THE
THIRD HUXLEY LECTURE.

LISTER.

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DELIVERED BEFORE THE MEDICAL SCHOOL OF CHARING CROSS HOSPITAL,

BY

LORD LISTER,

F.R.S., F.R.C.S.

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PREFACE.

This Lecture, delivered October 2nd, 1900, was published in *The British Medical Journal* of October 6th of the same year. As it so appeared, having been passed hurriedly through the press, it contained various inaccuracies, and I made arrangements for having it reprinted in separate form. I had finished correcting the proofs, when circumstances into which I need not enter led to delay, which has been since extended by several years of serious illness, so that I long abandoned all idea of the Lecture appearing again during my lifetime.

But it occurs to me that, though belated, it may still have interest for some of my professional brethren; and I have decided to issue it again as it was originally given.

LISTER.

February, 1907.

THE HUXLEY LECTURE.

WHEN the Council of Charing Cross Hospital did me the great honour of asking me to deliver the third of the Lectures instituted by them in memory of Huxley, the illustrious former pupil of their school, at the same time conveying their desire that the subject of it should be my own work, I at first reluctantly declined, on the ground that what I had done had been for the most part already published. But when the Dean, who assured me that he expressed the unanimous wish of his colleagues, urged me to reconsider my decision, I felt unable to refuse compliance with a request so very kindly made. It also occurred to me that, as my papers are scattered through a variety of media of publication, extending over a pretty long period, the earlier ones especially being probably little known to the present generation, it might perhaps be not without interest for me to refer on this occasion to some of the more salient of such observations as bear more or less directly upon the Antiseptic System of Surgery, while I should at the same time be complying with a wish that has been expressed that I should give some indication of the circumstances that led me to that subject.

As a Student at University College I was greatly attracted by Dr. Sharpey's lectures, which inspired me with a love of physiology that has never left me. My father, whose labours (*vide* "On the Improvement of Achromatic Compound Microscopes," by J. J. Lister, Esq., "Phil. Trans.," 1830) had raised the compound microscope from little better than a scientific toy to the powerful engine for investigation which it then already was, had equipped me with a first-rate instrument of that kind, and I employed it with keen interest in verifying the details of histology brought before us by our great master. When I afterwards became house surgeon under Mr. Erichsen, I applied the same means of observation to pathological objects.

One of the earliest records that I find of such work is in the form of sketches of the corpuscles in the pus in a case of pyæmia, which occurred after excision of the elbow in a little boy. The cancellated tissue of the humerus at the seat of operation and the adjacent part of the medullary cavity were seen, on *post-mortem* examination, to be occupied by thick, yellow pus, and similar fluid distended the brachial and axillary veins and their branches, including not only those leading from the bone towards the venous trunks, but also those proceeding from other parts of the limb, while the upper part of the axillary was plugged with a firm adhering clot. There was also suppuration in one knee-joint and multiple abscesses in the lungs. I was struck with the fact that the pus was to be found not only in the course of the channels leading from the original seat of mischief to the main trunk, but also in branches along which it must have advanced in the reverse direction in spite of the valves of the veins. The plugging of the axillary seemed also a very noteworthy circumstance. Sédillot had shown that multiple abscesses in the lungs were caused by introducing pus into the veins of an animal; and it seemed probable that the collections of pus in those organs in the present case had been of similar metastatic origin. Yet the plugging of the axillary, shutting off the pus in the veins from the general circulation, seemed inconsistent with such a view. I took careful Camera Lucida sketches of the constituents of the pus from the various situations in which it occurred; and I also made a record of the magnifying power employed, by sketching with the camera the scale of a micrometer placed upon the stage of the microscope. And I would venture to recommend this practice strongly to pathologists. The sketch which I then made is as valuable to me to-day as if it had been made yesterday. I see from my drawing what I noted at the time, that the solid constituents of the pus were in no case pus corpuscles such as we then knew them, and I also see that they were not leucocytes. I could not explain at the time the facts that I observed, but subsequent investigation has, I believe, made them intelligible.

An epidemic, as we termed it, of hospital gangrene occurred during my house surgeoncy, and I was charged with carrying out the treatment. This consisted in scraping away very thoroughly under chloroform the brown pultaceous slough and freely applying acid pernitrate of mercury to the exposed surface. The result was, as a rule, that, when the eschar caused by the powerful caustic separated under poulticing, a perfectly healthy granulating sore was disclosed which healed kindly under ordinary dressings. The only exception to this rule was in the case of a very stout woman, in whom the disease attacked an enormous wound of the forearm caused by an accident which had raised a very large flap of skin. In that case the caustic application removed indeed the pain and the extensive inflammatory blush; but when the slough separated, a small brown spot was seen at one place among the otherwise healthy granulations, and this spread with astonishing rapidity over the entire sore. The treatment was tried again and again with the same result, till, the deep structures of the limb having become seriously involved, Mr. Erichsen resolved to amputate. On the evening before the day fixed for the operation I again put the patient under chloroform and, after scraping the sore very thoroughly allowed the liquid caustic to lie in pools upon it for a quarter of an hour in order to destroy as effectually as possible all material in the sore which might otherwise infect the amputation wound. With a similar object I washed the skin of the limb thoroughly with soap and water, including the shoulder, where it had been decided to perform the amputation. The limb having been removed next day, the stump healed perfectly kindly. Here, as in the other cases, local treatment proved efficacious.

I was greatly struck with the clear evidence which these cases seemed to afford that the disease was of the nature of a purely local poison. In the hope of discovering its nature I examined microscopically the slough from one of the sores, and I made a sketch of some bodies of pretty uniform size which I imagined might be the *materies morbi* in the shape of some kind of fungus. Thus as regards that form of hospital disease, the idea that it was probably of parasitic nature was at that early period already present to my mind.

On visiting Edinburgh by Dr. Sharpey's advice in order to see something of Mr. Syme's practice, I was fascinated by the prominence that he gave to the pathological side of surgery as well as by his rare diagnostic judgment and his surpassing powers as an operator. Under him I had the unexpected great privilege of a second house surgeoncy, which extended over upwards of a year, and in the great Royal Infirmary I had ample opportunity for observing the behaviour of wounds under the most varied conditions. I was charmed with the superiority of the treatment of recent wounds which I witnessed there over the "water-dressing" which was used at University College after the precepts of Liston, who introduced it in place of what he termed "filthy unguents." Water-dressing, though cleanly when applied, was invariably putrid within 24 hours, and had to be changed daily. Mr. Syme placed pads of dry lint upon the bodies of the flaps, leaving the lips of the wound free for the escape of blood and serum, covering all with a single layer of dry lint and a retaining bandage which gently pressed the cut surfaces together. This dressing was left untouched for four days, during which union by the first intention proceeded undisturbed except in the track of the ligatures upon the blood-vessels, while the discharge found on changing the dressing was scanty and not specially offensive.

But highly successful as this practice was, it could not be continued in the further progress of the case. The ligatures were separated by a process of suppuration, which, even when the tissues had been healthy at the time of operation, became fully established in four days at the latest. The ligatures, on the other hand, were not fully detached till a later and variable period ; and so long as they remained they perpetuated the formation of pus in the depths of the wound, the retention of which by a dry dressing long continued would have involved disastrous consequences.

Thus, under the best possible management which the knowledge of those days permitted, suppuration was an inevitable attendant on nearly every wound ; and so long as it continued there was no security against the advent of one of the various specially unhealthy conditions, then quite inexplicable, which might ruin the results of the most beautifully planned and executed operations.

The very liberal regulations of the University and College of Surgeons of Edinburgh enabled me, on the expiry of my house surgeoncy at the Infirmary, to start a course of lectures on surgery, qualifying for the examinations of both bodies. The first subject with which I should have to deal was inflammation. The stasis of the blood in the capillaries, as the result of irritating applications, had been long studied in the transparent web of the frog's foot; and Paget had described similar phenomena in the wing of the mammalian bat. The latest contribution to the subject had been made by Wharton Jones, one of my former teachers at University College, who had received the Astley Cooper Prize for an essay in which observations were recorded leading him to the conclusion that the cause of the arrest of the red corpuscles in the capillaries of an inflamed part was contraction of the arterioles. According to this view, which he supported by very neatly executed experiments, the narrowing of the tubes of supply caused sluggishness of flow in the fields of capillaries supplied by them, and this permitted the red discs to aggregate and so obstruct the channels.

There could be no more doubt of the trustworthiness of Wharton Jones's observations than of the beauty of the drawings with which he illustrated them. But their relation to inflammatory stasis was not so clear; and I sought further light upon the subject by investigations of my own. My first attempt in this way may be described somewhat in detail. It occurred to me that it would be interesting, instead of the powerful irritants which had been usually applied in such investigations, to try warm water, the mildest of all stimulants to the human body. Having fixed a young frog upon a plate of glass on the stage of a microscope tilted at an angle of about 45°, one of the webs being extended in the field of view, I watched the effect of throwing a few drops of warm water upon the web by means of a syringe. The application of the water was little more than momentary; and as it flowed off immediately from the sloping surface, I could at once observe the result. This filled me with astonishment, and at first I could not understand what I saw. All appearance of blood-vessels—arteries, capillaries, and veins—had disappeared; the field being absolutely exsanguine. In a short time the circulation was resumed with greater freedom than ever; and on repeating the experiment I found that the first effect of the stimulus was a state of extreme constriction of the arterioles, which kept back the blood-corpuscles but allowed the liquor sanguinis to pass; so that the capillaries and veins, though retaining their former dimensions, were occupied only by the filtered plasma, itself invisible, while their walls were with difficulty discernible under the low magnifying power that I was using.

Thus was swept away at one stroke the latest theory upon the subject. The condition of contraction of the arterioles, which Wharton Jones had supposed to be the cause of the accumulation of the red corpuscles in the capillaries, had been present in the most perfect conceivable form; but the result had been the very opposite condition.

The explanation of Wharton Jones's mistake became apparent as I proceeded along the path which opened with so much promise. He had never experimented in a perfectly healthy state of the circulation, but had described with great accuracy what could occur only under morbid conditions. For I afterwards learned that the normal temperature of man is deadly to the cold-blooded frog. That animal, which under ordinary conditions exhibits very remarkable persistence of vitality even after somatic death, is killed by being held for about a quarter of an hour in the hand; and if one of its hind feet be similarly warmed, the blood-corpuscles will be found packed and stagnant in the vessels of the webs, as if mustard or any other powerful irritant had been applied to them.

If, on the other hand, in securing the frog for observation under the microscope, scrupulous care was taken to avoid needless exposure of the foot to the warmth of the hands, the threads for fixing the toes being tied by means of long forceps, and each half of the knot done separately, with a fair interval between them, a state of the circulation was seen which is, I believe, even to this day rarely witnessed. The white corpuscles, instead of trailing, more or less sluggishly, along the walls of the venous radicles—the normal condition, according to some modern text-books—move freely along among the red discs, and these being diffused through a due proportion of liquor sanguinis, the vessels present a pallor which would surprise anyone who had seen only the ordinary demonstrations of the circulation, but which might have been anticipated from the appearance, when in health, of the highly vascular sclerotic with its investing conjunctiva, "the white of the eye."

Such a method of arranging the foot could not be carried out if the animal were able to struggle; but this was effectually prevented in the following way:— The frog, wrapped in cold, wet lint, is held in the left hand, and the head, left exposed for the purpose, is depressed with the forefinger so as to stretch the ligament between the occiput and the first vertebra. The junction between the brain and spinal cord is then divided with a tenotome, after which the creature remains perfectly passive as long as may be desired. Comparatively dull though we know sensibility to be in an animal so low in the scale as the frog, it is a comfort to feel that this method must be attended with exceedingly little pain. That caused by the division of the cord is probably almost as momentary as the stroke of the tenotome; and sensibility as well as motion being abolished in the limbs, the creature cannot feel the tying of the naturally sensitive toes or the subsequent dragging upon them.

This arrangement had the further great advantage of allowing an irritant, even in the form of a drop of liquid, to remain undisturbed at the particular spot to which it was applied, instead of being diffused over the whole web by the movements of the limb. Under these circumstances the highly interesting fact was disclosed that, while the web generally was affected through the nervous system with active congestion, that is to say, with arterial dilatation and consequent very free flow of blood, the characteristic stasis was limited to the area on which the irritant acted directly. In spite of the widening of the tubes of supply, the blood-corpuscles tended to lag more and more behind the liquor sanguinis, till at length complete stagnation occurred. The obstacle to the onward movement of the red discs seemed to be caused by adhesiveness on their part. On careful examination, individual discs were sometimes seen attached to the walls of the vessels. The white corpuscles also showed a tendency to adhere to each other and to the vascular parietes; and this was seen in all degrees, from the disposition to trail along the venous radicles, before referred to as occurring under slight irritation, to piling up of colourless granular masses of leucocytes large enough to block a venous radicle.*

These appearances of the blood-corpuscles in the irritated area were such as were seen in blood examined outside the body between two plates of glass. I had observed similar granular masses of white corpuscles in blood from my own finger, as

* The accumulation of the white corpuscles in the vessels of an inflamed frog's web was described in 1841 by Dr. William Addison and Dr. C. J. B. Williams independently in the "Medical Gazette" of that year.

well as individual leucocytes adhering to the surface of the glass, along which, as has been since observed, they crawl by amœboid movements.

In the red corpuscles the tendency to mutual adhesion shows itself in different forms according to the species of the animal or its state of health. In the frog the prominence of the nuclei leads to very irregular grouping of the oval cells. In man the biconcave circular discs adhere under normal circumstances in that position which enables their moderate degree of adhesiveness to come best into play, the result being the well-known "rouleaux." The same is seen in the healthy blood of the cow. But in some animals, *e.g.*, the horse, the adhesiveness of the discs is so great that they stick to one another by the parts that come first into contact, producing dense spherical masses large enough to be visible to the naked eye, like grains of red sand. These, falling rapidly through the lighter plasma, leave the upper part of the liquid free from red corpuscles before coagulation occurs, thus giving rise to the buffy coat, whereas in the cow the delicate network of rouleaux remains suspended, and no buff occurs.

I am greatly surprised to learn that the cause of the buffy coat is stated in some text-books to be slowness of coagulation. Special slowness of coagulation does not occur in buffing blood; nor, if it did, would it explain the phenomenon. In whipped horse's blood the red discs aggregate into dense masses as in blood freshly drawn, and falling rapidly soon leave a deep layer of serum. In whipped cow's blood, rouleaux forming in the serum as in the plasma, there will be found, if the animal was healthy, only a thin superficial serous layer, even after the lapse of 24 hours.

I once drew blood from a donkey into two similar glass vessels, one empty, the other half full of water. The diluted blood and the undiluted clotted in exactly the same time. But whereas in the normal blood there happened to be an unusually thick layer of buff, comprising nearly two-thirds of the whole mass, the watered blood gave no buff, and the microscope showed that the red corpuscles had lost their natural adhesiveness.

Human blood, as is well known, shows the buffy coat in some states of inflammation. But it may also occur in anæmia.* And it may well make our profession humble to reflect that in days within living memory buffing of the clot was regarded as an indication for further withdrawal of the vital fluid by venesection.

To return from this digression: adhesiveness of the corpuscles, both red and white, was seen in the vessels of an irritated area of the frog's web, as in blood outside the body. But in a perfectly healthy part no such condition was observed. A string tied round a frog's thigh of course made the blood in the vessels of the foot motionless; but on the slightest

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*In the only case of anæmia in which I examined the blood microscopically I found the red discs extremely adhesive.

touch of the web the corpuscles, both red and white, moved along with the plasma with the most perfect freedom.

But I was not altogether satisfied with this evidence of their entire absence of adhesiveness within healthy vessels, because the aggregation of the red discs in the frog is of a somewhat indefinite character. I therefore sought further light upon the point in the mammalian bat. Having placed one under chloroform and extended one of its wings under the microscope, I temporarily arrested the circulation by compressing the main vessels of the limb; and on examining one of the veins I was much disappointed to see the red corpuscles of its contained blood aggregated. It seemed possible, however, that the part of the membrane which I was examining might be suffering mechanical irritation from pressure between the glass slide on which it rested and the cover-glass which it was necessary to use with the high magnifying power required for the bat's wing. For those were not the days of immersion lenses. I therefore made arrangements to guard against the possibility of such an occurrence; and now, to my great joy, I beheld the red corpuscles, which lay motionless in a considerable venous channel, distributed uniformly through the plasma, without the slightest appearance of aggregation.

The animal having been killed immediately afterwards, I examined a drop of blood from its heart. The contrast with what I had seen in the healthy living vessel was most striking; the red corpuscles presenting a degree of adhesiveness such as I had never before seen equalled, whether outside the body or within the vessels. When forced to separate from each other by pressure made upon the cover-glass, they became drawn out like threads of a viscid liquid before becoming completely detached. The animal had been suffering from a bad compound fracture in one of the wings. Whether the great adhesiveness of the red discs of the shed blood was due to inflammation caused by the injury, or whether such a condition is normal to the bat, as it is to the horse and the ass, I do not know.

By such facts it seemed to be established that the stasis of the blood in an irritated area, that is to say, the accumulation of the blood-corpuscles, both red and white, in the vessels of that area, is due to a tendency on their part to adhere to each other and to the walls of the vessels; that they do this by virtue of an adhesiveness or viscidity which they do not manifest at all within the vessels of a perfectly healthy part, and which, while varying in degree with the severity of the irritation, never seems to exceed that which is observed in blood outside the body.*

What was it that induced the blood-corpuscles to assume this adhesiveness under irritation? It was clearly not the result of direct action of the irritant upon them. When the inflammatory congestion, as

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* *Vide* "Phil. Trans.," 1859.

I ventured to term it, was not carried to its extreme degree, the corpuscles, though closely packed, still moving sluggishly along, successive portions of blood, as they passed through the affected spot, were successively affected in the same way, it might be for hours after the irritant had ceased to act. And some of the agencies which produced the effect, such as gentle warmth and mechanical disturbance in the shape of moderate pressure, were not of a nature to act chemically upon the blood cells, and could not possibly leave behind them among the tissues any active substance.

The tissues, as distinguished from the blood, were therefore the parts primarily and essentially affected by the action of the irritant. And we have seen that, in their relation to the blood-corpuscles, they approached more or less closely, according to the degree of the irritation, the behaviour of ordinary solids, such as glass, as distinguished from the living structures. The natural inference was that they had lost more or less, for the time being, certain special properties which they possessed when in active health as constituent structures of the living body. In other words, certain of their vital functions were temporarily in abeyance. I say temporarily because the extreme degree of inflammatory congestion, in which the capillaries appear as homogeneous scarlet threads of densely packed red discs, is susceptible of complete recovery by resolution if the action of the irritant has not been pushed too far.

The same conclusion followed naturally from a consideration of the properties of irritants. Greatly as they differ in their nature, whether physical, as mechanical violence, heat, and the electric shock, or chemical of the most varied characters, one feature they have all in common; if pushed far enough they destroy the tissues on which they act. Extreme inflammatory congestion is the state which they produce when their action is just short of the lethal degree; and it could hardly be doubted that the state of the tissues just short of death must be one of impairment of vital power.

This view was beautifully confirmed by a series of observations to which I was led by a most unlooked-for experience. Before I had adopted the method, which I have described, of obtaining a perfectly tranquil state of the frog's foot, I sought to study the local effect of an irritant by placing on the middle of the web a small piece of moistened mustard, which could not be shifted in position like a drop of liquid when the animal struggled. On removing the mustard after a while to observe its effects, I was astonished to see the part of the web on which it had lain, not only affected with inflammatory congestion, but totally different in colour from the rest of the web in consequence of a difference of arrangement of its pigmentary constituents. Where the mustard had rested, the pigment appeared as a delicate black network among the tissues, causing an extremely dark appearance; whereas in the rest of the web it was gathered into small round spots, which interfered little with the pallor of the other structures. I at once saw that I had before me direct ocular evidence of an effect of the irritant upon the tissues. The circumstance that I had applied the mustard to one spot only of the web, had revealed what had escaped the notice of the many previous observers who had studied the circulation in the frog. I afterwards learned that changes of colour due to pigmentary variation had been observed in Germany in the green tree-frog by Von Wittich, who had attributed them to contractions and relaxations of chromatophorous cells, more or less analogous to what is seen on a large scale, visible to the naked eye, in the skin of cephalopods. Very different were the real pigmentary functions in the frog. The colouring matter, which was in the form of granules of extreme minuteness, was contained in cells with offsets that rapidly broke up into ramifications of exquisite delicacy, anastomosing freely with each other and with those of other branches and of neighbouring cells, only visible when the frog was at the darkest, when they appeared, under the highest magnifying power at my disposal (a fine $\frac{1}{12}$ of Powell and Lealand's), as fine homogeneous black lines, in which the closely-packed granules were not individually discernible. Under these circumstances the bodies of the cells and their principal offsets were so cleared of pigment as to be almost colourless, so that it was difficult to define their contour.

On the other hand, when the animal was at the palest, the pigment granules were massed together into a circular disc, which did not occupy the whole of the body of the cell, being apparently grouped round its nucleus, while the offsets and their ramifications were quite colourless. Any intermediate degree between these extremes of complete diffusion and perfect concentration of the pigment granules might occur, with corresponding differences in the tint of the animal.

Camera Lucida sketching here stood me in good stead. I doubt if anyone would have credited my description had I not been able to support it by such evidence. For here was a function entirely new to physiologists. In muscular contraction the entire mass of the cell shrinks, and in ciliary action, the only other visible form of motion then known to occur in animal tissue, the part concerned moves as a whole, so far as we are able to observe it ; in the pigmentary changes the form of the cell remained unaltered, but one of its constituent materials was seen to be transferred from place to place among the rest. But drawings made with the camera of a cell in successive stages of concentration of the pigment admitted of only one just interpretation.*

* Max Schulze had not yet described the movements of animal protoplasm ; and if he had done so, this could have gone but a little way in explaining the phenomena described in the text. The gushing out of homogeneous pseudopodia from the granular body of an amœba may, however, be of an allied nature. I made attempts to see the movement of the pigment granules in cells in which concentration was going on

These changes in the disposition of the pigment accommodate the tint of the animal to that of surrounding objects. A dark frog placed in a white earthen basin in sunlight soon assumes a dull yellow colour, and a pale one is not long in becoming black in a covered earthen jar.

It was very interesting to find that light produces these effects, not by direct action upon the skin, but indirectly through the retina and optic nerve. A hood of black cloth, carefully arranged so as to exclude light from the eyes without obstructing respiration, entirely prevented a dark frog from becoming pale in bright sunlight. I was naturally desirous of ascertaining through what efferent channels the nervous impulse that caused concentration of the pigment on exposure to light was conveyed from the brain to the foot. Division of the sciatic nerve had no effect whatever upon the colour of the limb. I then tried cutting through all the structures in the thigh except the bone, the femoral artery and vein and the sciatic nerve. This also had no influence. But when I added to the latter procedure the section of the sciatic, the animal being then pale, it gradually grew dark below the seat of operation, till in no long

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but their extreme minuteness, together with the excessive rapidity of their apparent motion under the high magnifying power requisite, made them generally elude observation. I fancied I saw an indefinite rush of something through the clear space around the already accumulated mass, but I could not be sure. On one occasion, however, I saw some individual granules leave the mass and make excursions into the colourless liquid, as I could not doubt it to be.

time it presented from the toes to the wound as great a contrast with the rest of the body as if that part had been covered with a miniature black stocking. Thus the regulation of this function, which is probably closely allied to the action of the cells in nutrition, was not carried on exclusively through special nervous channels, as is the case with the contractions of the voluntary muscles, but one nerve could take the place of others in the duty.*

Light was not the only agency that induced pigmentary concentration. It might take place rapidly during struggling of the animal, and I once saw a frog grow pale in its efforts to avoid capture. Here mental emotion perhaps came into play, if we may use such an expression regarding the frog.

It seems quite astonishing that nervous action should make the pigment molecules rush thus rapidly to the centre of the cell from its remotest and finest ramifications. Yet a sudden gush of tears or outburst of perspiration, although familiar, is perhaps not less wonderful.

Concentration of the pigment took place, as we have seen, under nervous influence, and diffusion on its withdrawal. But diffusion was no mere passive phenomenon, such as might follow according to any ordinary arrangement of matter, when the agency that caused the grouping of the molecules ceased to operate. The transference of the granules from the

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* *Vide* "Phil. Trans.," *ibid.*

body of each cell to its remotest ramifications, and their close packing there, were an act such as a living organism alone could have effected. Pigmentary concentration and diffusion were vital functions of a profound character concerned with the relative distribution of different constituents of the cells. Yet from the very happy circumstance of the conspicuousness of the pigment, the results of their activity could be observed with the utmost facility, and their behaviour in relation to inflammatory congestion easily studied even under a low magnifying power.

The pigment cells pervade the skin and subcutaneous tissue of which the frog's web consists, and are especially numerous about the blood-vessels, round which their branches twine abundantly. They must, therefore, be acted on along with the vascular parietes by anything applied to the surface of the membrane. And to state shortly the result of many experiments, I found that any agency, physical or chemical, which caused the blood-corpuscles to lag behind the liquor sanguinis in the part on which it operated rendered the pigment cells in that particular area incapable of discharging their functions. Whatever might be their state at the time of the experiment, whether in full diffusion, complete concentration, or any intermediate condition, so they remained in the irritated spot, while in surrounding parts of the web, as in the body generally, they changed as usual in obedience to differences of illumination or other circumstances. At the same time they were not killed :

for if the irritation had not been too severe, they recovered their full activity when resolution occurred.*

Thus the pigment cells afforded ocular demonstration of the truth, to which I was otherwise led by inference, that an irritant, when producing inflammatory congestion, prostrates for the time being the vital energies of the tissues on which it acts.

It is to be observed that mere paralysis of the nervous apparatus of the irritated area would have been followed by diffusion of the pigment, as occurred after section of the nerves in the thigh, so that the suspension of diffusion as well as concentration shows that the special pigmentary functions had been arrested.

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* I have in rare instances seen an irritant cause diffusion from a state of concentration as a preliminary effect. This was unmistakably the case on one occasion when mustard was employed. The pigment was in an intermediate (stellate) state when the application was made. In a narrow ring round the mustard, where the volatile oil could only act extremely mildly on the web, the stellate condition gave place to complete diffusion ; whereas under the mass, where the irritant had acted at once with full energy, the stellate appearance remained unchanged. Inflammatory congestion, however, had been produced in the ring of full diffusion as well as in the more strongly irritated area. It happened that complete concentration afterwards took place in the rest of the web, while the irritated areas retained the appearances above described. It seems probable that the diffusion under the slighter irritation may have been the result of the nerves in the irritated part being paralysed before the pigment cells.

As is commonly the case with more specialised structures, the pigment cells are a delicate form of tissue, and are more readily killed than other constituents of the web. Hence, if care is not taken to avoid pushing the action of the irritant too far, it will be found, after resolution has taken place, that the pigment cells never recover ; the collections of pigment gradually lose their sharpness of outline and are ultimately absorbed, leaving a permanently white spot in the web.

It was of course a familiar fact that nerves may be temporarily paralysed by the direct action of pressure, cold and other agents upon them. But, so far as I am aware, it had not been known that the tissues generally are liable to be thrown into a state of suspended vital energy by injurious influences.

An experiment upon another form of tissue seems so illustrative of this subject that I am induced to relate it in detail. It was an attempt to study the effect of warmth upon the ciliated epithelium of the frog's tongue. It was easy to obtain the material for examination by gently scraping the surface of the organ and diffusing the product in a drop of water. Individual isolated cells were then to be seen with their cilia in motion, which might continue for a considerable period. But special arrangements were necessary in order to avoid killing them with the warmth, to which, as we have seen, the tissues of the frog are peculiarly sensitive. I succeeded by arranging them in a film of water between two delicate cover-glasses, the whole mass being so thin that it could be very quickly heated and as rapidly cooled. The object being placed under the microscope, I interposed a small cautery at a low black heat between the reflector and the stage and watched the result. The ciliary motion, which had been somewhat languid, became at once increased in rapidity, but resumed its former rate if the cautery was at once withdrawn. If, however, the application was somewhat longer continued, the active motion soon gave place to a state of complete rest, in which the cilia stood straight like the hairs of a brush. The hot iron being removed the instant that this effect was observed, slight indefinite movement soon began to show itself in individual cilia; and before long all were again in action as before the heat was applied. If the cautery was made somewhat hotter the motionless condition was produced almost immediately, preceded by a momentary period of excessively active motion. But if the warm application was immediately suspended, recovery occurred, as in the former case. And the same experiment might be repeated again and again on the same cells with the same results. But if the warmth was allowed to act for a slightly longer time, or the cautery was made still hotter, recovery never took place, and the bodies of the cells swelled up through endosmotic imbibition of water, having lost all life and obeying the ordinary laws of chemistry.

This simple experiment was in various ways instructive. It indicated that ciliated epithelium cells, like the pigment cells, when acted on by a destructive agency to a degree just short of that which is lethal, are thrown into a state in which their vital functions are suspended but not irretrievably lost. It also showed that the cells which compose the animal organism are individually capable of recovering from this state of suspended vital energy, without any aid from the general circulation or the nervous system.

It further illustrated the important fact that a most injurious agent when operating very mildly may stimulate function without impairing power.*

Active congestion, or arterial dilatation with consequent free flow of blood through the capillaries, is an early and prominent symptom of inflammation of a vascular part in man. Unlike the morbid condition which is produced by the application of irritants to the frog's web, it is brought about indirectly through the nervous system. A striking illustration of this was presented in a case which occurred at the period to which I have been referring. A schirrous mamma had been removed by transverse incisions, together with a considerable amount of integument; and the cutaneous margins had been brought together, in spite of a good deal of tension, by means of a few stitches. Two days later I found the lips of the wound gaping slightly; but the sutures, though subjected to much traction, were still holding; while the skin presented an inflammatory blush extending both upward and downward from the wound, so that it occupied an area of about 4 inches in breadth. I removed the sutures, and I particularly noticed that no blood escaped from any stitch-track. The procedure occupied about two minutes and (to quote from a note taken at the time) "no sooner had I done this than I observed that the

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* It would appear that all agents that act with destructive effect upon the tissues produce suspension of vital energy without loss of life when operating in a minor degree. Whether all such agents are also stimulants of function when in a still milder form is quite another question.

redness had almost entirely disappeared; most parts that were before apparently intensely inflamed being now pale." The irritating agents acted directly on only a minute portion of tissue; but they induced widespread active congestion, which subsided at once on their removal. Such results could only have been brought about through the agency of the nervous system.

As I before had occasion to remark, active congestion takes place throughout the frog's web when an irritant is applied to any part of it. It was, therefore, possible to study the phenomenon upon that animal. It was not at that time clearly known by what mechanism the constriction of the arterioles was effected, or by what part of the nervous system it was regulated. Kölliker had recently made his great discovery of the fibre-cells of involuntary muscle, and had described them as existing along with elastic tissue in the middle coat of the larger arteries; but the trustworthiness of his observations had not yet been by any means universally recognised, and the structure of the ultimate arterioles, as compared with the capillaries, had not been ascertained.

I found, on dissecting out the vessels from between the layers of the frog's web, and examining them with a high magnifying power, that whereas the capillaries showed only a thin, apparently homogeneous wall beset with occasional nuclei, the finest arteries exhibited three coats, of which the middle one was composed of muscular fibre-cells wrapped spirally round the lining membrane. A more efficient mechanism for their constriction could hardly be conceived.*

As regards the regulation of the arterial contractions, Bernard's classical experiment of inducing turgescence of the vessels of the ear by section of the sympathetic in the neck, and Waller's converse observation that galvanic stimulation of the distal end of the divided nerve made the distended vessels shrink and the ear assume unwonted pallor, had demonstrated the great fact of nervous control over the local circulation; but it was still a subject of discussion what part of the nervous centres exercised the function.†

In entering on the inquiry, I first divided the sciatic nerve, a proceeding which had been stated on high authority to cause relaxation of the arteries of the web. The immediate effect of its division was, indeed, some enlargement of their channels, but this very soon passed off. I then resorted to operations on the roots of the spinal nerves and on the medulla. And, not to weary you too much with details, I may say that removal of all that part of the spinal cord which gives off branches for the hind legs, caused the arteries of the web to relax completely and to remain permanently of about the same calibre as the veins. But if any portion that furnished nerves to the posterior extremi-

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* *Vide* "Trans. of the Royal Society of Edinburgh," Vol. XXI, Part IV.

† For authorities on this question, *vide* "Phil. Trans.," *ibid.*, pp. 607 *et seq.*

ties was allowed to remain, whether a little caudal segment or a small anterior part, the arteries resumed, after temporary dilatation, their ordinary and varying dimensions.*

It was thus shown that the cerebro-spinal axis is the centre that presides over the contractions of the arteries of the foot, and that the function is exercised by the entire posterior half of the cord

The very transient effect of section of the sciatic proved that, as is the case with the pigmentary functions, one nerve can take the place of others in the duty. And I found that even after division of all the soft parts of the thigh except the main artery and vein, the vessels of the webs soon recovered their contractile power; showing that the control of the cord over the arteries can be kept up in an extensive region through quite insignificant nervous twigs. We can thus understand how a flap of skin raised in a plastic operation in the human subject may have its circulation duly regulated through a narrow neck of attachment.

An experiment that greatly pleased Dr. Sharpey would seem to indicate that the vaso-motor function for the hind legs is also discharged by the most anterior part of the cord. A frog having been arranged as before described, the point of a fine needle, curved at the end, was introduced into the wound behind the occiput, so as to prick for an instant the divided

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* *Vide* "Phil. Trans," *ibid.*

medulla. The eye of the observer being over the microscope while this was done, the arteries of the web were seen to contract to complete obliteration of calibre, as in the first experiment with warm water.

The contraction of the vessels caused on that occasion by the application of gentle heat to the web was now explained as a "reflex action" through the spinal cord. Their dilatation under irritation remained to be accounted for. In describing that first experiment, I stated that the extreme constriction of the arterioles was followed by relaxation to a larger calibre than they had before the water was applied; suggesting the idea of fatigue after exertion. I have now to add that, if the warmth was longer continued, the subsequent relaxation was more marked and of longer duration; and if the water was made somewhat hotter the contraction that preceded the dilatation was so transient as to be barely discernible.*

We seem to have here an exact parallel to what occurred as the result of the action of heat upon the ciliated epithelium. And the natural view seemed to me to be that the ganglion cells of the cord concerned in the arterial contractions were affected by the nervous impulse conveyed to them by the afferent fibres according to the same law that governed the direct action of heat upon the epithelium cells; increased activity or suspension of function being

* Brief contraction of the vessels, followed by dilatation, had been previously observed by others as the result of the application of irritants to the frog's web.

induced according to the degree of energy of its operation. I incline still to believe that this was a correct interpretation of the phenomena of active congestion.

Inflammatory congestion also may be brought about by nervous agency. This fact being of fundamental importance, and not perhaps universally recognised by pathologists, I may describe briefly two unpublished experiments with regard to it which I did shortly after the time of which I have been speaking. Inflammatory phenomena being of a very languid character in the frog, I had resort to a higher animal. One of the experiments was simply passing a silk thread through a fold of skin in a rabbit's back and knotting the ends together. When 48 hours had elapsed, the animal having been killed, I removed the portion of skin concerned and examined its under surface. The thread was covered with a yellow line of lymph, around which there was intense scarlet redness for about a quarter of an inch in every direction, contrasting strongly with the paleness of the healthy structures around. And on microscopic examination I found that this depended (to quote from my notes of the time) "partly upon ecchymoses, but chiefly upon well-marked inflammatory congestion of the minutest vessels of the subcutaneous tissue and the deeper parts of the skin."

The other experiment was performed twenty minutes before the first, upon a part of the same animal which, being more sensitive, was more likely to show the effects of nervous disturbance. By means of a fine sewing needle I passed a delicate thread of silk through the superficial layers of the left cornea, and cut the ends off close with scissors. Next day the eye was much inflamed and its condition was aggravated on the day following, while the other eye remained healthy. As I have already said, the rabbit was killed on the expiry of 48 hours. This having been done by pithing, I at once divided the blood-vessels in the neck while the heart was still beating, so as to allow all blood that was free to flow to escape from the head. I then removed the two eyes and cut them both across transversely midway between the cornea and the optic nerve, and compared the inflamed eye with the healthy. I will not detain you with a description of the anterior halves of the globes, though they were very interesting, but will at once speak of their posterior portions, more remote from the part where the exciting cause had been in operation on the left side. In that eye the retina was much more readily detached than in the right, and showed small spots of ecchymosis, while the blood vessels were more conspicuous. The two choroids presented a striking contrast; "the vessel in the right eye" (to quote my notes again) "being not at all conspicuous, while in the left eye the membrane was scarlet; and this depended not merely upon fulness of the vessels but upon darker tint of their contents in consequence of excess of red corpuscles."

It is matter for discussion how inflammatory congestion is brought about by nervous action. It may be doubted whether active congestion could alone give rise to it, though it is by no means inconceivable that the excessive supply of the nutrient fluid might in time exhaust the tissues by over-stimulation, and so bring about more or less of that impairment of vital energy which we have seen reason to regard as the essential cause of the blood-corpuscles lagging behind the liquor sanguinis.

Or it may be that the nerves produce this weakening effect upon the tissues by immediate action upon them. From that point of view, the proof afforded by the pigment cells of the influence of the nerves over processes going on within cells seemed to me peculiarly interesting. And we can conceive of nervous impulse impairing their energies either by over-stimulation followed by exhaustion, or by immediate prostration of their powers as by an electric shock.

That the latter idea is not altogether out of the question seems to follow from a kind of experience familiar to surgeons. I will mention one instance of this which produced a great impression upon me. A healthy man, in the middle period of life, had been operated on by lateral lithotomy. All went perfectly well till about ten days had elapsed, when the renal secretion, which had passed through the wound since the operation, flowed for the first time through the natural channel. In those days, when lateral lithotomy was the routine treatment of calculus, it was well understood that the mucous membrane becomes in a few days unaccustomed to the urine, which then acts upon it with irritating effect, and the result may be a violent general nervous commotion in the shape of a rigor. This may be immediately followed by complete suppression of secretion by the kidneys; and if this does not pretty soon pass off it is fatal. Such was the case with the patient to whom I am referring. In spite of hot applications to the skin—which sometimes work like a charm in such circumstances, operating, as it would appear, by distracting, so to speak, the attention of the nervous system from the affected organs—that man died within a few hours of the rigor. On *post-mortem* examination the kidneys presented on section an appearance that I have never forgotten; scarlet redness throughout what in other respects appeared to be perfectly sound structure.

The previous healthiness of the patient seems to preclude the idea that this grave disorder of the kidneys could have existed before the rigor. We are therefore led to believe that the prostration of vital energy which inflammatory congestion implies was caused by the irritation in the urethra. If such was the case, the remoteness of the kidneys from the source of disturbance makes it certain that the disorder was brought about through the nervous system. This effect could not possibly be produced, like arterial relaxation, by failure of the nerves to act. For we know that the tissues retain their vital energies for a considerable period after entire severance from the body: as is illustrated by the success of Thiersch's method of skin grafting. We are, therefore, driven to the other alternative, and conclude that the inflammatory congestion of those kidneys was caused by nervous action upon the renal tissues. And the suddenness with which the effect was produced strongly suggests the view that the prostration of their vital power was the primary effect of an unwonted nervous impulse.

Abnormal effusion of liquor sanguinis from the vessels, another marked feature of acute inflammatory disturbance in man, would seem a natural result of any degree of inflammatory congestion. I used to illustrate to my class by a simple experiment the enormous increase which takes place in the pressure of a liquid upon the walls of a tube through which it is flowing, when an obstacle is opposed to its passage. When, therefore, the corpuscles begin to block the capillaries the plasma will naturally be forced in undue quantity through their porous walls.

When inflammation assumes an intense degree, the effused liquor sanguinis has the peculiarity of being coagulable, producing by its solidification the characteristic "brawny" swelling of the parts among which it is poured out. In this respect it differs from the normal plasma forced by pressure through the walls of healthy capillaries as the result of venous obstruction. Here the swelling has the "doughy" character of œdema, a condition also caused by inflammation of a mild degree. To that point I shall have occasion to refer again.

I designated by the title "direct inflammation" the morbid state produced by the direct operation of noxious agents upon the tissues, as distinguished from inflammation brought about through the medium of the nervous system. This distinction appears to me to be of great importance; and it enables us to understand what would otherwise be quite unintelligible. One beautiful instance of this is the behaviour of a recent wound in tissues previously healthy. When our means of arresting bleeding were less complete than they are at present, it was no uncommon thing to be summoned a few hours after an operation on account of hæmorrhage. It was a sad thing to have to tear asunder the lips of a wound already well glued together by lymph, in order to gain access to the bleeding point. This lymph was neither more nor less than liquor sanguinis which had been effused from the cut surfaces and had coagulated. From the quality of the effusion we should suppose that we had to deal with inflammation of a very intense character. Yet the lips of the wound were perfectly pale, entirely free from the active congestion which is the very earliest sign of inflammatory disturbance. How could this inconsistency be reconciled? Very simply, as I believe, by aid of the principles which we have been discussing. Mechanical violence is a noxious agency producing effects proportionate to its degree. A very blunt implement passing through the tissues kills the surface of the parts which it divides; and in former days we had to poultice a "contused wound" till the sloughs separated. A sharp knife does not destroy any part of the tissues, but it throws them in a microscopically thin layer into a state of intense inflammatory congestion, attended with effusion of coagulable liquor sanguinis. But this noxious agency is only momentary in its operation. It has no time to cause active congestion through the nervous system, but at once leaves the injured tissues free to recover by virtue of their own inherent powers. If the instrument be very sharp the layer of lymph will be very thin, unless some other disturbing cause come into play. But it is always sufficient in amount to serve the beautiful purpose of adhesion.

It is comparatively rarely that direct inflammation is met with thus pure and simple in practice. The two forms, the direct and indirect, are commonly more or less associated. Thus putrid discharge in a wound is an acrid irritant, as I once experienced personally in the keen smarting of an abrasion on the back of my hand, smeared accidentally with the pus of a stump that I was dressing. Hence during the period that elapses before the divided tissues are clothed with that wonderful protecting layer which we term granulations, such discharge causes direct inflammation in the structures on which it acts immediately, while it also induces in them and in neighbouring parts inflammation through the nervous system.

When Marious Sims had published his remarkable success with the silver suture in gynæcology, I resolved to give it a trial in general surgery. At that time, as assistant surgeon in the Royal Infirmary of Edinburgh, I had charge of the Lock Hospital; and one of the patients having an atheromatous tumour of the scalp, I removed it and brought the edges of the skin together with a silver stitch. No vessel required ligature, and the wound healed without suppuration. As the suture created no disturbance, I left it *in situ* for about ten days, when I took the patient over to Mr. Syme and showed him the skin about the wire perfectly pale and natural in appearance without a trace of discharge, whereas a silk stitch would within four days have infallibly caused suppuration, with surrounding redness. Mr. Syme at once recognised the importance of the facts, and from that day forward the silver suture was used for all wounds in the clinical wards, until, some years later, antiseptic measures caused it to give place to the more convenient and no longer hurtful silk.

In thinking over this striking difference between the effects of the two kinds of suture, it seemed to me clear that it depended on the silk imbibing blood and serum, which, undergoing decomposition in its interstices, grew more irritating the longer the process continued; whereas the metal gave no hold to the organic liquids, which were shed unaltered as fast as they were effused. From these and other analogous considerations, I taught my class at that time that decomposition of the organic liquids was the essential cause of suppuration.

The coagulation of the blood, while it is a matter of fundamental importance in physiology, has peculiar interest for the surgeon, on account of the special feature of coagulability of inflammatory exudations and the part played by lymph in the healing of wounds and various other pathological phenomena, such as the sealing of divided arteries by blood-clot. Towards the close of the investigations which I have been describing there was published another successful Astley Cooper Prize essay, " Coagulation of the Blood " having been the subject selected by the judges for the competition. The author of this dissertation, the late Dr. Richardson, propounded the new theory that the solidification of blood shed from the vessels was due to the escape of ammonia, which, as he believed, held the fibrin in solution. I was at first much struck by the evidence with which he supported this view, and my first experiments on the subject were made with a view to strengthening that evidence where it seemed to me weakest.

In one of these, a sheep having been placed under choloroform, I sought by means of a common tourniquet to constrict the thigh so extremely as to prevent the ammonia from escaping when the vessels were divided, and so keep the blood fluid in spite of amputation. Rigidity of the muscles prevented me from carrying out my intention ; but I tied a bandage firmly round the foot, below the joint where the butcher removes it, so as to retain the blood, and, as far as might be, the ammonia also. The foot being severed, I took it home, and, having raised a portion of the skin so as to expose a subcutaneous vein, I investigated the state of the blood in it. I found it indeed fluid, with one exception, full of significance, though I did not see its import at the time, viz., where the cord used by the butcher for tying the feet together had pinched the veins against the bone, there, and there only, was the blood in them coagulated. I remember being a little disappointed, as well as puzzled by that appearance. It was not in harmony with the theory in which I was at the time disposed to believe. And yet how replete were the facts with possible instruction! Compression of the veins had certainly given no opportunity for escape of ammonia. It is equally certain that the cord did not make the blood coagulate by any direct action upon it: for the cord, so long as it remained in position, kept the parts of the veins which it compressed empty of blood. It is clear that the effect was due to the action of the cord upon the walls of the vessels. Not that it had wounded them, nor is there any reason to suppose that it had killed them. No doubt if the animal had been released instead of slaughtered, the veins would in due time have recovered. But the mechanical violence which the hard round cord exerted, being pretty severe and long continued, had prostrated for the time the vital energies of the tissues on which it had acted; and we had, in coagulation of the blood, a repetition of the class of phenomena we had studied in the blood-corpuscles.

But how was it that the blood remained fluid in other parts of the vessels? To my surprise I found that the same continued to be the case for days afterwards. And thus accident led me to recognise what I afterwards found to be the general rule, viz., that the blood, though in mammalia it coagulates soon after death in the heart and main trunks, remains fluid for an indefinite period in minor branches. The clotting in the heart had been an object of familiar observation in *post-mortem* examinations in the human subject, and it seems to have been assumed that the same thing occurred throughout the vascular system.

The sheep's foot, with the blood retained in its veins by a bandage applied before the animal was slaughtered, afforded the opportunity for very simple, but instructive experiments on the nature of the relations between the living vessels and their contained blood. For that the veins retained their life, even after the lapse of more than 24 hours after severance of the foot from the body, was shown by their shrinking by muscular contraction on exposure.*

Thus I found that a piece of glass introduced into

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* As regards the ammonia theory, an experiment which proved universally convincing was this: Having exposed a vein in the sheep's foot, I pressed the blood out of it at one place, and applied liquor ammoniæ to the empty portion, protecting neighbouring parts of the vessel from the vapour with olive oil. After sufficient time had passed for the volatile alkali to fly off, blood was allowed to return to the part on which the caustic liquid had acted. There it soon coagulated: the very substance a mere trace of which should have kept it fluid according to the theory in question having brought about its coagulation by injuring the tissues of the living vessel.

a vein occasioned coagulation in its vicinity. The end of a sewing needle pushed through the wall of a vein otherwise uninjured, became after a while encrusted with a layer of fibrin deposited upon the part within the vessel, while the rest of the blood in it retained its fluidity.* On the other hand, having injected air into the vessels on another occasion, I found seven hours later that their contents were a frothy mixture of blood and air, the walls of whose bubbles were fluid, but solidified when shed. Sir Astley Cooper had been of opinion that the living vessels kept the blood within them fluid by acting in some way upon it—in other words, his view implied that the blood had a spontaneous tendency to coagulate, which was held in check by the active operation of the living tubes that contained it.† Facts such as I have just mentioned seemed to me to indicate that the ordinary solid was the active agent: determining the formation of fibrin as a thread does the deposition of sugar candy; while the healthy living tissue had the

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* The results of experiments of this kind vary considerably according to the time which has elapsed after the foot was removed from the body: for the blood undergoes pretty rapid impairment of its coagulability within the vessels of the severed part, and finally loses it altogether. It then, of course, remains fluid long after the veins have lost all life.

† Brücke, of Vienna, who had also competed for the Astley Cooper Prize, had arrived at a similar conclusion. He experimented largely with the turtle's heart, which, as in cold-blooded animals generally, retains its life long after removal from the body; the blood in its cavities at the same time retaining its fluidity. I had not seen Brücke's important essay when the experiments referred to in the text were performed.

remarkable peculiarity of being destitute of this general aggregating property of solids, behaving rather like the self-repelling particles of gases.*

It was not only in vessels of small size, like those of the sheep's foot, that the blood remained fluid in parts severed from the body. I found that the same was the case in veins of the dimensions of the jugular of the ox or the horse, and this in spite of their entire detachment from surrounding structures. The vessel being exposed after the animal had been felled at the abattoir, two ligatures were applied in order to retain the blood in it, after which it was removed and taken home with as little disturbance as possible. The blood in it retained its fluidity for upwards of 24 hours, affording opportunity for most instructive experiments. Of these I must content myself with describing one. A portion of an ox's jugular with its contained blood being held vertically, the upper part was removed along with its ligature, and the lips of the now open venous compartment were held apart with forceps by aid of an assistant, while a thin glass tube, of rather smaller calibre than the vein and open at both ends, was passed down into the vessel with the utmost steadiness, so as to disturb the blood as little as

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* It has since been shown, by Freund, of Vienna, that an indifferent liquid, such as liquid paraffin, has a similar negative behaviour in relation to coagulation ; so that, by proper management, blood may be kept fluid in a vessel of ordinary solid matter having its interior smeared with that substance. Professor Haycraft arrived about the same time at a similar conclusion regarding castor oil.

possible. The upper end of the tube had been drawn out with the blow-pipe to much smaller size and a short piece of indiarubber tubing adapted, so as to admit of clamping with catch-forceps. When blood appeared at the end of the caoutchouc tube the clamp was applied. The whole apparatus was then rapidly inverted and the piece of vein removed, leaving the blood in a vessel of ordinary solid matter without any contact of living tissue. The glass tube was steadily clamped to a retort stand, and its orifice covered with a loose cap of guttapercha tissue to exclude dust, after which all was left undisturbed for 24 hours. On then turning out the blood, I found it all fluid except a layer of clot about one-eighth of an inch in thickness, which encrusted the interior of the tube, and also a little clot at the surface, which might be explained by some drying on account of the imperfect fitting of the cap. The fluid part of the blood soon coagulated.

The result of this experiment seemed to me of itself sufficient evidence that the blood requires no action of the living vessels to maintain its fluidity, and that the hypothesis of such action was superfluous.

At the same time the extreme care required in order to ensure the success of such an experiment indicated the subtilty of the influence of an ordinary solid in bringing about coagulation. A very simple experiment, performed in a butcher's establishment on the way from my father's house at Upton to deliver the Croonian Lecture before the Royal Society, illustrates the same thing. I received blood from the throat of an ox into two similar open earthen jars (gallipots), and slowly moved a clean glass stirring rod through the blood of one of them for a second or two, and then left both vessels undisturbed.

In the course of a few minutes the blood that had been thus gently and briefly stirred was a mass of coagulum, while the unstirred blood was still fluid, except a thin layer of clot encrusting the wall of the jar. In course of time it also coagulated completely. Now we know, from the experiment with the ox's jugular, that coagulation is propagated with extreme slowness, if at all, from a clot in blood perfectly undisturbed. The earlier coagulation of the main mass of the stirred blood was, therefore, not caused by propagation of the process from a layer upon the surface of the jar, but must have been the result of the brief agency of the glass rod.

A little before the delivery of the lecture referred to,* I became aware of the recent very important observations of Schmidt, who showed, as had been foreshadowed many years previously by Andrew Buchanan, of Glasgow, that normal liquor sanguinis does not, as had been supposed, contain fibrin in solution, but only one constituent of that substance, termed by Schwann Fibrinogen,

* *Vide* the Croonian Lecture on the "Coagulation of the Blood," "Proceedings of the Royal Society," 1863.

the other constituent being derived from the blood-corpuscles. The ordinary solid, therefore, in determining coagulation, does not cause the deposition of fibrin already formed, but so influences the corpuscles as to make them give up an ingredient necessary for the formation of that insoluble body.*

With this further light upon the subject, the conclusions derived from the experiments to which I have referred seem to explain the special coagulability of the exudation in intense inflammation. Under intense irritation the capillary walls will naturally be affected by the noxious agency as the veins of the sheep's foot were by the constricting cord, and, like them, will act upon their contained blood as if they were ordinary solids. The plasma of that blood will therefore receive from the blood-corpuscles the material requisite for forming fibrin, and, passing through the pores of the capillaries with that addition, will constitute a coagulable exudation.†

On the other hand, if irritation is less severe, although the corpuscles acquire more or less adhesiveness, involving corresponding obstruction to the flow through the capillaries and consequent undue passage of liquor sanguinis through their walls, the

* Regarding the corpuscular elements of the blood which are concerned in supplying to the plasma the materials necessary for the formation of the fibrin and the chemical interactions of those substances, various important researches have since been conducted, in which I have had no share.

† I once ascertained the coagulability of a drop of clear fluid which had exuded from a recent contused wound, by drawing the point of a needle through it, to which it yielded threads of fibrin.

constituent tissues of the vessels are not reduced to the condition in which they act like ordinary solids in relation to coagulation. This seems to follow from the uncoagulable character of the effused fluid. For we know that what used to be termed the serum of œdema or hydrocele is simply the normal plasma.

Adhesiveness of corpuscles and coagulation are both brought about by the operation of noxious agents upon the tissues of the part concerned. But it by no means follows that they are in all respects analogous phenomena. We have seen that normal blood has no innate tendency to coagulate, and needs no action of the tissues upon it to ensure its fluidity. But the blood-corpuscles may be naturally adhesive bodies, possessing a viscosity only kept in abeyance by some influence exerted upon them by the living tissues in their vicinity: and such appears to be really the case.

A very interesting observation which I made long ago, but to which I have not before directed attention in this point of view, shows that an extreme degree of adhesiveness of the red discs may exist within a blood-vessel the walls of which are in perfect health with reference to coagulation. If a horse's jugular vein, obtained in the manner I have described, is suspended vertically, the blood in it remains fluid for an indefinite period, but the red corpuscles soon fall from the upper parts of the fluid, leaving a buffy layer of plasma, readily seen through the translucent wall of the vessel. And this behaviour of horse's blood implies, as we have seen, a high degree of adhesiveness of the red discs.

If we compare this with the perfect absence of grouping of the red corpuscles which was observed within a vein of the bat's wing, in spite of their extreme adhesiveness in the same animal in blood shed from the body, we cannot but be greatly struck with the contrast. As regards the circumstances of the two vessels, we see that in the bat's wing the vein was of small calibre, and was in its natural relations to surrounding structures; whereas the horse's jugular was of very large dimensions and isolated from the rest of the body.

It seems impossible that the adhesiveness of the corpuscles in the jugular vein was the result of isolation of the vessel from other structures. For adhesiveness of corpuscles is not occasioned in the frog's web by amputation of the limb; nor is it produced in the human subject by complete detachment of a portion of tissue; as is clearly shown by the persistent healthiness of a piece of skin entirely transplanted in skin-grafting. We are therefore forced to the conclusion that the adhesiveness of the red discs in the horse's jugular, as contrasted with its complete absence in the vein of the bat's wing, was due to the larger size of the vessel in the former case. And the only way in which it seems possible to interpret this difference of behaviour of the corpuscles in the two cases is to suppose that they possess an innate and normal viscosity which is kept in abeyance by some action of the healthy tissues; this action having a limited range of operation, so that, while effective for vessels of small size, it fails to influence the mass of blood in a large venous trunk. And I may remark, in passing, that it is only in the smaller vessels that absence of adhesiveness of the corpuscles is essential for the free transmission of the blood.

The mobility of the black pigment granules of the frog has often struck me as extremely remarkable. Perfect absence of any tendency to aggregate on their part must be fully as essential to the freedom with which they move through the exquisitely delicate ramifications of their containing cells as want of adhesiveness of the blood-corpuscles is to their free transit through the capillaries, and I cannot but think that the two phenomena must be analogous. It may be, for aught we know to the contrary, that the pigment granules may be themselves living entities. Their uniformity in size is in favour of such an idea. Our fathers would have been greatly astonished to learn that the chlorophyl grains of vegetables were, as has been shown in recent years, living organisms, multiplying by division like the nuclei of their containing cells: and though the pigment granules are much smaller, they must be greatly surpassed in minuteness by many microbes which, though hitherto invisible to us, we believe from analogy to be the causes of some infective diseases. But however this may be, the perfect mobility of the pigment granules seems to me a special property which they possess as constituents of the healthy living body; in other words, to use once more the expression which in the present state of our knowledge is indispensable, a vital property.

If this be so, we understand what would otherwise be very unintelligible, viz., that when the pigment cells have their functions temporarily suspended by a noxious agent, the granules do not become diffused as they do when simply withdrawn from the influence of the nervous centres, but remain exactly as they were before the irritant was applied, whether fully concentrated, completely diffused, or in any intermediate state. If we suppose that the pigment granules, like the blood-corpuscles, acquire under irritation a tendency to mutual aggregation which they do not possess in health, it follows, as a matter of course, that when vital energy is suspended by the noxious agency, they will adhere together and retain their relative positions.

After being appointed to the Chair of Surgery in the University of Glasgow, I became one of the surgeons to the Royal Infirmary of that city. Here I had too ample opportunity for studying Hospital diseases, of which the most fearful was pyæmia. About this time I saw the opinion expressed by a high authority in pathology that the pus in a pyæmic vein was probably an accumulation of leucocytes. Facts such as those which I mentioned as having aroused my interest in my student days in a case of pyæmia, made such a view to me incredible, and I determined to ascertain, if possible, the real state of things by experiment. I introduced into a vein of a living horse a short glass tube open at both ends, containing a piece of silver wire in which was mounted a little bit of calico, which I thought likely to give rise slowly to putrefactive change; shutting off the portion of vein concerned from the general circulation by means of ligatures. After the lapse of some days I removed the venous compartment and found that the blood in it had undergone very remarkable changes. The limits of this lecture (which have been already too widely extended) make it impossible for me to enter into details, as I had hoped to have done, regarding the researches of which this was the commencement. I must content myself with stating the conclusion to which I was led at the time I am speaking of, and which was confirmed by later investigation, viz., that the introduction of septic material into a vein may give rise to the rapid development of large nucleated cells which, growing at the expense of the original constituents of the coagulum, convert it entirely into a thick yellow liquid. The pus so formed contains corpuscles which, like those which I sketched in the early case at University College, are not pus corpuscles in the ordinary sense or leucocytes, but the variously-sized, more or less granular nuclei of the large cells, the pellucid bodies of which constitute the so-called liquor puris. Into the question of the origin of these rapidly-proliferating cells I must not enter. This process of genuine suppuration of the blood-clot removed all the difficulties I had felt in interpreting the *post-mortem* appearances in pyæmia, and also its clinical features.

Having become familiar with the appearances of these cells in suppurating coagula, I was able to recognise them in acute abscesses in the human subject, and to demonstrate them to others by mixing carmine with the pus, so as to render clearly defined the limits of the pellucid bodies of the cells, which otherwise would have been regarded as liquor puris.

I am, of course, aware of the great importance of the emigration of leucocytes, discovered by Cohnheim, and rendered immeasurably more interesting by Metchnikoff's observation of their phagocytic powers; and I know that collections of pus have often such an origin. But I am quite satisfied that this is not the exclusive mode of pus formation, and that it is often produced by the proliferation of cells, as was first taught by my illustrious predecessor in this chair of two years ago (Professor Virchow), in the "Cellular Pathologie."

While these investigations into the nature of pyæmia were proceeding, I was doing my utmost against that deadly scourge. Professor Polli, of Milan, having recommended the internal administration of sulphite of potash on account of its anti-putrescent properties, I gave that drug a very full trial as a prophylactic. I have notes of a case in 1864, in which, after amputating the thigh for disease of the knee-joint, I gave 10 grains of the sulphite every two hours from the time of the amputation ; and when, on the sixth day, an ominous rigor occurred, I doubled the frequency of the administration. Death, however, took place nevertheless, and this was by no means my only experience of such disappointment.

At the same time, I did my best by local measures to diminish the risk of communicating contagion from one wound to another. I freely used antiseptic washes, and I had on the tables of my wards piles of clean towels to be used for drying my hands and those of my assistants after washing them, as I insisted should invariably be done in passing from one dressing to another. But all my efforts proved abortive, as I could hardly wonder when I believed, with chemists generally, that putrefaction was caused by the oxygen of the air.

It will thus be seen that I was prepared to welcome Pasteur's demonstration that putrefaction, like other true fermentations, is caused by microbes growing in the putrescible substance. Thus was presented a new problem: not to exclude oxygen from wounds, which was impossible, but to protect them from the living causes of decomposition by means which should disturb the tissues as little as is consistent with the attainment of the essential object.

It has been since shown that putrefaction, though a most serious cause of mischief in wounds, is not its only cause. In other words, it has been proved that there are microbes which produce septic effects without occasioning unpleasant smell. But the principle that first guided me, still retains, I believe, its full value, and the endeavour to apply that principle so as to ensure the greatest safety with the least attendant disadvantage has been my chief life-work.

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