Part First.

ORIGINAL COMMUNICATIONS.

ARTICLE I.—*On Sponge-Grafting.* By D. J. HAMILTON, M.B., F.R.C.S.E., etc., Pathologist to the Edinburgh Royal Infirmary; Lecturer on Pathology in the School of Medicine, Edinburgh.

IN a former paper ("On the Process of Healing," *Journal of Anatomy and Physiology*, vol. xiii., 1879) I made the statement, and endeavoured to show experimentally and otherwise, that the vessels of a granulating surface are not newly formed, but are simply the superficial capillaries of the part which have become displaced. They have been thrown upwards as granulation loops by the propelling action of the heart, because the restraining influence of the skin has been removed.

One of the great functions of the skin is to counteract the tendency which the superficial vessels have to be pushed outwards, and a similar restraining action is conferred upon the deeper branches by the fasciæ which surround them. These hold the vessels in their proper places, and overcome the tendency which there is to peripheral displacement.

Whilst getting the information for that paper, and subsequently when studying the subject of organization and healing still further, I was much struck with the similarity of the process of vascularization as seen on a granulating surface, and that which occurs when a blood-clot or a fibrinous exudation is replaced by a vascular cicatricial tissue. Later on in this paper I shall have to refer to the process of organization of blood-clot and of fibrinous lymph more fully, but at present will merely observe, as a preliminary measure, that blood-clot or fibrinous lymph plays merely a mechanical and passive part in any situation where it becomes replaced by a fibrous cicatrix, and further, that their vascularization is not owing to new formation of bloodvessels, but rather to a displacement and pushing inwards of the bloodvessels of surrounding tissues. Being convinced that the blood-clot or fibrinous lymph, before organization takes place, was just as so much dead matter in a tissue, it occurred to me that if we could employ, instead of blood-clot or fibrinous lymph, some dead porous animal tissue, it, also, would, in the course of time, become vascularized and replaced by cicatricial tissue. For long I could not think of any animal texture which would subserve this purpose; but an accidental circumstance in the summer of 1880 which came under my notice suggested to me that sponge would in all probability, if placed under proper conditions, fulfil the object in view.

The reasons on which I grounded this hope were, firstly, that it is a porous tissue, and in this respect would imitate the interstices of the fibrinous network in a blood-clot or in fibrinous lymph. In the second place, it is an animal tissue, and, like other animal tissues, such as catgut, would, if placed under favourable circumstances, become absorbed in the course of time. Thirdly, that it is a pliable texture, and can, consequently, be easily adjusted to any surface, or be cut of convenient size to be placed in a cavity. If, therefore, the blood-clot or fibrinous exudation merely acts mechanically in the process of organization, there is no reason why sponge or any other porous texture should not similarly become vascular and organized.

I resolved, accordingly, to see whether this theory would stand the test of experiment; and probably, before going further in the way of explanation, it will be well to give an account of some of the experiments which I have made, so as to afford an idea of the objects aimed at.

Through the kindness of Dr Watson, Messrs Bell, Chiene, and others, I have had opportunities of carrying on this investigation during the last twelve months, and I have to offer them my sincere thanks for affording me the means of doing so.

Experiment No. 1.—The subject of this was a female patient who had been admitted into the Chalmers Hospital during the summer of the year 1880, suffering from several ulcerated wounds on different parts of the body. The largest of these was situated on the outside of the left leg. It was circular in shape, and five inches in diameter by from half an inch to three-quarters deep. The edges were indurated, slightly raised, and in some places undermined. There was still a cellular tissue slough at the deepest part of the wound, which gave the whole ulcer a somewhat putrefactive odour. The rest of the floor was in a granulating condition.

The other wounds were of a similar character, but of smaller size. They were situated, one on the scalp, and another further down the leg. They looked very much like ulcers of a specific character, although the patient denied any such history. The largest of them—that on which the experiment was made—had evidently resulted from a huge cellular tissue slough. The patient was admitted with the expectation of having the leg amputated if the wound would not heal by ordinary means.

The usual antiseptic dressings were at first applied, but very little progress was made in its contraction. On 3d August 1880

I filled the wound, while in the above described condition, with one large piece and several small pieces of very fine sponge prepared by dissolving out the siliceous and calcareous salts by means of a dilute mineral acid (nitro-hydrochloric), subsequently washing in liquor potassæ, and then finally steeping for some months in 1 to 20 solution of carbolic acid in water. There is not any necessity for steeping it so long in the carbolic solution: it had been accidentally lying in it for this time. The sponge in the central part of the wound rose a little higher than the edges, so that at its greatest thickness it must have measured at least from half to three quarters of an inch, and five inches wide. The sponge was made to fit the wound very accurately, and was inserted beneath the undermined edges. A piece of green protective was placed on the surface, and, above this, lint soaked in a 1 to 20 solution of carbolic acid in glycerine, with a little tincture of lavender in it. The whole was covered by a pad of boracic lint. An ordinary bandage was applied. The patient was kept in bed, with the limb at absolute rest.

On the following day it was redressed. The sponge was partially soaked with purulent discharge, but there was not any marked putrefactive odour. It was dressed as before.

On 5th August there was a distinct putrefactive odour. It was dressed as formerly, but, in addition, the wound was irrigated with a 1 to 40 carbolic solution. This was continued throughout the progress of the experiment, and at one time, when the putrefactive odour became great, a 1 to 20 solution was employed. Oakum was now used as a top dressing over the glycerine and carbolic acid. The sponge at its shallowest part appeared to be slightly red in one or two points, and the undermined edge had extended for a short distance further over it.

On 6th August the sponge was irrigated as before, and, in addition, was gently squeezed so as to remove any waste products which were contained in it. Opposite where the cellular tissue slough was situated there seemed to be a considerable quantity of discharge given off. The whole sponge was now completely soaked with the discharge, and, further, it was noticed that its edges were adhering to the granulating surface. At one part it looked almost as if the edge of the sponge were dissolving. This may have been caused by its having been to a certain depth imbedded in the granulation tissue, and appearing thinner on that account.

On 8th August, or five days after the application of the sponge, the wound seemed to have shrunk a little. There was very little putrefactive odour, but still the protective tissue was discoloured. The thin parts of the sponge felt very firm, and their interstices were evidently filling with organizing tissue. If the surface was pricked it bled freely. Healing seemed to be going on in two ways, namely, from the edges towards the centre, and from below upwards. The edge of the sponge at the thinnest part also seemed to be dissolving as it became infiltrated with the new tissue. Its surface, moreover, was covered by a grayish-coloured pellicle, very much like that seen on the surface of some wounds healing under antiseptics.

During the treatment of the case iodide of potassium was given internally, from which marked constitutional benefit seemed to be derived.

From this time onwards the sponge rapidly became filled with organizing tissue, until on 29th November there was only a small piece of it to be seen on the surface. As soon as it became vascular and filled with new tissue the epithelium spread over it. There did not seem to be any difficulty in getting the epithelium to spread over it whenever the underlying surface was of a proper nature, that is, whenever it became filled with young and vascular connective tissue elements. On this day (29th November) the circumference of the limb at the part which had healed was 21 inches, while at a corresponding part in the other limb it measured only 19 inches. The difference was not caused by œdema, as the limb was perfectly free from this, and had been kept bandaged and in the horizontal position. It was evident that the cause of the increase was the tumour-like mass of new tissue which had now supplanted the sponge.

On 5th January 1881 I showed the patient, through Dr Watson's kind permission, to the Medico-Chirurgical Society, at which period the sponge had entirely vanished, and there was merely a superficial, typically healthy granulating surface, measuring about 1½ inch in diameter. Dr Clark, Resident Surgeon at the Chalmers Hospital, whom I have to thank for latterly superintending the dressing of the case, informs me that a small piece of the sponge, the last vestige of it seen, at last became dissolved at its attachments and separated.

In the healing of this wound it seemed that, instead of the edges and surrounding skin being drawn downwards and towards the centre, as in the usual process of cicatrization, the reparative material had in reality grown up within the interstices of the sponge, and so had filled the vacuity caused by the cellular tissue slough. It appeared to be, in every sense of the term, *a process of healing up* instead of contracting down.

This first experiment showed me that if sponge be placed over a granulating surface its interstices will, in the course of time, become filled with bloodvessels and cicatricial tissue, just as in the case of a blood-clot, and, ultimately, that the whole of the sponge will disappear in the wound, leaving an organizing mass of new tissue in its place. The vacuities in the sponge appear to be specially adapted for allowing of this, and the framework of keratode affords support to the young vessels which are formed within it.

It further showed that even where the wound continues in a putrescent condition organization will still go on. In the case of the blood-clot, putrefaction tends to destroy it; in that of the sponge, its texture being more resistant, it does not seem to make much difference. The cellular tissue slough which lay at the bottom of the wound, as previously mentioned, must have been the chief cause of the continuous putrefaction which resisted all antiseptic remedies.

Experiment No. 2.—The second case in which I had an opportunity of seeing what would happen if a sponge were left on an abraded surface was where a large piece was employed as a compress over a wound resulting from the excision of an epitheliomatous tumour in the neighbourhood of the lower jaw. The sponge was employed as a compress for a few days; and after this, finding that it had become adherent, the superfluous parts of the sponge were clipped off, leaving a button-like portion over the wound. The patient expressing a desire to go home to the Western Highlands, he was dismissed with the fragment of sponge adhering and forming an excellent protection to the wounded surface. As to what further happened to it I have not had any tidings.

Experiment No. 3.—The next experiment was carried out under Mr Bell's direction in the Royal Infirmary, after seeing the subject of the first experiment at the Medico-Chirurgical Society. There happened to be in one of his wards a patient suffering from an intractable ulcerating wound of old standing on the left leg. It had been previously healed and had again broken out, and there was great cicatricial contraction of the surrounding parts. Several methods of treatment had been employed, but apparently with no benefit, the cicatricial contraction of the skin and deep tissues around preventing the wound from closing. There was not much loss of tissue at the ulcerated part, so that the wound, although it presented a scooped-out appearance, did not show the same enormous vacuity as in the first case. It did not seem to be a very promising case for carrying out the experiment, but, nevertheless, seeing that it was proposed to amputate the limb if it would not heal, Mr Bell thought it right to make a trial of sponge-grafting. The object in doing so was to grow sufficient young tissue to allow of the necessary contraction, and at the same time to afford a healthier—that is, a more embryonic—surface for the epithelium to spread over.

The wound measured $2\frac{1}{2}$ inches by 2 inches, and on 8th January of this year it was covered by a layer of fine sponge rising a little higher than the level of the skin. It was dressed with Listerian antiseptics, but, at the time of application, was in a septic condition, and remained so throughout. The patient's age was 29.

In from a week to a fortnight after application it had taken a firm hold on the exposed surface, and Mr Bell noticed in dressing it that it appeared to be slightly vascular, and bled when pricked.

The daily record of the case it will be unnecessary to follow out; but suffice it to say that it shortly became filled with young vascular cicatricial tissue, which grew up from below, filling the cavities of the sponge, as in the first case. The discharge from the wound was considerable, and remained of a septic nature throughout the course of the organization.

The patient in time was dismissed with the sponge completely organized and the wound healed. There did not, moreover, appear to be any injurious stretching of the parts, the newly formed tissue having allowed for this.

Experiment No. 4.—A short time after the commencement of this experiment, Mr Bell admitted a woman into his wards who suffered from a large recurrent cancer of the mamma. He had previously excised the primary tumour, and this had been the first recurrence. Several of the axillary glands were now enlarged and apparently cancerous.

On 3d February Mr Bell excised the tumour, and in doing so required to remove a large portion of the surrounding skin, and to dissect the parts close down to the ribs. A large gap was thus left, which, instead of allowing to cicatrize in the ordinary manner, he filled with a piece of fine sponge. The enlarged glands were removed at the same time. The operation was conducted antiseptically.

On 13th February, ten days after the operation, the sponge was noticed to be vascular. There had been a little serous discharge from it, but the wound and discharge had remained perfectly aseptic, even although such a large mass of a material so liable to foster putrefaction as sponge had been imbedded in the tissues.

I ought to have mentioned that the sponge had been carefully prepared in carbolic acid before being applied, and, of course, the very conditions which would encourage putrefaction would, *cæteris paribus,* be a hindrance to it if no living septic matter were contained in its interstices. There is therefore no difficulty in keeping the sponge aseptic in a wound provided it be so at the time of introduction. The size of the portion placed in the wound in this case was, roughly speaking, twice that of a crown-piece.

When the sponge became vascular it rapidly filled with embryonic cicatricial tissue, until in the beginning of July it had entirely disappeared, and nothing remained but a granulating surface the size of a shilling, partially covered by a pellicle of epithelium. There was, in the place of the sponge, a somewhat hard mass of tissue.

Seeing that the tumour had recurred, Mr Bell naturally became anxious about the hard feeling which the new-grown mass presented, supposing that possibly the cancer tissue had penetrated into the sponge, and had there found a convenient medium within which to develop and grow.

X 300 DIAMS.

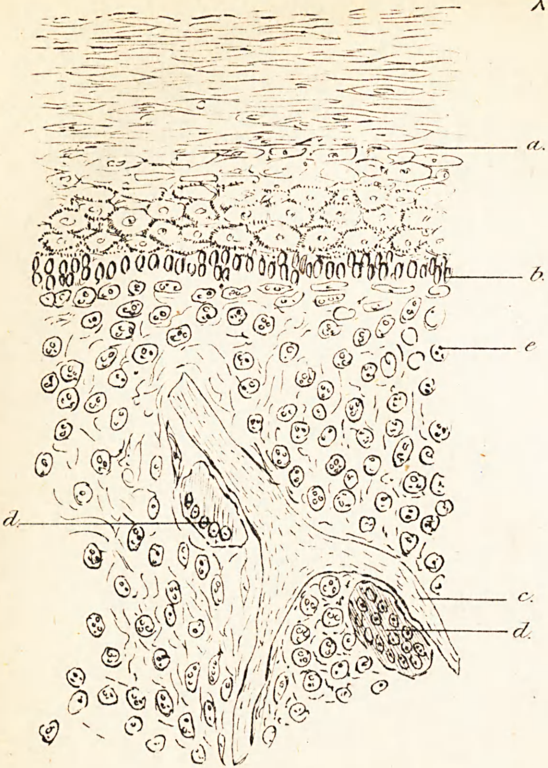


Fig. 1.

x 350 DIAMS.

Fig. 2.

In order to ascertain what the exact condition of the part was, he clipped out a small portion covered by a blue pellicle of young epithelium and gave it me for examination. It is noteworthy that, in clipping it out, the patient did not feel any pain, so that, probably, nerves had not found their way into the new mass.

I made some sections of the little piece of tissue, both when fresh and after being placed for forty-eight hours in Müller's fluid, drawings from which are shown in Figs. 1 and 2. In Fig. 1 is seen a piece of the section magnified about 300 diams. At *c* is noticed the keratode framework of the sponge as it appears with this magnifying power, while adjacent to it is shown the embryonic connective tissue (*e*), which has filled the interspaces and surrounds the framework. The surface of this new tissue is covered by a layer of epithelium (*a*), with a complete germinal layer (*b*). The epithelial cells, as so often happens in healing wounds, presented well-marked serrated edges.

The whole of the sponge interspaces were filled with what would be generally called young connective tissue cells, as seen at *e*, Fig. 1; but what was still more remarkable was the extraordinary number of very large giant cells (*d*) which lay in the same situation. A little piece of the sponge somewhat deeper in the wound is represented in Fig. 2, where *a* is again the sponge framework, while all round it, and sometimes adhering closely to it, lie great numbers of giant cells. They are of very large size, as may be seen from the drawing, which represents them as magnified 350 diams. There were in some of them as many as thirty nuclei, and every nucleus had one or more very bright nucleoli, without there being any apparent intranuclear plexus. Around these lay spindles and round cells of a connective tissue type. In fact, the appearance was like that of a typical giant-cell sarcoma. As will be seen from the drawing, there does not appear to be any absorption space in the sponge skeleton (*a*) at the point where the giant cells are attached, and hence I can hardly believe that they were acting as osteoclasts are supposed to do in absorbing and hollowing out a cavity in bone matrix. I should have expected that after this time, three to four months, they should have showed some action of this kind if they really possess such a function, but nothing of the kind was visible. It is possible, and I am open to further conviction on this point, that the portion of sponge examined, being superficial, had not been a sufficiently long time organized to allow of absorption taking place by the erosive action of the giant cells.

Whatever the action of these giant cells may be in the organizing tissue, the observation remains true that in nearly every instance in which I have had an opportunity of examining an excised portion they were present, and usually in great abundance.

The sponge framework appeared somewhat altered from its usual homogenous aspect. It was marked by many little lines (Fig. 2, *a*), and, at its ends, was thinner than usual (Fig. 2), appearances which seemingly indicated that it was dissolving. That such will be the ultimate result I cannot fail to believe. Being an animal texture, it will, like catgut, in course of time undergo tissue digestion.

Experiment No. 5.—Although these cases were all successful as instances of sponge-grafting, it is right that reference should be made to another case which proved unsuccessful, and to notice the cause of failure. The patient was a man who was under Mr Chiene's care in the Royal Infirmary. He suffered from an old necrosis of the lower end of the tibia communicating with a wound of considerable size. At the bottom of the wound the exposed and apparently dead extremity of the bone was visible, while the surrounding parts had an unhealthy, somewhat sloughy appearance. There was not any granulating surface at any part. The cavity was filled with a plug of sponge, but after being kept on for several weeks it did not seem to have formed any attachment. The reason was apparent; the parts could not furnish sufficient embryonic tissue to pierce into the sponge and to organize it. There were not any underlying bloodvessels to penetrate into its interstices. Under such circumstances only one result could be expected, as I told Mr Chiene when he proposed applying it, namely, that there could not be any permanent attachment.

These comprise the experiments which I have made in the human subject; but, in order to carry out the inquiry still further, I have performed certain experiments on animals, with a view to studying the process of sponge organization under more favourable circumstances. My friend Dr Woodhead, who had been working in my laboratory in the commencement of the winter session, undertook to get the experiments carried out for me in Professor Stricker's laboratory in Vienna. I have to offer him my warmest thanks for the trouble he took in getting the experiments performed, and also to tender the same to Professor Stricker for the interest he showed in the experiments, and for placing his laboratory at Dr Woodhead's disposal.

One set of experiments consisted in placing pieces of sponge within the peritoneal cavity and leaving them there for various periods of time, while another set comprised the introduction of the same into muscular parts. A third series of experiments was made by inserting two thin glass plates with a layer of sponge between them into the subcutaneous tissues, while Ziegler's original experiments (*Centralblatt,* 1874, Nos. 57 and 58), of inserting these beneath the tissues without any sponge intervening, were also repeated. Whether the sponge was placed in the peritoneal cavity or in a muscular part, the result, where the case went on favourably, was invariably the same, namely, that the sponge in a few days after insertion began to organize in the same manner as I had found to occur in the human subject.

Fig. 3.

J. Bartholomew, Edin.

The following description of the appearances presented is, however, taken from a sponge which had been in the abdominal cavity for a period of *ten days*. There was considerable peritonitis, and this occurrence, either of a local or general nature, is extremely liable to be set up in all such experiments on the peritoneum of the lower animals, chiefly from the difficulty of avoiding septic contamination. The sponge, as generally happens, was found to be adherent to a loop of the intestine. The union was so firm that it could with difficulty be detached. Throughout the abdominal cavity there was a considerable quantity of fibrinous lymph, but the part of the sponge not attached to the intestine was only partially covered by it. The greater part of the unattached surface was still quite porous, and did not present any evidence of organization.

On cutting into it, after it had been hardened in Müller's fluid, there was seen to be a layer of dense newly formed tissue at the attached edge of the sponge, about a quarter of an inch thick. The rest of the sponge was porous, and did not seem to be much altered in appearance.

Sections were now made through different parts of the sponge, and one of these, magnified 50 diameters, is represented in Fig. 3. The part represented is taken from where the newly formed tissue was greatest.

In all the experiments I have made, the first thing noticed is the infiltration of the interstices of the sponge with a certain amount of fibrinous lymph. The canals do not become occluded by it, but fibrin with entangled leucocytes is found adhering to the sponge framework (Fig. 3 A, and Fig. 4 *a* and *b*). The cicatricial tissue, however, gradually invades the apertures of the sponge subsequently to this, and, as will be afterwards more fully shown, displaces the fibrin and destroys it. In a section made from the interior of such a sponge there are always to be seen two distinct areas. The internal is the part which has been in the first instance filled with fibrinous lymph, while the other, the external, is that which is becoming pervaded with cicatricial tissue. These two areas are distinctly seen in Fig. 3. From A to B (inclusive) is seen the sponge framework infiltrated with fibrinous lymph, while the area comprised within C is the cicatricial or organizing layer invading the sponge and displacing the fibrinous lymph. At B there intervenes a very granular layer, which, as will be pointed out, is composed of broken down fibrin and leucocytes.

The line of demarcation between the fibrinous and organizing layers was in all cases perfectly distinct. In no instance was organization found to commence within the interior of the sponge among the primarily effused lymph. Without exception the cicatricial elements grew into the sponge in the form of a distinct layer, springing from the intestine or other tissue to which it had become attached. From this attachment bloodvessels also arose, which, along with the cicatricial elements, were the means of bringing about the organization.

Let us examine a little more closely, in the first place, a piece of the sponge comprised within the area A (Fig. 3), that is to say, the portion which is infiltrated with fibrinous lymph. A small piece of it is seen more highly magnified in Fig. 4. Lying in the sections of the "incurrent" and "excurrent" canals formed by the sponge skeleton there is seen to be a network of fibrin (*b*), while in its meshes are contained many blood-leucocytes (*a*), all more or less in a state of disintegration. The disintegration, however, of these and of the fibrinous network was much more evident at a point nearer to the cicatrizing layer (B, Fig. 3), where the whole network of fibrin, after becoming invaded by the connective tissue elements found in the cicatrizing part, seemed to fall to pieces and to be absorbed. I was not able to discover any cell other than a leucocyte in this lymph-infiltrated portion of the sponge. There was, further, not a vestige of a bloodvessel to be noticed.

Within the cicatricial layer (C, Fig. 3), however, the appearances were very different. As this layer had arisen from the intestine, it will be well to describe in what state the different coats of the intestine were, as the connexion between the cicatrizing layer and the bowel will then be better understood. The mucous and submucous coats of the bowel appeared to be unaltered, and the same can be said of the muscular coat, as may be noticed in Fig. 3, E. All the changes which had ensued in the texture of the bowel appeared to be concentrated in the serous or peritoneal coat.

From studying the appearances in different stages, as seen in various portions of the sponge, the first thing noticed in the serous coat was that its bloodvessels became much distended. At the same time they also became unduly tortuous, so that each vessel could be seen to have a markedly undulating character. The fibrous tissue around these also became œdematous, as shown by the surrounding wide connective tissue spaces.

On examining these distended vessels in other parts, long straight offshoots could be seen arising from them and running directly upwards into the cicatrizing layer (Fig. 3, C and *e*, *e*). The large number of these was in some parts very remarkable, forming, as seen in the drawing, a dense bundle in certain places. For a considerable distance after they left the parent trunk in the peritoneal or subperitoneal tissue they gave off only a very few divisions. Nearer the fibrinous layer, however, they could be seen to give off branches enclosing wide meshes, and at the extreme internal limit of the cicatricial layer they ended in a network of wide loops (Fig. 3, *b*, and Fig. 5, *a* and *b*).

Now, the convex side of these loops was, without exception, always towards the distal extremity of the vessel, the concave towards the proximal (Fig. 5, *b*), and in no instance could I find anything but loops in this situation. I could not see the slightest

X 350 DIAMS

Fig. 4.

X300 DIAM.S

Fig. 5.

J. Bartholomew, Edin.r

evidence of these bloodvessels ending in free extremities. There was always a complete afferent and efferent vessel. When such a loop reached the sponge framework it was pushed into it, often some distance in advance of the cicatricial elements which usually surrounded these vessels. It still, however, maintained the character of a complete capillary loop, and I was unable to detect anything like a free, newly formed, and pointed offshoot.

While the loops were always filled and usually distended with blood, it sometimes happened that the stem leading to or from them was comparatively empty. It seemed as if there had been greatest pressure upon the extremity of the loop, and as if the afferent and efferent vessels had been stretched and so rendered anæmic. On examining other portions of these vessels for any evidence of sprouts from their sides, I must say that I could not detect anything of the kind. It might have been expected that at this time (ten days), if these vessels were newly formed, the offshoots described by Arnold (*Virchow's Archiv*, vol. liii. 70) and others, should have been distinctly visible. After the most searching examination, however, I must confess that nothing of the sort presented itself.

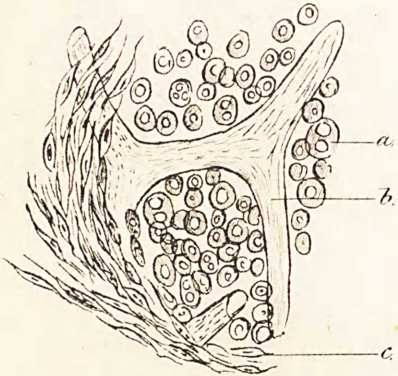
Another curious point, if these vessels were newly formed, was that the stems leading up to the capillary loops at the edge of the cicatricial layer possessed, in many cases, a completely formed adventitious coat. Arnold certainly refers to this circumstance in what he considers to be newly formed vessels in keratitis vasculosa, but whether those which he noticed having this appendage were actually newly formed is a matter of doubt. As regards those seen in the sponge, at least, possessing an adventitia, I shall have to give quite a different interpretation in the summing up of the facts of this paper in the sequel. Suffice it at present to state that the vessels at the invading extremity of the cicatrizing part were always in the form of loops, that these loops could be seen to be pushed into the spaces of the sponge, and, further, that even at the extremity of this part they presented the appearance of fully developed capillaries, without any evidence of offshoots branching from them.

I noted a significant phenomenon supporting the theory that the bloodvessels were pushed into the sponge as loops, namely, that when the convexity of a loop came in contact with the sponge framework, instead of one of its pores, a curvature formed on the vessel at the opposing point (Fig. 5, *c*), and on each side of the obstacle there was pushed in a secondary loop (Fig. 5, *d*) similar to that from which both had arisen. By this process of invagination, as it were, it seemed to me that the sponge became first vascular. A capillary loop was pushed against the sponge. If it happened to run into a pore it was driven further and further inwards, but if it abutted against an arm of the sponge framework the vessel became invaginated, and a secondary loop formed on each side. Whether another method of vascularization—by formation of new vessels—ensues at a later period, I cannot say; but certainly, ten days after being implanted in a tissue, everything seems to favour the idea that the vascularization is caused by already formed vessels becoming much elongated, and being subsequently pushed into and invaginated against the framework of the sponge.

The area in which the bloodvessels were contained I have named the "cicatrizing layer," because it was in reality the layer which contained the organizing elements. The character of the cellular structures found in this cicatrizing layer was (1) chiefly that of round cells (Fig. 6, *a*) several times larger than a leucocyte, (2) spindle cells (Fig. 6, *c*) developed from these, and (3) giant cells of great size (Fig. 2, *b*). The large round cells (Fig. 6, *a*) always contained at least one nucleus, sometimes two or more. They had also a very well defined border. Different stages of development were met with between the round and spindle cell. The cellular elements were in all respects identical with those met with in organizing inflammatory products. The giant cells, as in other cases, lay in very close contact with the sponge framework, and were frequently twisted round it.

Besides the above-mentioned cells, however, there were, as Arnold has described in parts becoming vascular, masses of coloured blood-corpuscles in certain spots, which, looking at the distended condition of the neighbouring capillary loops, and the localized character of the collection, I cannot regard otherwise than as extravasations. Various interpretations have been put upon the occurrence of these collections of coloured blood-corpuscles by Cohnheim, Arnold, Stricker, and others; but surely it is only reasonable to suppose that where such intense hyperæmia exists, as in a panophthalmitis, for instance, or in the case under consideration, small extravasations are only to be expected. In other parts, however, depôts of what undoubtedly were blood-leucocytes were to be seen, more particularly in the subperitoneal tissue, and there was good evidence to show that they had escaped from the distended vessels.

Are these leucocytes, however, to be looked upon, as Cohnheim (*Allgemeine Pathologie*, Band i. S. 29) does, as the elements out of which the larger round, or, as he calls them, "epithelioid" cells, above described, are developed? In speaking of the organization of inflammatory products in his lectures, he has the following:—"Certain it is that all further development is dependent upon the large epithelioid cells, closely related to which are the large giant cells, although the latter are much less numerous. The more rounded epithelioid cells, on account of their sending out processes, become spindle and stellate in shape. The processes grow and become further metamorphosed, chiefly in that they split and become converted into fine fibres and fibrils. From each end of a spindle cell there is then produced a pencil of fine, wavy, attenuated fibres, but



X 300 DIAMS.

Fig. 6.

X 350 DIAMS.

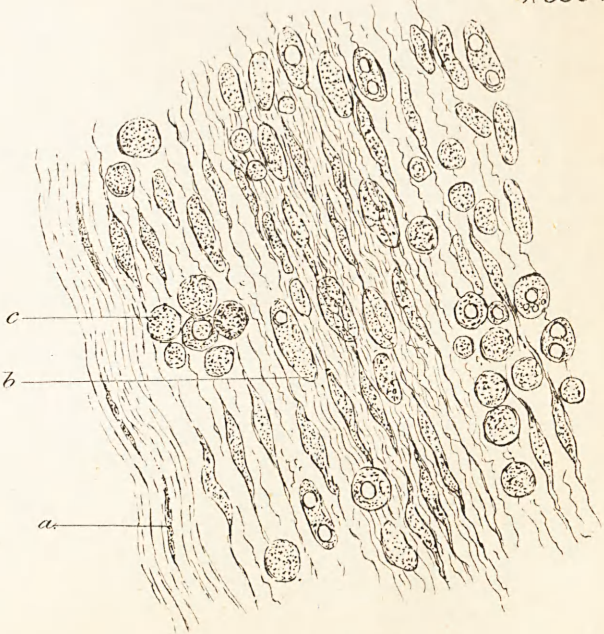


Fig. 7.

J. Bartholomew, Edin^r.

the broad side of the cell can also give rise to fibres which develop out of its protoplasm. From the fact that the fibres from different cells lie side by side, complete bundles of fibres result, to which, as a rule, several cells belong. The remainder of the protoplasm becomes converted into a fixed cell, which lies in the spaces between the bundles of fibres." He, therefore, clearly traces the origin of a newly vascularized cicatricial tissue to the transformation of these large epithelioid cells.

As regards the origin of the new cicatricial tissue, the question, therefore, comes to be—Whence do these epithelioid cells arise? This question is fully gone into in the work above mentioned, on several of the preceding pages, but, I cannot but think, with somewhat of a biassed mind. The whole object of the author seems to be, by keeping to one line of argument, or by want of sufficiently wide and accurate observation, to endeavour to prove that they are derived from blood-leucocytes which pass out of the newly formed bloodvessels. The fact of there being a possibility of any mode of origin other than this is never taken into consideration, the only point which the author cannot explain being why, in ordinary progressive inflammation, large numbers of these are extruded from the vessels and infiltrate the part without having any tendency to form fibrous tissue. He regards the formation of new bloodvessels as essential for the genesis and growth of the "epithelioid" cells. Without this they would be destroyed by fatty degeneration (p. 287). He further describes the method by which leucocytes become transformed into these "epithelioid" cells. He believes that what Ziegler has observed—namely, the enlargement of "individual pus cells by the absorption of others" (p. 285)—throws a great deal of light upon the subject, and, further, that these epithelioid cells, apparently by over-nourishment, may become converted into giant cells.

Now, although this theory of the origin of the new tissue has been accepted by many pathologists as correct, yet it seems to me that the evidence showing that a blood-leucocyte can become converted into a bundle of fibrous tissue is not proved by anything which the supporters of this doctrine have brought forward.

In the first place, if it is true that an over-nourished leucocyte will form fibrous tissue, why is it, then, that, when immersed in the richest of nourishing fluids, the blood, there is not only no inclination to form fibrous tissue, but not even a tendency to overgrowth? Nothing approaching the size of the "epithelioid" cells is reached. It might be urged that there is some special condition in the blood itself or bloodvessel which prevents their growing to an inordinately great size. Why, then, is it that, after they leave the bloodvessels in the natural course of the circulation and enter the lymph spaces, where they are bathed in nutritive pabulum, they still do not enlarge, still do not form fibrous tissue?

To any unbiassed observer who will take the necessary care in looking at such an organizing tissue as the sponge from which Fig. 3 was drawn, I cannot conceive that the origin of the large epithelioid cells should remain a matter of doubt. In Fig. 7 I have represented a few of the fibres from the fibrous tissue of the subperitoneal coat at the part where the sponge had become attached. What is the signification of the enlargement of every fixed connective tissue corpuscle upon these bundles of fibrous tissue, their polynucleation, their giving birth to a progeny of new cells, the accumulation of these cells in depôts, their subsequent wandering into the newly forming cicatricial mass? Are we totally to ignore such appearances, and say with Professor Cohnheim that the connective tissue corpuscles remain unaltered in such a part, or at least that they are not the progenitors of the cells out of which the cicatricial tissue is produced?

I presume that the supporters of such a theory will not deny that the cells of young growing connective-tissue tumours have a close resemblance to the so-called "epithelioid" cells already mentioned. Will they say that *these* are formed from leucocytes? Would they deny that such can be traced to an excessive activity of the connective tissue corpuscles of the part in which the tumour has originated? Why, then, where there is the most distinct evidence to support it, are they so averse to admit that the connective tissue elements in the neighbourhood of an organizing inflammatory tissue, such as Cohnheim refers to, are also the origin of the so-called epithelioid cells? Even although a believer, in former times, of the current theory of fibrous tissue formation from leucocytes, I cannot find, in all the search which I have made after facts to support it, a single instance in which it could be said, "Here is a leucocyte undergoing fibrous tissue transformation." On the other hand, I have overwhelming evidence to prove that in vascularized newly formed tissues the new connective tissue corpuscles are derived from old connective tissue, and that the so-called epithelioid cells are the direct offspring of the connective-tissue cells of the part.

Where, then, was the connective tissue layer derived from in this case of a sponge attached to the intestine? From the peritoneal and subperitoneal tissues and from the endothelium covering them. It was from the connective tissue nuclei lying upon the bundles of fibrous tissue in these that the progeny of new "epithelioid" or connective tissue cells mainly arose. The whole of the fibrous tissue of these parts was opened out and to a certain extent destroyed (Fig. 3, D). Its place was taken by a layer of young cicatricial elements a quarter of an inch thick. The proximate cause of this unusual activity of the connective tissue will be explained afterwards.

It has already been stated that at the free edge of the cicatricial layer the fibrinous network which filled the interior of the sponge had broken down, and the contained leucocytes had also fallen to pieces. The part to which I refer is seen in Fig. 3 at B, while the same part, more highly magnified, is represented in Fig. 5. It was very interesting to notice how the loops of the bloodvessels brought with them "epithelioid" cells, and how, after the former were projected into the interstices of the sponge, the "epithelioid" cells and spindle cells (Fig. 5, *i* and *g*) made their way into the meshes of the fibrinous network (Fig. 5, *e*) and rapidly destroyed it. Layer by layer the fibrinous lymph was thus removed, until the whole of the sponge canals came to be filled with the cicatricial tissue.

Such were the usual appearances seen when a sponge was left in the abdominal cavity. In some rabbits experimented upon, however, the sponge had first become infiltrated with pus. This had caseated, and, as a result, I am informed by Dr Woodhead that general tuberculosis was excited. Such sponges were practically solid, and in all respects were similar, as regards powers of organization, to a caseous mesenteric gland. Their interstices were filled by a solid, resistant, caseous mass. When this occurred the sponge never showed any tendency to organize, but became encapsuled by a layer of cicatricial tissue. The extreme periphery of the sponge was organized, this having happened apparently before caseation had occurred, but only for a very short distance. The interior was filled simply by caseous *débris* and shrivelled pus corpuscles.

The reason of this, as will be more thoroughly shown, undoubtedly was that the interstices of the sponge had become filled by a solid and hard material which as effectually resisted the entrance of bloodvessels and cicatricial elements as the solid texture of a caseous lymphatic gland or other caseous mass would. I have never seen any evidence of caseation of the sponge and its contents in the human subject, and must account for its occurrence in the rabbit by the well-known liability which there is for purulent collections to become caseous in these and certain other animals.

Another set of experiments was made by placing pieces of sponge between the muscular parts of animals, with very much the same results as those seen when it was left in the abdomen. In some, extensive organization had taken place, in others caseation had occurred, accompanied by encapsuling of the sponge, but without much organization of its substance. I regret that these pieces of sponge were merely inserted between the fibres of a muscle, and were not made to occupy the place of a portion which had been excised. This would make, I believe, a most important difference in the result.

Several other experiments were also made by placing a thin layer of sponge between two thin glass plates, and inserting this into the subcutaneous tissues. The results from this method of experimentation, however, were not satisfactory. The best results, as regards organization, have been obtained by simply placing a portion of sponge in a natural cavity, or in a part where there has been *loss* of tissue, as in those experiments recorded as made upon the human subject. In these the organization was completely successful, and took place without suppuration where the wound was fresh; but where inserted so as to cause pressure on adjacent parts, and thus to interrupt the circulation, the sponge seemed to act injuriously, and induced profuse suppuration. Experiments on the human subject, when made in a fresh wound, are also more successful than those in animals, because the wound can be kept aseptic, which is a very difficult matter to accomplish in the lower animals.

Organization of Blood-Clot.

Such being the facts derived from these as yet somewhat crude experiments, it seems to me that not only may they have a certain utilitarian value, but also that they open up a new field for investigation in the study of healing and growth. We have all been familiar for many years with the subject of skin-grafting, where a few young epidermic cells, placed upon a proper surface, will live, grow, and cover it. John Hunter's experiment of grafting the cock's spur on to the stump of the cock's comb was the first authentic indication we had that such a thing was possible. Of course the two sets of facts connected with skin-grafting and what I have called "sponge-grafting" are in no respect comparable, because, in the former, living epidermic cells are placed on a vascular surface and are simply nourished by it, so that they continue to live and grow, while, in the latter, the sponge merely acts a passive part in supplying a framework in which organization may take place. No one, I think, will say that a sponge, after it is deprived of its sarcode, is a living tissue; and yet we have seen that it is quite as capable of becoming organized as a blood-clot is.

When, however, we come to examine how a blood-clot organizes, the fact that a sponge may also be utilized for the growing of a new tissue is only what would be expected. Any porous substance will similarly fulfil this purpose, although sponge, owing to certain qualities, seems at present to me to possess peculiar advantages.

When blood is effused and coagulates on an abraded surface it will, as originally pointed out by John Hunter, and more fully demonstrated by Lister, in the course of time, become vascular, and, finally, apparently converted into cicatricial tissue. How is this accomplished? Where do the cicatricial elements come from?

For some time past I have studied with great care what occurs in this so-called organization of blood-clot, and am now fully persuaded that blood, after being effused from a bloodvessel, merely acts as a passive agent in bringing about organization—it serves the same purpose as the sponge framework. Any vitality which its leucocytes may have exhibited immediately after the blood has been effused, is, in a short time, lost. In the mere act of coagulating a great many of the leucocytes are destroyed, as Schmidt has shown, and remnants of these are always found in any fresh clot. In giving up their fibrin ferment they fall to pieces. Hence in a blood-clot there are always relatively fewer colourless blood-corpuscles than in an equivalent quantity of blood before coagulation.

What, then, does take place when such organization of blood-clot in a wound occurs? The first thing that happens when blood is effused on a granulating surface or into a tissue is coagulation. At least, such is the first thing seen when organization is going to occur. Blood which remains fluid when effused into a tissue is either all immediately absorbed, or becomes encapsuled by a layer of fibrous tissue. Suppose, then, that such a mass of blood has coagulated in or upon a recent wound, the next thing seen is that the bloodvessels of the underlying parts begin to dilate and to become tortuous. The connective tissue corpuscles around them also commence to show unusual signs of activity. The interfibrillar spaces become œdematous, and each connective tissue corpuscle rises up from the bundle on which it is placed. It then divides into several new cells, and the young brood so produced finds its way into an interfibrillar space. After the distention of the bloodvessels has existed for some time blood-corpuscles of both kinds are seen to wander out through their coats.

The next change perceived in the now tortuous and distended bloodvessels is that they are displaced and pushed outwards towards the clot which is lying on the surface of the wound. The blood-clot is an excessively porous substance. It is more finely porous than the finest sponge. The fibrin forms a network containing only a few blood-corpuscles, while the serum is squeezed out of, or drains away from, the interstices. It is, therefore, a tissue which, if its assumed vital properties be laid aside, is extremely like a sponge in its structure, each being composed of a delicate framework with large and small meshes.

The bloodvessels which have been pushed outwards from the neighbouring parts bear with them great numbers of the actively proliferating connective tissue corpuscles derived in the above-described manner from the neighbouring connective tissues. Coming in contact with the blood-clot, these vascular loops penetrate into its interstices, and the cells which abundantly surround them very soon fill its interfibrinous spaces. Almost immediately after this has taken place the fibrinous network disappears—it falls to pieces—and blood-corpuscles of both kinds can be seen, at the edge of the clot, to undergo a similar fate. They become granular, apparently in some cases fatty, and then disintegrate.

The vascular loops, surrounded by their tissue-forming cells, continue to penetrate further and further into the clot; and as successive meshes of the fibrinous network are filled by them, so they appear to cause its destruction, until the whole clot becomes in this way removed, its place being taken by new vessels and the above-described cicatricial elements. The latter soon elongate into spindle cells, and these, in from three weeks to a month, become transformed into fibrous tissue.

It was from observing the merely passive part played by the blood-clot when undergoing organization in wounds, in bloodvessels, and in other parts, that I was led to suppose that a porous substance like sponge, if applied under the same circumstances, would serve a similar purpose.

Organization of Fibrinous Lymph.

Fibrinous lymph, or, as it is sometimes called, a "false membrane," is simply a modified blood-clot. It is composed of a network of fibrin with leucocytes more or less abundant, and a certain number (often many) coloured blood-corpuscles. It is a blood-clot with a disproportionate mixture of the elements; for while the fibrin and leucocytes are in great abundance, the coloured blood-corpuscles are relatively few. In certain instances even the leucocytes are so few in number that the false membrane appears to consist almost entirely of a dense mass of fibrin. Such a false membrane, as seen on the pleura or peritoneum, for instance, in pleurisy or pericarditis, is extremely porous; it has quite a sponge-like consistence.

Suppose such a sponge-like mass of fibrinous lymph to be effused into the pericardium, how is it that the permanent organization of a fibrous adhesion is accomplished?

It was formerly supposed, and it is still held by many, that the fibrinous lymph has some inherent property of forming fibrous tissue. Such a fallacy, however, only requires a little careful observation for its exposure. Fibrinous lymph has no more power of forming *per se* a fibrous tissue than blood-clot or a piece of sponge has. If we were to place within the pericardial sac a layer of sponge instead of an effusion of fibrinous lymph, I have little hesitation in saying that a permanent fibrous adhesion would be produced between the epi- and pericardial surfaces just as well as by the agency of fibrinous lymph. For, seeing that this fibrinous lymph is nothing more than a modified blood-clot, it is only reasonable to suppose that its histogenetic powers would not be greater than those of such a sanguineous effusion.

The first thing that occurs in the formation of a pericardial or pleuritic adhesion is that the two fibrin-coated surfaces come together and coalesce. A fibrinous union is the result. But in the course of a few days the vessels on each side of the cavity become distended, just as in the sides of a wound with an organizing blood-clot within it. They also become tortuous, and very soon the capillaries on each side of the cavity are seen standing out at right angles to the surface. They are surrounded by young cicatricial elements, and within a few days are pushed into the fibrinous lymph and organize it. Organizing layers thus invade the lymph, both from the pericardial and epicardial surfaces, and gradually produce absorption of the fibrin and leucocytes on each side. The two cicatricial layers, after the lymph has all been removed, meet; they grow together like the two sides of a wound, and a permanent fibrous adhesion is the result. The same process may be observed in the formation of a fibrous adhesion between any two parts of a natural cavity. The method of union is the same as that by which a wound heals when fibrinous lymph or blood-clot is interposed between its surfaces.

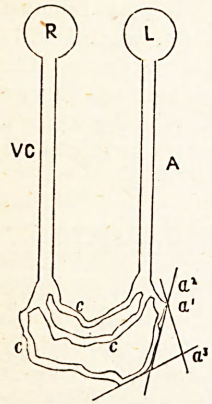
What is the Cause of the Organization of the Sponge in the Experiments just related?

From what has been recorded there cannot be any doubt that sponge, if placed under proper conditions, will cause the building up of a mass of cicatricial tissue. The reason for this, or the principle on which the sponge becomes infiltrated with young cicatricial elements, does not, however, at first sight appear to be so clear. For why a porous dead substance should of itself have the power of building up a mass of new tissue containing many bloodvessels seems, at any rate, a strange problem in tissue metamorphosis. The following explanation which I am about to give has become more and more convincing to me by the observation of many collateral circumstances.

Every part of the body is under a certain blood-pressure. The expulsive action of the heart, opposed by the elasticity of the tissues, strikes a balance at a certain mean pressure. Under such circumstances a cavity, in the strict sense of the term, whose walls are not rigid is a physical impossibility. All the so-called cavities, such as the peritoneum, pleura, or pericardium, must necessarily either have their surfaces in accurate apposition or must be filled with some resistant material which will counterbalance the pressure of the blood on their various sides. If a separation were to occur between the surfaces of the pericardium, the pleura, or the peritoneum, then the immediate effect would be the transudation of fluid from the bloodvessels to fill the vacuity until the pressure in the cavity were equal to that of the bloodvessels ramifying in its walls; or, if this were prevented, then the *capillary loops* on either side of the cavity, not meeting with sufficient support from the mutual pressure of the two walls, would tend to be pushed inwards so as to fill the vacuity.

Every capillary in the body has a tendency to be pushed further and further outwards from the heart as a pumping centre, as may be explained by the accompanying diagram.

Let L represent the left side of the heart, and R the right. The blood, leaving the left ventricle by the aorta (A), will be diverted from running in a straight line only in so far as it is opposed by certain forces. In completing the circulation it is so acted upon by these forces that it runs back through the vena cava (V C) in exactly an opposite direction from that in which it passes down the aorta (A).



The opposing force which determines this entire change in the direction of the bloodstream is to be found in the walls of the bloodvessels; for if we suppose *c*, *c*, *c* to represent capillaries, it is evident that it is by their intervention that the reversal of the stream occurs.

Now, it is apparent that as the blood would, practically speaking, continue to run in a straight line unless it were for the intervention of the curved bloodvessels, it must follow that the stream will impinge against the coat of the vessel at points a^1, a^2, a^3, and will tend to drive the vessel outwards. That this displacement does not actually occur is, I hold, the result of the resistance of the fasciæ and skin, which so bind the capillaries down in their places that eversion is prevented. In the case of a cavity, such displacement is prevented by the mutual compression of the various sides.

There are many facts which prove that a restraint of this kind is required in order to prevent capillary displacement, and the following may be taken as examples. If, for instance, we remove the skin and leave the part exposed, the almost immediate effect is that the surface begins to granulate; and if we study how these granulation vessels are formed, it is evident that they are nothing more than the superficial capillaries of the subcutaneous tissues which have been displaced and elongated by the pressure of the blood within them. There is not any evidence in such a case to show that the bloodvesssels are newly formed. The loops can be seen in all stages of eversion. That these capillary loops, further, are not, as is generally supposed, a provision of nature towards reparation, is shown by the fact that the larger they grow the less rapidly healing proceeds. They require to become *atrophied* before healing will commence. This is shown to be the case even better by the fact that wounds of non-vascular parts, such as the cornea, heal much more quickly than those of vascular, and also that a wound heals quicker by the first intention than by the second. Granulations, if not otherwise utilized, undoubtedly are one of the great obstructions to a wound healing.

Another example bearing upon the point in question is seen in the healing of wounds by the first and by the second intentions. Make an incision in a tissue, bring the edges together so as to exert mutual pressure, keep the part free from irritation, and the two injured surfaces will rapidly unite without granulating. Expose the surfaces of such a wound by separating them, and do not apply any counter-pressure, and the whole of the superficial capillary loops, which have lost the restraining influence of the tissues, will be everted as granulations.

Thirdly, there is not any tendency to granulation on the pleural or peritoneal surfaces nor on the mucous membrane of the bladder. Separate the adjacent surfaces, however, and expose them, and they will begin to granulate like the surface of a fresh wound.

The vessels of the brain are restrained in their position by the resistance of the cranial vault and membranes. Remove these resisting media, and the brain is seen to pulsate in the first instance, and then is forced out in the form of a hernia.

The granulations in an ulcer of the leg are larger when the limb is dependent, because there is more than ordinary pressure exerted upon them by the weight of the whole blood-column. The tendency to ulceration on the leg is simply an expression of the effects of increased pressure upon the resistant skin. In order to relieve this pressure and to avoid ulceration, we raise the limb and place the patient in the recumbent position. The cause of the ulceration is that the balance which naturally exists throughout the whole body between the expulsive action of the heart and the resistance of the tissues has been disturbed and is in favour of the former. The cellular tissue infiltration which precedes the formation of an ulcer is simply a mass of granulations. The vessels within it are all much distended; they are under an undue pressure, and are ready, when the skin is destroyed, to burst out in the form of capillary loops. We must remove the undue capillary tension by counter-pressure or by raising the limb before the balance can be again struck between the expelling force and the resistance. If, on the other hand, an unduly great amount of contracting cicatricial tissue should result after healing is complete, then the balance between the two may be again disturbed in an opposite direction, and a shrinking of the limb follows.

Lastly, as another example of the displacing action of the heart upon the bloodvessels, we may take that of the different length of the limbs and stature of the body in a blood-vascular animal of the same genus and species. Why is it that in different individuals there is such a difference in stature, such a contrast in the length of the limbs? May it not be that the cause of it in reality is that the propelling action of the heart is specially vigorous in those of great stature, and the resistance of the tissues slight, while in those of small stature the reverse conditions are present. Why is it that growth goes on up to a certain age? May it not be that the heart is relatively more powerful than the delicate stretchable tissues of youth, but that as adolescence is reached the tissues become sufficiently rigid to counteract the heart's action; while in old age, again, the balance is actually on the other side, the heart becoming weak, the tissues more rigid, and a consequent shrinking taking place.

Much the same thing is seen in plants. When growth is most active the plant is in a cellular, pliable condition. Its interstices are easily distended by the ascending sap, which, rushing upwards, will no doubt tend to push out the plant further and further; while, as it becomes older, and as more woody fibre is formed within it, a stable condition is reached, which, if carried to an extreme degree, ends in the atrophy and death of old age.

There therefore seems to be very good reason to believe that there is a constant tendency to displacement of the bloodvessels throughout the body, and that this does not take place oftener than actually happens is due to the resistance of the tissues. The fasciæ bind down those which are internal; the skin has the same effect on those which lie superficially. It is only necessary to remove these restraining influences in order that the phenomenon of eversion and elongation of the bloodvessels should manifest itself.

If it be granted that this theory is correct, it goes far to explain how a porous substance, such as a sponge or blood-clot, may become organized if placed under certain conditions. We have already drawn attention to the fact that the peritoneal, pleural, and other so-called cavities are in reality not to be looked upon as such. Their parietes keep up a mutual pressure, so that no vacuity is left.

If, however, we open one of these cavities and place within it a porous substance such as a sponge, then we entirely alter the conditions. By so doing we leave within the space a body filled with minute pores, in which the pressure must be very much less than that of the bloodvessels in the walls of the cavity in which it is contained; and, further, if we suppose the pores to be filled with air when introduced, this air will in all probability become absorbed, or at any rate it will be capable of great compression. In the course of time it would undoubtedly become removed and its place perhaps be taken by water vapour. The pores of such a substance will afford insufficient support to the bloodvessels ramifying in the walls of the cavity in which it is contained. These bloodvessels will consequently tend to become displaced and pushed into the pores, for the same reason that granulation loops are pushed outwards on a part from which the skin has been removed. The first thing that ought to be seen in such a part would be dilatation of the bloodvessels in tissues immediately adjacent to the sponge. Then they should become tortuous. The tortuosities should be forced upwards or inwards, as the case may be, and then they should become elongated and their meshes widened. That such actually occurs in the vascularization of the sponge may be seen from the drawings and the description which I have given. That new formation of bloodvessels may subsequently occur I will not deny, although I have never seen it in any of my experiments. That the primary means of vascularization, however, is from the old vessels of the part becoming elongated and pushed inwards, I believe is thoroughly borne out by what can be observed. The principle holds good in any part of the body, that if you remove the resistance, the bloodvessels will protrude; if you apply counter-pressure, they will be restrained.

The same method of vascularization prevails in the application of a sponge to a wound of an external part. Here the resistance in the form of the skin has been removed, and the granulation loops are pushed into the sponge porosities. Were the body applied not porous, then of course the effect would be to restrain the vessels instead of encouraging their evagination.

It might be said, however, if this theory be true, if bloodvessels will become protruded in this way when the resistance of the skin is removed, why do they not grow on indefinitely without the application of a porous body such as a sponge or a blood-clot. In certain cases granulations do become so exuberant as to rise up above the level of the skin; nay, they may form a little wart-like growth in some situations and under certain circumstances. Their growth, however, is generally cut short for various reasons, two of the most important being the spread of epidermis over them, and the constriction of the healing part of the wound. There is another reason, however, which prevents their growing on indefinitely, namely, that they require a framework to act as a support, and to which they may become attached very much as a climbing plant does to a trellis-work.

We all know that if a climbing plant does not meet with the necessary support its growth is impeded and the whole health of the plant is impaired. Tendrils, if they do not meet with a support, dry, become woody, and finally die (Sachs, *Text-Book of Botany*, p. 777). The circulation in such a plant must be seriously interfered with if the plant is allowed to grow along the ground instead of in its naturally upright condition. It seems to be very much the same with granulation capillaries. In some of my preparations tendril-like bundles of spindle cells can be seen to twist round a portion of the framework of the sponge, and, being fixed at the other end to a capillary loop, to support this, and in some cases apparently to contract and pull it outwards. In certain instances I have seen a rope-like bundle of spindles twisted round a piece of the sponge framework and attached at each end to a small capillary vessel, which it was pulling further and further towards the interior of the sponge. If such a support is not given it can be easily seen that the granulation loops, when they become of a certain length, would tend to fall over. Their circulation would thus be impeded, and the loop would probably die or become abortive. The sponge or blood-clot, however, affords a most serviceable trellis-work to which the ends of the loops may become fixed, so as to allow of their circulation going on with as little impediment as possible. The structure of the sponge is thus excellently adapted for the purpose of growing new tissue, because its framework is so delicate and its porosity so great.

I would therefore conclude that the sponge acts in a twofold manner in inducing new growth of tissue, firstly by its porosity allowing the vessels to gain entrance, and, secondly, by its framework affording a support for the capillaries to climb upon.

It might be said, however, if you place a sponge in a peritoneal or pleural cavity, will fluid not be effused into it and so equalize the pressure within the interstices of the sponge and the vessels on the wall of the cavity? If such did happen, then I believe the sponge never would organize. I have already quoted experiments in which it became filled with pus and then caseated, and in which there was not any effort at organization. The same thing would happen if it became filled with serous fluid. One of two things must happen if placed in such a cavity: either fluid must be effused so as to fill the interstices and thus to equalize the pressure, or bloodvessels and cicatricial tissue will have to do so. In all those cases in which organization has taken place the sponge was not filled with fluid, although, of course, a certain amount was always present, and in those which were applied to an external part the opportunity for the exodus of fluid was quite free, a considerable quantity being given off as discharge.

The next point that has to be accounted for is the cause of the great cellular proliferation and invasion of the sponge. It has been related that the sponge, in the first place, shows a few leucocytes in its interior, but that subsequently these, along with the fibrinous lymph which accompanies them, give place to a layer of much larger "epithelioid" cells, which gradually invade the sponge from the periphery. These, as can be seen from Figs. 3 and 5, form a dense layer round the bloodvessels. Why are these formed? What is the cause which excites their development. Professor Cohnheim would answer that they are leucocytes which have exuded from the vessels. I have very little hesitation in replying, that although a few leucocytes are mixed up with them, the greater number do not exude from the bloodvessels, but are derived from the connective tissue.

Almost simultaneously with the hyperæmia of the serous coat of the intestine, in those cases where the sponge was laid in the abdominal cavity and became attached to the bowel, it could be observed that the connective tissue corpuscles showed unusual activity and began to assume a germinal character. In Fig. 7 is represented a small portion of the subserous fibrous tissue of the intestine opposite the attachment of a sponge. Bundles of fibres are seen, with great enlargement of the fixed connective tissue corpuscles upon them. At *a* is noticed a fixed connective tissue corpuscle, lying between and upon the bundles of fibres, becoming enlarged and granular, while at *b* is seen one of the same which has undergone still greater enlargement, and whose flat surface is rendered visible by its superficial position. Others are spindle-like bodies, owing to their being looked at on edge between two bundles. In many of them two nuclei are visible. There was almost always one such nucleus, although it was frequently much obscured from the excessive granularity of the corpuscle. When these bodies became larger they could be seen to elevate themselves from the bundle on which they lay, in the same manner as can be observed in the fibrous tissue out of which a young sarcomatous tumour is growing. They then lost their attachment to the bundle, and moved off in rows or arranged themselves in masses (*c*). They subsequently became polynucleated, and germination, with the most active division of the cell, followed with great rapidity. In the superficial part of the serous coat the whole of the fibrous tissue had become destroyed by this means, the remains of its fibres being dragged towards the sponge by the everted blood-vessels. The cells thus produced were typical "epithelioid" cells, as Cohnheim describes them, and it was by the further enlargement (a simple overgrowth) of these that the giant cells were formed.

The leucocytes and coloured blood-corpuscles, on the other hand, which could be seen exuding from the vessels in certain places, remained as such; and although they in many cases became mixed with these other cells of connective tissue origin, yet they never became any larger, either by over-nutrition or by the coalescence of several together. The cells of connective tissue origin, on the other hand, could be traced through all the stages from their point of origin to the time when they elongated into spindles. The rapidity with which they divided was very much like that seen in a young sarcoma. In fact, at certain parts of this cicatricial layer the appearance was identical with that of a round-cell sarcoma.

How is it, then, that the activity of these fixed connective tissue cells was aroused? What influence was it that brought them into this embryonic state of multiplication? The question, to be gone into properly, would require a special treatise, and I do not intend entering into the complete evidence on the subject at present. It will be sufficient to state that, after examining into the subject with great care, I cannot find any other cause than that the part was overnourished. The distended state of the vessels would allow a greater amount of fluid to escape from them, and that fluid would have a richer composition than ordinary serum—it would, like an inflammatory effusion, be almost pure liquor sanguinis. This, being poured out in great quantity, would undoubtedly, as always happens, induce a special activity in the cellular tissue elements, and would, as may be seen in any such case, induce an overgrowth of their substance with subsequent proliferation. Even in a simply œdematous part the same thing can be noticed to a certain extent; but if the fluid effused should be richer than mere œdematous fluid, should it be pure or nearly pure liquor sanguinis containing an excess of albumen, then I have never failed to see, in such circumstances, appearances similar to the above. It is just a question whether a constructive inflammation does not owe its new tissue simply to an excessive quantity of a highly nutritious fluid exuding from the inflamed bloodvessels and overnourishing the tissue elements.

There is the closest relationship between what we call œdema and what is known as inflammation. The difference is one of degree. In the former a comparatively thin fluid, so to speak, is poured out and induces a certain amount of germination in the tissue elements. In the latter an extremely rich fluid—in fact, the liquor sanguinis—exudes, and, accompanying this, and, I hold, in great part due to it, is produced an appearance such as that shown in Fig. 7. It may be said that similar appearances are seen in non-vascular parts when stimulated; but what parts can we say are non-vascular? If the cornea be taken as an example, it may justly be said to be devoid of bloodvessels; but has it not the most exquisite plexus of lymph-channels capable of conducting into it fluid poured out by the neighbouring bloodvessels? Is not swelling of this connective tissue from distention of its interfibrillar spaces with a rich lymph fluid one of the prominent signs of its inflammation? And if so, does it differ in any material respect from a vascular part under the same circumstances? The study of the cornea as a non-vascular tissue is quite a superficial distinction. It does not possess bloodvessels, but they are in abundance all round it, and its nutritive supply must be influenced by the condition of the bloodvessels at the periphery just as much as a fascia or a tendon with bloodvessels thinly scattered throughout them. Complicated as the subject of proliferation as a result of inflammation may be, it seems to me that the cause of all such proliferative phenomena can be reduced to that of over-nutrition. Under normal circumstances the supply of nutritive fluid is commensurate with the demand. If from any cause this becomes abnormally increased, excessive growth is the result.

I would, therefore, say that the bloodvessels are the primary cause of the vascularization of the sponge, and that they bear into its interior actively dividing connective tissue corpuscles derived from neighbouring connective tissues, and that it is out of the latter that the new cicatricial tissue is evolved. The bloodvessels are the primary, the connective tissue elements the secondary factors in the organizing process.

Some Suggestions as to the Application of Sponge-Grafting.

Having once recognised the principle that a porous body may become vascularized and be the medium for the construction of new tissue, the application of the method to various purposes naturally suggests itself. In applying any porous body with a view to this organization certain points must always be kept in mind. The porosity of the body must be such that all the canals freely communicate. Sponge is exquisitely suited for the purpose on account of the free anastomosis between its channels, but many other substances might be utilized in the same way. I have of late thought that charcoal or calcined bone might be employed in certain cases. For one purpose at least such a solid framework would be useful. Where it is desired to prevent contraction of the newly formed tissue when it cicatrizes, where it is of moment to retain the newly formed tissue of its original bulk, then a solid framework must be employed. A solid framework will, I feel sure, organize just as a sponge would, and will have the special quality of preventing cicatricial shrivelling. When once incorporated with the tissue it will not cause any more irritation than the calcareous matter of a bone does. A dead body of this kind is not of itself an irritant. It is the injurious application of it, or the septic matter which it may introduce, which gives rise to the mischief.

Such a solid framework, it strikes me, would be particularly useful for forming new bone. One of the great dangers of a simple periosteal detachment operation is that the future bone is not sufficiently bulky and strong. By supplying a solid framework of this kind we would avoid this, and the formation of bone would proceed within it just as well as in the spaces of cartilage or the meshes of a fibrous tissue. Bone is nothing more than a fibrous tissue modified by being impregnated by calcareous and other salts. The particular elements which go to form bone are nothing more than connective tissue corpuscles, and by supplying a framework of the above nature for these to ramify within, bone might be grown to an almost unlimited extent. The sponge framework, I should think, although I have not as yet had any practical experience in the matter, would be rather too yielding, and would be liable, when infiltrated with bone elements, to contract. Whether the formation of bone would commence early enough to prevent this I do not know. It is quite possible that it might.

Wherever it is applied, it must be always remembered that the sponge or other framework must be employed merely for the purpose of *filling a vacuity*, otherwise it will cause great inflammation, and the efforts at organization will not proceed. My experiments so far have shown me that, if thrust between two portions of a muscle, for instance, without a portion of the muscle being excised, organization does not proceed nearly so equally as when a piece of tissue is removed and the sponge merely takes its place. The reason is obvious. If thrust between the muscles of a part it will, especially when it gets softened by the juices of the tissues, tend to swell, and, by pressing on neighbouring bloodvessels, will interrupt the circulation within them and so induce an inflammation. Where it merely fills a vacuity, however, the case is very different, and organization will then follow.

Before being applied it should always be rendered antiseptic, and, of course, this specially holds good of its application to a fresh wound. Every one will admit that nothing is more conducive to putridity in a wound than a septic sponge, while, if applied in an aseptic, or rather antiseptic, condition, and dressed with the view of retaining it so, it can be kept, as shown in one of my recorded experiments, perfectly free of putrefaction through a period of several months.

So far as I see at present, the method of "sponge-grafting" seems excellently suited for growing new tissue where that is insufficient to cover a part or to allow of stretching, but whether it may not have a wider range of application remains for future experience to demonstrate. The only objection which I perceive to its application is the somewhat long time required to organize it. During the first ten days I found that a part of a sponge placed in the abdomen had organized from an eighth to a quarter of an inch, but it always happens that one part organizes quicker than another, and hence, although in a large wound one part may thoroughly organize in, say, a month, other parts of the same sponge require longer. I cannot see, however, what objection there would be to the patient going about, if this were practicable, after the sponge had once become fixed. On the contrary, I should think that this might actually, in certain cases, exert a beneficial influence upon the organizing powers of the tissues.

List of Illustrations.

Fig. 1.—Portion of sponge from Mr Bell's case of excision of the mamma three months after the operation : *a*, new epidermis ; *b*, germinal layer of same ; *c*, a portion of the sponge framework somewhat attenuated at the end ; *d*, giant cells ; *e*, round connective-tissue cells filling the sponge interstices and underlying the new epidermis.

Fig. 2.—Portion of same sponge as in Fig. 1, deeper down : *a*, sponge framework ; *b*, multinucleated giant cells ; *c*, round and spindle connective-tissue cells occupying the intervals between the giant cells.

Fig. 3.—Section through the side of a sponge left in the abdominal cavity for ten days, and which had become adherent to the bowel : A, the interior of the sponge, which is filled with fibrinous lymph, but has not as yet organized ; B, portion of the same adjacent to the cicatrizing layer (C), in which the fibrinous network is becoming destroyed by the invading cicatricial elements and bloodvessels ; C, the cicatricial layer derived from the peritoneal and subperitoneal tissue of the intestine (D) ; D, the remains of the peritoneal and subperitoneal tissue of the intestine, showing the bloodvessels sprouting from them ; E, muscular coat of the intestine ; *a*, fibrinous lymph lying in the meshes of the sponge ; *b*, a capillary loop being pushed into a space in the sponge ; *c*, giant cells adhering to the sponge framework (*g*) ; *d*, cicatricial elements passing into the sponge along with the bloodvessels ; *e*, the straight vessels running off at right angles to the intestine ; *f*, vessels in subperitoneal coat in a distended and tortuous condition.

Fig. 4.—Portion of same sponge as in Fig. 3, taken from the centre, showing the infiltration with fibrinous lymph : *a*, leucocytes ; *b*, fibrinous network ; *c*, framework of sponge.

Fig. 5.—Portion of same sponge as in Fig. 3, at the extreme edge of the cica-

trizing layer ; it corresponds to the part comprised within B in Fig. 3, but is more highly magnified (300 diams.) : *a*, capillary stem leading up to capillary loop (*b*) ; *b*, capillary loop being pushed into the sponge framework ; *c*, portions of the sponge framework ; *d*, a capillary loop rising up on each side of a portion of the sponge framework ; *e*, the fibrinous lymph breaking down as the sponge is becoming invaded by the young cicatricial elements ; *f*, a bundle of spindle cells twisted round a piece of the sponge framework ; *g*, cicatricial elements accompanying the vessels ; *h*, a leucocyte in the fibrinous lymph ; *i*, cicatricial cells invading the fibrinous lymph.

FIG. 6.—Portion of the sponge framework taken from a part which had cicatrized ; it corresponds to the area marked C in Fig. 3, only more highly magnified : *a*, cicatricial cells occupying the spaces of the sponge framework ; *b*, the sponge framework ; *c*, some spindle cells twisting round the framework.

FIG. 7.—A portion of the subperitoneal fibrous tissue taken from same sponge as that represented in Fig. 3 : *a*, fixed connective tissue corpuscles beginning to enlarge : they look like spindles when seen on edge between two bundles of fibrous tissue ; *b*, the same, more enlarged, and seen on their flat surface ; *c*, a group of large epithelioid cells formed from these.

ARTICLE II.—*Report of Fourteen Cases of Completed Ovariotomy.* By ANGUS MACDONALD, M.D., Lecturer on Midwifery and the Diseases of Women and Children, Medical School, Edinburgh; Physician and Clinical Lecturer on Diseases of Women, Royal Infirmary, etc., etc.

(*Continued from page* 334.)

CASE VII.—Mrs B., æt. 30, married four years, mother of three children, was admitted to Ward XVI., old Royal Infirmary, on 30th of January 1879, complaining of pain and distention of the abdomen. She began to fail in health towards the end of the previous October. She experienced great pain in right side of the abdomen, accompanied with fever, and at the same time noticed that her belly began to swell. She was ultimately seen by Dr John Playfair, who recommended her to the Infirmary.

Condition on Admission.—Patient was pale and thin. Some œdema and swelling of the whole right leg, more especially near the ankle. Abdomen presented appearance of an eight months' pregnancy. The superficial abdominal veins were much distended and very large. Measurement round umbilicus, 35 inches. Percussion yields a dull note, except over a portion of the abdomen extending from ensiform cartilage to a part two-thirds the distance from that to umbilicus. Percussion at the flanks also comparatively dull, but not absolutely so. Fluctuation and fluid impact thrill over the whole of the abdomen. Palpation does not cause much pain, except over a single spot midway between umbilicus and anterior superior spine of right ilium. The uterus was rather drawn upwards, was movable, and sound passed $3\frac{1}{2}$ inches into its cavity, causing some pain. There was no perceptible change of resonant