lymphatic glands in the body. The muscular and fibrous wall of the vessel opens out, and, becoming greatly increased in amount, forms the capsule and trabecule, whilst the cell-elements of the connective tissue forms the framework of the adenoid mass we call lymphatic gland. The substance is composed of lymphoid corpuscles, multiplying with a rapidity which is measured by their food-supply from capillary blood-vessels and the passing stream of chyle, whilst their detachment is in proportion to the amount of distension by passing chyle. The greater the amount of chyle, the greater is the amount of corpuscles added to it as it passes, each corpuscle being derived, both in substance and properties, from a pre-existing one, or as in the original development from the differentiated protoplasm of the endothelial cells.

Dr. Klein has described small cells which bound the stomata of serous membranes, cover the surface near the stomata, and often extend along considerable tracts of their surface. These are smaller than the ordinary endothelial cells, and germinate freely under ordinary healthy conditions; but in such unhealthy states as are induced by the presence of pieces of gutta serena or irritating substances injected into the peritoneal cavity, they germinate with great rapidity, and form large villous projections on the surface of the membrane, the newly produced cells falling into the cavity or presenting themselves in large numbers in the adjacent lymphatic vessels.

Thus, in the same way as, in lymphatic and other blood-forming glands, white corpuscles of the blood are continually formed and thrown off into the stream of chyle or lymph, so under both normal and abnormal circumstances, the cells bordering the stomata and covering parts of the surfaces of serous membranes multiply rapidly, whilst in inflammation, not only these lymphoid cells, but the branched cells of the matrix also, undergo very active proliferation. The natural food-supply of such cells is derived from the blood, the amount and

rapidity of circulation of which is largely increased in some stages of inflammation.

I now ask your attention to the structural relations of the walls of blood-vessels to the tissue-elements. The most cursory examination of blood-glands, such, for instance, as the spleen and the red marrow of bones, shows an important adaptation of these parts to each other. Ordinary capillaries, which are really little more than spaces between the elements of tissues lined by endothelial cells, loosely cemented together at their edges, have, frequently, sinuous spindle-shaped or angular dilatations upon them, whilst their walls have projecting processes directly continuous with the branched connective tissue corpuscles of the adjacent parts, a connection which shows the close similarity of the lumen of the vessel to the spaces of areolar tissue, whilst the endothelial cells of the vessel correspond to the less numerous, but similarly flattened endothelial cells of the spaces, and to tendon and corneal corpuscles, which cover in an equally sparing manner their respective tendon or corneal spaces. Indeed, the whole lymphatic system, with its lymph canalicular spaces, and its definitely walled vessels, is neither a new nor an added system, but a part, and a most important part, of the general vascular system of the body.

If we trace a small artery in the spleen, we see the tissue of its wall opened out into spaces occupied by lymphoid cells, a veritable mass of adenoid tissue involving the whole or part of the circumference of the vessel; and when at length the vessel ends, it empties its blood into the spaces of the pulp, bounded and supported by the flattened, branched, endothelial elements of the walls of the commencing veins. Where the adenoid masses, the Malpighian corpuscles, of the walls of the arteries, abut upon the pulp-tissue, there is no separation, the elements of the adenoid reticulum and those of the walls of the venous sinuses being continuous; whilst the lymphoid cells of the adenoid tissue are free to mix with the venous blood in the sinuses. Here, as in the case of the lymphatic glands, the organ is subjected to great distension after the absorption of food, which not only leads to the formation and separation of large numbers of new lymphoid elements, but, at the same time, the cellular protoplasmic elements of the venous sinuses become very active, take up old coloured corpuscles, break them down, and set free their variously oxidated remains into the bloodstream. The vascular arrangements of the spleen, at the same time as they tend to retard the flow of the blood, are, no doubt, highly advantageous for the completion of the changes which the blood undergoes in the organ; whilst the necessarily tardy flow of the blood is, no doubt, compensated by the large size of both the artery and the vein, and the loss of force by the rhythmical contractions of the organ, so beautifully demonstrated by Dr. C. S. Roy. Lymphatic glands also have a muscular capsule and muscular trabecule; but, as yet, we have no evidence of their having rhythmical contractions.

I cannot pass without mention the largest living mass of protoplasm in the body, the liver; at one period employed in the production of blood-corpuscles, and then half the weight of the body. Originally formed upon the vitelline veins, and subsequently transferred to the umbilical, and then to the portal vein, as each in turn becomes the recipient of the food-supplies, there can be no doubt that, whilst its function is mainly to make and maintain the blood, its methods of action still involve great physiological secrets.

From the preceding considerations it is plain that, at certain special parts of the circulating system for lymph and blood, lymphoid or white blood-corpuscles are produced in adenoid tissue from pre-existing corpuscles, at a definite rate. If Quincke be correct in his supposition, that the duration of the functional activity of red blood-corpuscles is not longer than two or three weeks; we have in this a measure of the required reproductive capacity, for in healthy conditions a balance of the absolute and relative numbers of the corpuscles is very accurately maintained.

But this does not always happen. My late esteemed teacher and friend, Dr. Hughes Bennett, in his original description of leucocythemia, pointed out that an amazing relative increase of white in relation to the red corpuscles of the blood occurs in connection with enlargement of various of the blood-forming organs, and the disease is now universally recognised. In the second case which came under the notice of Dr. Bennett, I had the pleasure of making the examination, and of recording and sketching the microscopical characters of the blood in the *Pathological Reports* of the Royal Infirmary of Edinburgh. In that case the spleen, liver, and intestinal glands were all enlarged.

In this disease there is a greatly increased production of lymphoid cells, in situations where there is abundance of nutritive material; and this increased formation of corpuscles is possibly attended by a conversion of fewer white into red blood-corpuscles than ordinary, thus greatly increasing their numerical disproportion.

As lymphoid cells can also be produced in large numbers in and

near the stomata and on the surface of serous membranes, it is probable from such sources that the pus-corpuscles of empyema and peritoneal effusions arise. And it may be asked whether the amœboid cells which migrate through the walls of the blood-vessels on the onset of inflammation possess the power of multiplying on surfaces which are now supplied with a largely increased amount of blood.

This is improbable, for many reasons. Actual observation of such multiplication has not yet been satisfactorily obtained. Dr. D. J. Hamilton, in the record of his very interesting observations on the healing of ulcers and sponge-grafting, says that he has carefully watched the exuded leucocytes, and has never seen them get larger, either by overnutrition or coalescence.

Ranvier, who thinks it probable that lymph-cells are connective tissue-cells set free from adenoid tissue, believes that they will neither move nor multiply except when freely supplied with oxygen; that the free supply of oxygenated blood by the capillaries of lymphatic and other blood-glands is the means of their multiplication, and that the absence of oxygen in the lymphatic vessels stops it. He sees in the rapidity of the circulation of blood an explanation of their migrating in small numbers only in health, whilst, on the slowing or arrest of the circulation in inflammation, they migrate in large numbers, and, getting beyond the reach of the supply of oxygen, disintegrate and cause coagulation of the plasma. He points to the experiment of introducing fragments of phosphorus under the skin, without arousing inflammation and migration of leucocytes, as indicating that the phosphorus has taken up the oxygen present, and destroyed the amœboid movement necessary for migration, and thinks that the effect of cold in checking exudation is due to a similar action. Whatever the influence of oxygen on the manifestation of the vital movement of lymphoid corpuscles, it is certain that lymph differs widely from blood in containing a mere trace of oxygen.

In the formation of an acute abscess, the part is hot, painful, and swelled; exudation and coagulation of the exuded matter occur, with migration of leucocytes through the vascular walls; the pain becomes more severe and throbbing, and the heat greater than before; next day, there is indistinct fluctuation from the formation of pus, and from this time the pain and heat lessen, and the matter makes its way by softening and degeneration to the surface. The greater heat and pain preceding the formation of pus indicate greater distension of the vessels and greatly increased exudation; or that the larger supply of blood which increased the pain and tension, had furnished the food for the more rapid generation of lymphoid corpuscles.

When in diffuse phlegmon punctures are made one day, and discharge thin serous fluid, and the next day the whole areolar tissue is distended with pus, there is little room for doubt that a rapid generation of lymphoid corpuscles has taken place at that very part, and produced the pus. If this happen in one instance, it is probable that in other cases, too, pus is either formed by rapid proliferation of connective tissue corpuscles, or that it is the result of rapid formation of corpuscles from those which first migrated, and that the primary cause of this is an increase of the normal attraction of the tissue for the nutritive matters of the blood, where the lymph-stream flows more slowly, and the corpuscles drag lazily along the wall, then penetrate it, and escape with the plasma in large amount, at a time when the cement between the endothelial cells has softened and the spaces occupied by it have become widened.

But, whatever be the cause, let us not lose sight of the main phenomena: millions of lymphoid corpuscles have been rapidly produced somewhere, and they have been produced from pre-existing corpuscles of the same kind. It will scarcely be suggested without evidence, that the whole circulating blood has taken on either an entirely new, or certainly an unwonted, action in order to supply more lymphoid corpuscles than ordinary to the particular part where we find them accumulate; and it is little less difficult to maintain, that because of some local injury a multitude of lymphatic or other blood-glands at a distance have produced a greatly increased quantity of corpuscles to migrate into the injured spot. We know that the period when the corpuscles of blood-glands multiply rapidly and fall off in large numbers into the circulating current is the period of tension and turgescence of such glands—a tension and turgescence produced by an extraordinary afflux either of blood, or of both blood and chyle. We cannot dissociate, either here or anywhere else, increased activity from increased supply of nutritive material, and we have no ground for supposing that there is an increased supply of nutritive material to the blood-glands because of a distant local injury. What remains? The admission is now as full and complete as I could wish in the instance of cartilage, that whatever changes take place in it are the results of the exercise of its own, and of no borrowed, power; and though some of the old leaven clings to the accounts we get now and then of the

living actions of bone and tooth, I have no doubt that what is true of a living tissue easily made the subject of observation is true also of more complex ones with whose elements other accessory tissues are mingled.

In the seats of formation of pus we have been considering, the corpuscular and formed tissue-elements are ordinarily bathed in lymph transuding through the cement-spaces of the endothelium of their vessels, and having amongst it, here and there, amoeboid corpuscles. Now, a greater amount of blood than ordinary circulates through the vessels; these are dilated; the cement between their endothelial cells is of greater bulk and softer than ordinary; the fluid plasma and lymphoid corpuscles of the blood pass out into the tissue, which, becoming tense and having its vitality impaired, acts as foreign matter to the effused fluid, and leads to the disintegration of some of its corpuscles, and coagulation. Meantime, the supply of nutritive material increases; the redness, heat, and throbbing become more intense; the part becomes firm and brawny with its increasing mass of corpuscles; and then, the violence of the action being over, and the vitality of the central part of the mass lessened by the tension; pallor and oedema, with great relief from pain, succeed; softening, degeneration, and solution of both tissue and exudation occur, and the fluid mass approaches the surface and points.

If it seem strange that the same process should produce necrosis at one part and rapid growth and multiplication of corpuscles at another, let us recollect what happens in the healing of ulcers. The surface is no longer supported by firm skin, therefore its vessels dilate, and exudation occurs freely. Stimulated to unwonted activity, the connective tissue corpuscles multiply rapidly; they first form rounded, then spindle-shaped cells, and ultimately the fibres, corpuscles, and ground-substance of the new connective tissue of the cicatrix; whilst the exudation and the migrated corpuscles it contains disintegrate and soften into pus which escapes on the surface. As the healing proceeds, the epithelial cells at the edge of the ulcer divide and produce others like themselves, which gradually extend over the surface and cover the newly formed connective tissue corium with an equally new epithelial layer, both having respectively been derived from similar pre-existing tissue. The newly formed cicatricial tissue scarcely equals the old in bulk, therefore the surface is generally below the surrounding level, the ulcer healing down, not up, as Dr. D. J. Hamilton has expressed it in his admirable demonstration of the changes attendant on the healing of an ulcer in the *Journal of Anatomy and Physiology* for July, 1879, from which I have freely extracted these details.

Let us turn for a moment to the peritoneal surface on which such a proliferation of cells as we have been considering has been going on for some time, and we shall have no difficulty in understanding that, whilst effusions may be absorbed by it with great rapidity as long as its stomata are healthy, when these are obstructed or obliterated by masses of proliferating corpuscles, the diaphragm, pump as it may, becomes entirely powerless to empty the sac of its fluid contents.

A very interesting case occurred to Dr. Whittle of this town, in which obstruction and rupture of the thoracic duct led to the passage of the whole chyle into the abdominal cavity for many months; the surface of the peritoneum was everywhere studded with tubercles, and in consequence, absorption of the fluid could not take place. It was removed by tapping at intervals in quantities of twenty pints or more.

The importance of the physiological arrangement, by which the lung is irrigated by lymph from the pleural to the vesicular and bronchial surfaces, has, I think, not been sufficiently appreciated. The application of cold to the surface of the body produces general congestion of the lung, taking the form of pneumonia, pleuritis, or bronchitis, in different persons, according to their respective liabilities to these diseases. But the addition of one of these diseases to another which has been primarily produced, is not as easy to explain by reference to their entirely different capillary blood-vessels, as by the great freedom of communication of their lymph-passages.

Salivary secretion, discharged after stimulation of the chorda tympani of a salivary gland deprived of circulating blood, is no doubt derived from lymph, previously stored in the gland itself; but under normal conditions this exalted action of the gland-tissue is attended by the circulation of a greatly increased quantity of blood through it, a notable instance of afflux of blood attendant on increased vital activity of the tissue. The case of muscular tissue is exactly similar.

I presume there can be no doubt that the increased activity of the circulation leads to increased transudation of lymph, which, however, does not coagulate, because the healthy limit has not been passed. But if the lymph had transuded into tissue which had been previously damaged, or damaged by the exudation itself, it would have coagulated, as the veritable exudation of inflammation does.

When we call to mind that the cellular elements of capillary walls

are continuous with the framework of lymph-spaces, which themselves communicate through the endothelial cement with the lumen of the capillary tube, the continuity seems to reduce the question, whether the phenomena of inflammation depend on increased vital attraction of the tissue for blood, or on some altered vital action of the vessels, to one mainly of words.

Yet the separation which is effected by the endothelial cement between the circulation of red blood-corpuscles in capillary vessels, and that of lymph and white corpuscles only in lymphatic spaces, is a real separation—a separation by a living colloidal septum of great liability to change. It suggests the necessity of a supply of oxygen and red corpuscles to some tissues, whilst others, such as cornea, have all their vital needs supplied by fluid plasma and white corpuscles.

If I have occupied much of your time on matters which I conceive to involve fundamental principles of physiology, and its twin-sister pathology, and made free use of vital action, of which we cannot hope to learn more than the manifestations, let me plead the powerful influence of early impressions gathered from a most revered and philosophical teacher, the late Dr. Alison, who held that the essential peculiarity of inflammation is a peculiar perversion of nutrition or of secretion.

In the very pleasant examination of the border-ground of physiology and pathology which the writing of this address suggested, nothing has been more forcibly brought before me than the clear insight which the painstaking and accurate investigations, and the genius of Sir James Paget, gave him long years ago into many vital phenomena which seemed startling when afterwards they were spoken of individually. Thus, in his lectures at the College of Surgeons, from 1847 to 1852, he demonstrated many of the conditions under which exudations coagulate or are restrained from coagulating,—conditions which Sir Joseph Lister's subsequent careful experiments have more fully elucidated: in connection with the conversion of lymph corpuscles into granule cells, inflammatory globules of Glüge, a change first demonstrated by Reinhardt and independently by Sir Andrew Clark, he pointed out that it is impaired nutrition, fatty degeneration, not death, which leads to absorption; he described most graphically the hardening of the wall of an abscess by coagulation of plasma, which neither the exuded corpuscles nor the fluid plasma alone could effect, and followed this by a clear account of the subsequent liquefaction of the hardened mass by what he styled "liquefactive degeneration," a great feature in Dr. Ziegler's more modern description and demonstration of what happens in the formation of a blister from a burn, and in the disappearance of clots of blood; and in the same lectures Sir James pointed out that granulations and clots of blood hinder the healing of wounds, leaving it for Dr. Hamilton only quite recently to prove this by irresistible microscopical evidence.

Knowledge derived from experience is never more interesting than when confirmed by scientific examination. Dr. Hamilton's paper on sponge-grafting recalled some of the earliest lessons of my professional life under a very able surgeon, the late Mr. R. C. Botham of Chesterfield. He taught me to treat foul ulcers of the leg in working men by scrupulous cleanliness, a pad of lint steeped in solution of chloride of lime on the ulcer, then oiled silk, and a constantly applied bandage, making equal pressure from the toes upwards, and kept wet with solution of chloride of lime. The success of this treatment was most marked, and I now see that, beginning with an absolutely clean surface, the dressings acted antiseptically, they prevented the contact of the atmosphere, and afforded the support which Dr. Hamilton has shown to be so essential for healing wherever the restraining pressure of the skin has been removed.

Dr. Cory's unfortunate success in vaccinating himself with matter taken from the cow-pox pustule of a syphilitic child will lead to a reconsideration of the respective powers of development of the different constituents of the blood, and to the relations of its white nucleated, to its coloured non-nucleated, constituents. At the last meeting of the British Medical Association, Dr. Schäfer called attention very pointedly to the function of reproduction of the nucleus of a cell, and it is long since Dr. Beale showed the great power of the germinal matter as compared with that of the formed material of tissues. Yet for years the startling proposition has been maintained that syphilis is alone communicable in vaccination by the coloured non-nucleated formed constituents of the blood. Every medical man knows the potency of the lymph taken early from a vaccine-vesicle as compared with that obtained in the later stages when the lymph-corpuscles have degenerated into pus. And the previous considerations which I have urged upon you show that these lymph-corpuscles, accumulated in the vaccine-vesicle, have been produced in this local inflammation either by migration and subsequent multiplication of the white corpuscles of the blood, or by active proliferation of the

connective tissue corpuscles of the part; in either case, from germinal matter, active living protoplasm, if not by the direct agency of the nucleus of such matter.

Recalling Mr. Goodsir's happy demonstration that the cells of lymphatic glands are developments of the epithelium of lymphatic vessels, and Dr. Klein's beautiful tracing of the continuity of endothelium, and the corpuscles of connective tissue at the fenestræ of omenta and in other situations, we recognise the family relationship between the lymph corpuscles, which, when detached, constitute white corpuscles of the blood, the endothelium of serous membranes so often found germinating abundantly, and the connective tissue corpuscles which Dr. Hamilton has figured and described as multiplying with great rapidity when stimulated by the agents causing inflammation, and unduly fed by a largely increased afflux of blood.

If it be asked why syphilis does not more frequently follow vaccination, the reply is simply that the greatest care is taken to select none but perfectly healthy children for the collection of lymph, and that it is possible that when lymph has been collected where syphilis, though present, was not recognised, the results may not always have been referred to their proper causes.

This leads me to mention the most difficult, exciting, and important problem of the day; whether other diseases than small-pox can be deprived of their virulence by vaccination.

You are aware with what ardour M. Pasteur has espoused the affirmative side of this question, and it was very natural that having had a certain amount of evidence that infectious diseases of animals may be deprived of their fatal effects by previous vaccination, he should have been led to hope that what is true of one is true of all, and that in this way, even hydrophobia may be deprived of its horrors.

The exceedingly careful researches of Dr. Klein, described with such accuracy of detail that they may be followed by any one, have shown that there are numerous pitfalls in the way of such inquiries, and that we are yet very far from being able to foresee the end of them. Yet the progress made gives great hope for the future, for careful experiments, by Drs. Klein and Roy, and by Dr. Burdon Sanderson and Mr. Duguid, have clearly shown that sheep inoculated with anthrax blood of white mouse, cattle inoculated with anthrax blood of the guinea-pig, and cattle inoculated with anthrax blood of the South American bischach, are, for a time at least, insusceptible of a fatal attack of the malady.

Dr. Klein has found that the virus which communicates swine disease is a form of bacillus which he has been able to cultivate out of the body in various ways, and which is capable of forming spores when exposed to the air. But though the organs of a dead animal swarm with the bacilli, these soon degenerate and become harmless, without forming spores, if the body be not cut; and this happens equally whether the body be interred or not.

From long experience, I am satisfied that the bodies of persons who die of small-pox or of puerperal or other fevers may be dissected without harm if properly prepared.

Dr. Burdon Sanderson has suggested the possibility of the determination of the morbid process in contagious diseases by an action similar to the spontaneous arrest of septic fermentations by the development of members of the aromatic group of chemical compounds destructive of any further manifestation of the vital activity of septic microphytes; and he has undertaken to direct a series of researches on this subject.

On the one hand, what can be more alarming than that, under certain conditions, living organisms of the utmost minuteness enter the body, and multiply with a rapidity with which fungi alone can multiply, corrupting the blood, causing local coagulations, obstructions of vessels, abscesses, and death: and, on the other hand, what can be more comforting than Dr. Sanderson's happy reference to the manner in which salivary, gastric, or pancreatic digestions furnish the means of their own arrest, and to the similar manner in which the organisms containing the virus of contagious diseases prepare the means of their own destruction.

Surely the day will come when it will be seen that gratitude and reverence are due to such men as Pasteur and Koch, and Sanderson and Klein, rather than that they should be assailed with insult, and hindered by mischievous legislation, as if they were criminals rather than benefactors of the whole human and animal races.

Let me mention certain circumstances which, I think, indicate that we are on the eve of great simplification and extension of our knowledge. It was a great step when the late Master of the Mint taught us the difference between crystalloids and colloids, and many of the laws of diffusion and osmosis. It led the way to an intelligent investigation as to how, in the process of digestion, colloidal starch and albu-

men are fitted to pass through the membranous walls of the alimentary canal. We have found that contact with a mere trace of saliva or pancreatic or intestinal secretion suddenly converts starch into sugar, and that a large number of other organic matters produce a similar result. Bernard showed by experiment how different cane, grape, hepatic, and diabetic sugars are in their relation to the economy; that starch and sugar are converted into fat by the liver; and that, by an insignificant lesion of the medulla oblongata, temporary diabetes can be produced. And we know, further, that, during the conversion of starch into sugar, there are many almost insensible stages. The process is influenced by numerous conditions which require investigation at every step, to enable us to trace these substances at their entrance into the economy, in the regions where they contribute to the production of heat and motion, and until their final deposition or discharge in some more highly oxidated form.

Similarly, I would suggest the most careful observation, not by one person, but by everyone in his own sphere, of the conditions under which albuminoid matters are changed, whether after their entrance into the upper or lower end of the alimentary canal; of those under which they pass into the blood, circulate, and become tissue; also of the forms under which they reappear in their variously oxidated conditions in the urinary excretion in health and disease.

The marvellous differences between albumen of the egg and serum, and albumen washed free from salts, or when changed into acid, or alkali-albumen; the modes of production of peptone and its varieties; the differences in the conditions and results of the action of the gastric, pancreatic, and intestinal secretions; and, very specially, the appearance in the urine in disordered or diseased conditions of albuminoid substances yielding reactions, showing that the variety of forms in which these substances appear are no less numerous or closely related than those of the varieties of sugar and starch, all point to the necessity of rigorous investigation, and to the possibility of presenting these substances and their various alternations in a light far more simple than has yet been suspected.

It is, unfortunately, the custom in this country to leave such investigations to be undertaken by private individuals, very few of whom have the necessary physiological and chemical knowledge, and fewer still have also the requisite time and means at their disposal. That we have men admirably fitted to direct and aid, or to conduct such inquiries, is plain from the researches of Simpson and Thudichum; and the aid rendered by Gamgee, Ralfe, and T. C. Charles. And I am not without hope that the public spirit of this great country may yet be aroused by the expressed opinion of the President of the Royal Society, as to the duties of the State in such matters; and that something worthy of the nation may yet be done to aid the teaching of science, and to promote scientific inquiry.

STRATFORD-ON-AVON COMBINATION.—Mr. Fosbroke has again to request his authorities to invite the urban districts (Stratford-on-Avon and Evesham), for which he acts as health-officer, to authorise him to combine his reports on these boroughs with those on the rural districts. It is obviously desirable that Mr. Fosbroke's "résumé upon the sanitary state of the whole district" should be issued "in a collective form;" and we trust that his authorities, if they have not already done so, will do their best to further this end. But a feature in the annual report for 1882 which furnishes even greater cause for regret is, that the authorities did not instruct the subdistrict registrars to make returns of births to the medical officer, who was thus unable to calculate any birth-rates, and consequently to give full particulars as to infantile mortality—a subject of special interest in any report upon the sanitary condition of a district. The vital statistics are necessarily somewhat brief. The respective death-rates in Stratford-upon-Avon, Alcester, and Evesham were 13.1, 15.8, and 13.3 per 1,000. It is satisfactory to note that these rates show little variation from the extremely favourable ones for the previous year. The zymotic death-rate in Stratford was .8, in Alcester 1.4, and in Evesham 1.1. The increase, as compared with 1881, was in Alcester due to whooping-cough, and in Evesham to "fever." An outbreak of typhoid fever in this latter district is surrounded with considerable interest. After no little investigation it was ascertained that all the persons attacked—with one exception, and that doubtful—had attended a "regatta." Subsequent inquiry led to the conclusion that the water used for "spirits," lemonade, or ices, was the root of the evil, having been drawn from a polluted well. Mr. Fosbroke expresses his belief that the propagation of typhoid fever through the agency of lemonade is unique, though he points out that the competent authorities who have criticised his report admit that his explanation of the outbreak was the correct one.

THE will of Dr. George James Hilbers, of Cavendish Place, Brighton, has been proved, and duty paid on personal estate exceeding £17,500.