ARTICLE III.—*On the Textural Changes which Occur in Inflammation of Serous Membranes.* By WILLIAM TURNER, M.B., London, F.R.C.S.E., Senior Demonstrator of Anatomy in the University of Edinburgh.

IN a Lecture delivered before the President and Fellows of the Royal College of Surgeons of Edinburgh on the 27th February 1863, and published in the April number of this Journal, I gave an account of the more important investigations made during the past few years into the mode of origin of the new cells formed in the course of certain pathological processes. In this lecture were incorporated various observations of my own on the same subject.[1] Among others I recorded some observations which I had made on the origin of the corpuscles of the coagulable lymph—the so-called inflammatory exudation corpuscles—in a case of inflammation of the pleura. Since that time I have availed myself of such opportunities as have presented themselves to prosecute additional inquiries into the process of inflammation in serous membranes, and in this communication I purpose recording the results of my observations made on various specimens of inflamed pleural and peritoneal membranes.

To carry out successfully an inquiry into the nature of the inflammatory process in a serous membrane, the attention of the pathologist should not be confined to the examination of the lymph coating its free surface, or to the mingled liquid and solid products lying in the serous cavity, but the membrane itself should be carefully inspected, not only at its free surface, but for some distance into its substance. This may be efficiently done by making sections through its entire thickness, and carrying the knife even into the subserous connective tissue. If a portion of the subjacent healthy texture is thus included along with the diseased in the section, the observer is enabled to make, in the same preparation, and from the same locality, a comparison of the healthy tissue with that in which the characteristic inflammatory changes have taken place. I have been in the habit of making these sections with a Valentin's knife, spreading them out carefully on a glass slide so as not to disturb the relations of the structures, and adding acetic acid and glycerine to assist in promoting the transparency of the parts.

The textural elements which enter into the formation of a serous membrane are epithelium and connective tissue. The epithelium consists of a simple layer of pavement epithelial cells. It rests on the subepithelial connective tissue. In the connective tissue, both the white and yellow fibres exist, the latter in considerable numbers. The connective tissue is always more compact immediately beneath the epithelium than in the parts further removed from it, from which circumstance the membrane-like appearance described as the basement membrane results. In the deeper parts of the texture the gradual blending of the connective tissue of the serous membrane

[1] See also the new edition of Paget's Lectures on Surgical Pathology, p. 287.

with the looser subserous connective tissue may be traced. The amount of this latter tissue is greater in the parietal than in the visceral portions of a serous membrane. In tracing the effects produced by the inflammatory process, the changes which take place both in the epithelial and connective-tissue elements of the texture ought to be studied.

In the specimens of inflamed pleura I have examined, the membrane was thickened and swollen, and covered by a soft layer of yellowish, flaky inflammatory lymph, which could be readily scraped off with a knife. When the lymph was removed an abundant bright red mottling of the membrane was noted. When the inflammatory lymph was examined microscopically, it was seen to be composed of small, pale, faintly granular cells, such as are familiar to all pathologists as products of the process of inflammation, and are described sometimes as the corpuscles of inflammatory lymph, at others as exudation corpuscles.

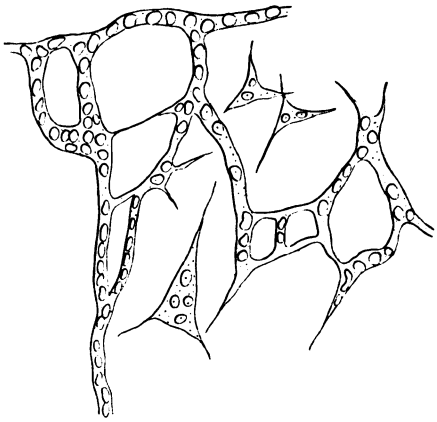
I have no observations to offer on the changes which the epithelium had undergone in the course of the inflammation. It had either been shed from the surface of the membrane into the cavity, or its characters had been so altered that it was no longer recognisable. Two opinions have been put forward, and supported by observations, of the part which the epithelium takes in the early stage of inflammation of a serous membrane. According to Dr Julius Cohnheim,[1] some of whose observations were made on animals killed the day after he had irritated the peritoneum, the epithelial cells were found to be increased in size, more opaque, with no longer a mosaic arrangement, but lying next each other as large round globules, with a large shining nucleus. In some cells fatty degeneration had begun, and this could be traced in others up to the stage of disappearance of the cell membrane, and destruction and resolution of the cell into granules. Dr E. Neumann's observations[2] agree with those of Cohnheim as far as relates to the degeneration and shedding of the epithelium cells. Dr Rindfleisch,[3] again, regards the epithelium as not necessarily destroyed by fatty degeneration at the commencement of the inflammatory process, but as assisting in the production of the new-formed cells of the inflammatory lymph. He induced artificial peritonitis in a rabbit, and found that the epithelial cells had lost their normal, six-sided, flattened form, that their corners had become rounded, and their shape was more globular. The contents also were more opaque, and commencement of nuclear division was observed. Rindfleisch considers that there is a direct metamorphosis of the epithelial scales into cells which, through their rounded form and divided nucleus, resemble pus-corpuscles. Even if these conclusions of Rindfleisch's be accepted, I cannot but think that the part which the epithelium plays in the production of the cells of the inflam-

[1] Virchow's Archiv, vol. xxii. p. 516, 1861. [2] Ibid. vol. xxiv. p. 202, 1862.
[3] Ibid. vol. xxiii. p. 519, 1862.

matory lymph is comparatively unimportant, and that it is the subepithelial connective tissue we are more especially to look to as the seat of their formation.

When sections through the inflamed costal pleura were examined, before the addition of acetic acid and glycerine, a confused mass of new-formed cells mingled with the proper fibres of the sub-epithelial connective tissue in apparently inextricable confusion was seen. But after the addition of the above reagents had caused the white fibrous element of the tissue to disappear, the transparency of the textures was promoted, and the arrangement and relations of the new-formed cells could be followed, especially in those parts of the section where the elastic fibres were at a minimum. The new-formed cells were small, pale, and rounded, with faintly granular contents, and closely corresponded in their characters to those existing in the inflammatory lymph coating the free surface of the membrane. In those parts of the sections which lay immediately beneath this free surface, the cells were crowded together in great numbers, and formed closely packed rows or clustered masses. But somewhat deeper they were not so densely set, and here, therefore, their mode of arrangement could be more satisfactorily studied. To attempt to describe all the variations which they presented in the numerous sections I examined, would be tedious and of little practical value, but a general description may be attempted. In many places they were so disposed as to form a network, more or less close, which possessed greater or less degrees of irregularity in the size and form of its meshes. For the most part the cells were arranged in rows, though here and there they lost the linear disposition, and formed small clusters. The cells succeeding each other in any given row were either in contact, or almost in contact,

Fig. 1.



though occasionally intervals of somewhat greater extent existed between them. These cell networks evidently did not lie free in the

interstices of the texture, but were enclosed by an investing membrane, which appeared to constitute a tubular system possessing numerous anastomoses, though here and there the tubes gradually terminated in long pointed processes (Fig. 1). Cell-containing tubular networks presenting modifications of the plan just described and figured, could be followed through the greater part of the thickness of the inflamed costal pleura, though in some places the numerous yellow elastic fibres prevented the arrangement from being so closely traced. The constancy of these arrangements shows, I think, that these cell-containing tubular networks are not mere accidental occurrences in inflammations of the inflamed pleura, but are evidently due to something in the anatomical configuration of the part which determines that the new cells produced in the course of the inflammatory process should arrange themselves in such a manner. The numerous investigations, more especially by Donders, Virchow, and Von Wittich, which have of late years been conducted into the structure of the connective tissue, supply us with a means of giving a satisfactory explanation of the mode of production of these cell-containing networks. For it has now been demonstrated that there exists in the connective tissue, in addition to the ordinary well-known fibres, a distinct nucleated corpuscular element, the individual corpuscles of which give off processes and possess most commonly a fusiform or stellate shape. Between the processes of adjacent corpuscles, frequent anastomoses occur, so as to occasion a networklike arrangement in the texture.

The extended observations of Virchow, Billroth, C. O. Weber, Förster, and others, have shown that in the production of pus-cells and other pathological new formations, the corpuscles of the connective tissue play a most important part. If this texture be examined in the early periods of the inflammatory process, the single nucleus of the connective-tissue corpuscle may be seen to be constricted in the middle, as if dividing, or to have divided, into two or a greater number. The corpuscles themselves are enlarged and

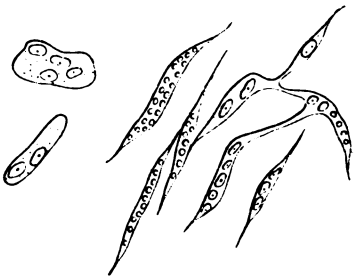
Fig. 2.

swollen, and contain two or more small, pale, faintly granular, cell-like bodies, corresponding in appearance to the cells which consti-

tute so essential a constituent of the inflammatory lymph (Fig. 2). With the further continuance of the inflammation the corpuscles swell out more, and become more distorted in shape; their anastomoses become larger and more distinct; the new cells formed in their interior are greatly multiplied, and instead of being collected merely in clusters at the spots which correspond to the original bodies or central parts of the corpuscles, they extend in rows along the interior of the dilated anastomosing processes. And in this manner arises an arrangement, of which Fig. 1 affords an illustration. At a still later period the proliferation of the nuclei of the connective-tissue corpuscles has increased to such an extent, and the new cells formed are so numerous, that the part seems to be altogether composed of these new productions, and all trace of their mode of origin is lost.

In the layer of pleural membrane investing the surface of the lung, the textural changes were not so satisfactorily traced as in the costal pleura, for the membrane was highly charged with small granules, which, from their form and the manner in which they refracted the light, were evidently fatty. Sections through the pulmonic pleura, even after the addition of acetic acid and glycerine, did not, as a rule, become so clear as to enable me to trace the arrangement of the new-formed inflammatory products in a very extended portion of any single section. The subjacent lung tissue was also much congested. But in limited parts of some of the sections the outlines of the corpuscles of the connective tissue could be traced, and the nature of their contents examined. Not unfrequently they contained fatty granules, which were sometimes arranged in single or double rows. Many variations, however, in the apparent disposition of these granules occurred, according as the corpuscles themselves possessed the stellate or fusiform shape. When the corpuscles were completely filled with these fatty granules, and when at the same time the intermediate texture was highly charged with them, nothing but a confused granular mass could be recognised. In other places, however, the corpuscles were free, or

Fig. 3.



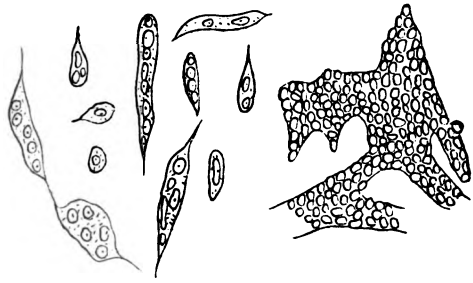
almost free, from fatty particles, and then other changes besides those of fatty degeneration could be traced.

In Fig. 3 a group of corpuscles is represented, some of which exhibit the fatty degeneration above described; whilst in others the phenomena of nuclear multiplication may be observed. In some of my sections, which included portions of the subjacent lung-tissue, a few flattened cells were seen (see the left hand of Fig. 3) floating free in the fluid in which the preparation was lying. In these cells nuclear multiplication had also occurred. They had all the characters of tessellated epithelium, and, it may be conjectured, were the loosened and separated epithelial lining of the air-cells of the lung.

The peritoneal membrane I examined had evidently been subjected for a longer period to the influence of the inflammatory process than the various specimens of inflamed pleuræ just described. The lymph on the surface was drier, tougher, more resisting, and not so easily scraped off with a knife. When vertical sections through the membrane were subjected to microscopic examination, no trace of the original epithelial covering could be seen. My observations were made, therefore, on the sub-epithelial connective tissue. The yellow elastic fibres formed so large a constituent of the deeper layers of the peritoneal membrane and of the subserous connective tissue, that the inflammatory changes were in these parts difficult to follow out. But in portions of the texture, situated between these deeply-placed elastic fibres and the original free surface of the membrane, many satisfactory views of the textural changes were obtained. Next the free surface, *i. e.*, in the part of the membrane presumably the longest inflamed, multitudes of new-formed cells, resembling those making up so large a part of the inflammatory lymph, were closely massed together. Somewhat further removed from the free surface, the new-formed cells were arranged in a linear manner, the rows of cells lying parallel to the free surface. When these rows were not too closely crowded together, so that they could be analyzed into groups, indications of an investing membrane for each group could be traced. In other parts of the sections the new cells formed irregular networks, closely comparable with those described in the inflamed pleuræ, and illustrated by Fig. 1; and outside the rows and clusters of cells, a distinct sharp line, such as an investing membrane would produce, was observed. When the network was close it was not easy to follow it far, and the difficulty of determining the presence of an enveloping membrane was proportionally increased. Further away from the free surface of the inflamed membrane the new-formed cells were much fewer in number, the departure from the normal appearance of the part was not so great, the corpuscles of the connective tissue, which had here undergone comparatively slight alteration in form, could be distinctly recognised, and in them the phenomena of nuclear multiplication, resulting in the production of broods of new-formed cells, were observed. In Fig. 4 some of these slightly altered corpuscles are represented. Such views are

of interest, not only from the positive evidence they afford of the intra-corpuscular origin of the cells produced in the course of the

Fig. 4.



inflammatory process, but from the assistance they give us in arriving at a satisfactory interpretation of the more complicated linear and network-like arrangements met with in some other parts of the sections.

On the right hand of Fig. 4. I have sketched a group of new formed cells, of the mode of origin of which at first sight it may appear difficult to give an explanation. But I would submit that such a group is produced by abundant nuclear multiplication in one or more adjacent connective-tissue corpuscles, for it still presents an approach in its form to the radiated system of anastomosing processes, so characteristic of those bodies, though necessarily much obscured by the distortion occasioned by the production of such a mass of new-formed cells.

From these observations I hold, with Virchow, that in inflammation of serous membranes the cells of the "coagulable lymph," produced so largely during the progress of the inflammation, take their rise from the pre-existing nucleated cellular elements of the texture, and that in their production the corpuscles of the connective tissue play the leading part. In none of my preparations, either of these or other inflamed tissues, did I see anything to satisfy me that the new-formed cells originated in an aggregation of visible granules or molecules in an exudation poured out into the interstices of the textures. On the other hand, the intra-corpuscular origin of these cells was in so many cases distinctly recognisable, and in others their linear network-like arrangement, with occasional clusters, was in such strict conformity with the disposition of the pre-existing corpuscles in the connective tissue, that I had no doubt that the pathologically new-formed cells owed their origin to the nucleated corpuscular structures normally present in the texture. And, in conclusion, I may state that the general result arrived at from these and most other recent observations on the inflammatory process is, that "an explanation of its phenomena is not to be looked for by referring them to actions of the extreme vessels, but to a disturbance of the forces which naturally exist in the extra-vascular portions of the inflamed part."[1]

[1] John Goodsir: Anat. and Path. Observations, 1845; p. 43.