RESEARCHES ON THE NORMAL AND PATHOLOGICAL
HISTOLOGY OF SURFACE ENDOTHELIUM AS EXAMINED BY
THE METHOD OF SUPERFICIAL HORIZONTAL SECTION.

THESIS.

Submitted to the University of Edinburgh, for the
Degree of Doctor of Medicine,
by

JOHN ADAMSON HONEY DUNCAN, M.B., C.M.

32 Morningside Drive.
Edinburgh.

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1. INTRODUCTORY NOTE. METHODS EMPLOYED.

The changes which occur in the cells of the endothelial lining of the pleura, the pericardium, and the peritoneum, as a result of disease, are practically unknown; at least, they have scarcely been recognised, if one may judge from the scantiness of the literature on the subject. In fact, there is little or no literature at all, bearing on the pathology of endothelium.

This imperfect study of the pathological changes is doubtless, owing, in a great measure, to the want of a suitable method, for the making of preparations, showing a large area of the endothelial surface, and, being at the same time, sufficiently thin for making closer observations on it. Such morbid appearances, as have been seen and described in endothelial cells, have been almost all made out by means of vertical sections of tissues lined by them. Accordingly, it has occurred to me that, by adopting a different method, some of the morbid changes which have taken place in these cells, might be better elucidated. The method referred to and which I have therefore adopted, in my investigations, is that which has been introduced by Dr W. F. Robertson and which he has designated "Surface or Superficial Horizontal Section". This method he employed in studying the morbid changes which lead up to the formation of false membranes, on the inner
aspect of the dura, and the observations, thus made by him, have increased our knowledge of the structural changes taking place, near the surface, in a way the former method of vertical section entirely failed to do.

In this Thesis, therefore, I propose to describe the normal structure and the pathological changes coming under my own observation, as shown in the various microscopical preparations I have made by superficial horizontal section, and in a few instances by vertical section.

Until within the last few years, the histology of endothelial cells appears to have been entirely studied by examining thin transparent membranes lined by them; such as pieces of the omentum or the mesentery of the lower animals, in the case of the peritoneum, or, by stripping off a thin piece of the pleura, and examining it under the microscope, after suitable staining. Obviously very thin tissues were required for this purpose, and it was not always possible nor easy to procure such, sufficiently thin, to enable enough light to pass through them so as to allow the endothelial cells to be adequately seen. Such structures, for example, as the pericardium or the pleura in man, are too thick for this method of examination; hence the structure of the endothelial lining, and the morbid appearances in it failed, in my opinion, to be studied in a satisfactory
manner, although the cells in these membranes are believed to be of the same character as those in the peritoneum. Moreover, any pathological changes taking place in the cells could only be made out by making vertical sections through the entire thickness of the membranes. But the method of superficial horizontal section enables a much larger number of cells to be seen, and that in their entirety, while vertical section shows only a comparatively few cells, and generally but a small part of each and in profile, while it also overlooks many lesions and does not allow all the changes which may occur in the cells to be observed. Anyone, therefore, who has examined endothelial cells, in specimens obtained by the two methods, must, I think, have little difficulty in deciding, all things considered, in favour of Superficial Horizontal Section.

Nevertheless, vertical section has certain advantages, e.g., in studying inflammatory processes, upon the surface, it is, of course, essential, to make vertical sections, in order to show the changes taking place at a deeper level.

Again, it is useful as a comparative method. Thus when granulations form, on the surface of the serous membranes, the cells, though showing as a rosette shaped, flattened mass of proliferated cells, on horizontal section, are seen to be distinctly elevated
above the surface when vertical section is made.

Further, vertical section is important in ascertaining the various alterations which take place in the dimensions of the cells, points, which have formed the subject of investigation, by several writers, in examinations they made of the shape, the cells of the pericardium, the pulmonary pleura, and the bladder undergo, during changes in the volume of the organs lined by them; that is, during states of systole and of diastole, or of contraction and distension. But this subject will be referred to again when the Normal Structure is being considered.

(a) Method of Superficial Horizontal Section.

The method of Superficial Horizontal Section, however, is sometimes difficult of application. It consists in cutting away the tissue of the serous membranes, parallel to the surface, so that a large area of endothelium is obtained, in the specimens. It is carried out by first of all making a pool of dextrine solution, on the top of the freezing table of the microtome and then freezing it hard, by means of the ether hand spray. A smooth surface and one sufficiently broad to contain the whole surface of the endothelial lining of the piece of tissue about to be cut, is then obtained by shaving away the top of the frozen dextrine.

This hardened tissue, cut into small pieces, and which
may have been previously soaked, for twenty four hours, in a solution of dextrine or not, is then dried by laying it on blotting paper. A small fragment of the tissue is next laid, with the endothelial surface downwards, on the frozen dextrine, slight pressure being used with the finger so as to get the entire surface in contact with it. The tissue is then frozen on to the dextrine by means of the ether hand spray, and is gradually cut away with a sharp knife, until a sufficiently thin section is left. The knife is then lowered (if the Swift microtome is used) below the surface of the section and the dextrine again sliced away, this piece carrying the section with it. The sections are then allowed to soak in water to remove the dextrine.

There are one or two points in making the section worth alluding to. Firstly, the knife must be very sharp, otherwise ragged, unequal sections will be obtained. Secondly, in connection with such fibrous tissues as the peritoneum, and the parietal pleura, it is important not to freeze the tissues too hard, as they become very brittle, and are then liable to crack across and jump off the dextrine during the process of cutting. Thirdly, the knife must be perfectly horizontal, and parallel to the stage; otherwise, the section will be unequal in thickness. Fourthly, the visceral pericardium (from which I have made most of my sections in
studying the endothelium of that surface) can be frozen quite hard as it cuts very readily, not having much supporting connective tissue. When it is remembered that one section only, can be obtained from each square block of tissue, it can be easily understood that some care must be taken in the cutting, in order to avoid frequent failure.

(b) Hardening of Tissues.

At the commencement of my researches, I hardened the tissues in Heidenhain's corrosive sublimate solution; but, as I did not get such good results by this method as that obtained by potassium-bichromate and formalin, I abandoned it and throughout all my work, I have used the latter. The tissues are placed for twenty four hours in a ten per cent solution of formalin, with two per cent potassium-bichromate. At the end of that time, the bichromate and formalin are poured off, and the tissues washed in water for a few minutes. They are then placed in two per cent pure bichromate until required for use. I found then that at the end of other twenty four hours the endothelial elements were perfectly fixed. After allowing them to harden for that length of time I cut many sections with quite satisfactory results.
(c) Staining of Tissues.

In almost all cases, I have used Ehrlich's haematoxylin as a nuclear stain and eosin as a contrast stain. Silver nitrate I employed in only one or two cases, as I did not find it of much advantage, the endothelial cells being as a rule, easily made out after staining with the haematoxylin and eosin. In a good many of the sections, I found the intercellular substance very evident.

In removing the tissues from the cadaver for the purpose of examination, it is most important that the serous surfaces should not be handled, as, if the surface is in any way rubbed the endothelium is very apt to be removed, and a false idea conveyed to the mind afterwards, regarding its absence in certain parts of the section. The best method to adopt is to take a pair of forceps and seize hold of the tissue at one part, and cut out as much as is required. This should be done, if practicable, before the organs are removed from the body. All superfluous blood should also be removed by allowing a stream of water to run gently over the tissue.

II. MATERIAL EXAMINED.

For the material obtained for the purpose of examination in connection with this Thesis, I am indebted to Drs Fleming and Welsh of the pathological depart-
ment of the Royal Infirmary, to Drs Rutherford and Easterbrook of the Royal Edinburgh Asylum, and also to Dr Anderson of the Crichton Royal Institution, Dumfries, to all of whom my best thanks are due. I may state that I obtained all the material (with the exception of six serous membranes, received from Dr Anderson) by personally attending the post mortem and removing it myself. I thus made sure that the endothelial surfaces were in no way injured. I may also state that the cases have been in no way specially selected, but were taken from the post-mortem room as opportunity occurred, and the observations and conclusions presented in this thesis were made by examining one hundred and one serous membranes taken from fifty one cases.

When I took up the subject of the pathology of endothelial surfaces, I resolved to limit myself to the study of the pleura, the pericardium and the peritoneum along with, in a few instances, that of the dura mater, believing that the examination of these surfaces, in a sufficient number of cases, would enable me to observe many changes, and draw suitable conclusions from them. As the pathological conditions met with, however, are complicated, in many instances, and difficult of explanation, I have refrained from expressing any very decided opinions on their cause contenting myself, as must be done, with merely describing the appearances shown in the various sections.
I hope, however, at some future time to resume consideration of this subject, as I feel convinced that many morbid conditions still require to be investigated.

I have examined the dura mater only in some cases of insanity from which I, at the same time, obtained the serous lining of the pleura, the pericardium and the peritoneum. In studying the pericardium, I invariably chose the visceral surface, as I found sections from it more easily cut, owing to its containing much less fibrous tissue than the parietal surface. The pleura in all cases was studied on its parietal surface, with the examination of the visceral surface, in addition, in one case viz. that of pneumonia. The peritoneum was always examined on its parietal surface. As far as I can ascertain, no systematic attempt has been made to study several of the serous surfaces taken from the same case. I believe, therefore that by examining the endothelial surfaces by the method of surface section previously alluded to, new ground is entered upon, and an entirely new field of research opened up.
The following is a list of the cases I examined.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age</th>
<th>Surfaces Examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Choreic Insanity.</td>
<td>61</td>
<td>pericardium.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pleura.</td>
</tr>
<tr>
<td>2. Acute Phthisis.</td>
<td>34</td>
<td>pericardium.</td>
</tr>
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<td>3. Do. Do.</td>
<td>48</td>
<td>pleura.</td>
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<tr>
<td>4. Do. Do.</td>
<td></td>
<td>pericardium.</td>
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<tr>
<td>5. Do. Do.</td>
<td></td>
<td>pleura.</td>
</tr>
<tr>
<td>6. Tubercular Pleurisy and</td>
<td></td>
<td>peritonitis.</td>
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<tr>
<td>Tubercular Peritonitis.</td>
<td>15</td>
<td>pleura.</td>
</tr>
<tr>
<td>7. Chronic Phthisis with empyaema.</td>
<td>20</td>
<td>pleura.</td>
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<tr>
<td>8. Pneumonia.</td>
<td>21</td>
<td>peritonitis.</td>
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<tr>
<td>9. Do.</td>
<td></td>
<td>pleura.</td>
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<tr>
<td>10. Do.</td>
<td>52</td>
<td>peritonitis.</td>
</tr>
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<td>11. Cerebral Hemorrhage.</td>
<td>68</td>
<td>pericardium.</td>
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<td></td>
<td></td>
<td>pleura.</td>
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<td></td>
<td></td>
<td>peritonitis.</td>
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<tr>
<td>Disease</td>
<td>Age</td>
<td>Surface Examed</td>
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<tr>
<td>13. Tubercule of Peritoneum</td>
<td></td>
<td>peritoneum.</td>
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<tr>
<td>14. General Paralysis of Insane</td>
<td>48</td>
<td>pericardium.</td>
</tr>
<tr>
<td>15. Do</td>
<td>47</td>
<td>pleura.</td>
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<tr>
<td>16. Epilepsy</td>
<td>44</td>
<td>pericardium.</td>
</tr>
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<td>17. Do</td>
<td>33</td>
<td>pleura.</td>
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<tr>
<td>18. Do</td>
<td>40</td>
<td>pericardium.</td>
</tr>
<tr>
<td>20. Insanity (Pathol.)</td>
<td>39</td>
<td>peritoneum.</td>
</tr>
<tr>
<td>Disease</td>
<td>Age</td>
<td>Surface Examined</td>
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<tr>
<td></td>
<td></td>
<td>pleura.</td>
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<td></td>
<td></td>
<td>peritoneum.</td>
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<tr>
<td>23. Senile Insanity</td>
<td>70</td>
<td>pleura.</td>
</tr>
<tr>
<td>24. Do. Do.</td>
<td>70</td>
<td>pericardium.</td>
</tr>
<tr>
<td>25. Senility</td>
<td>71</td>
<td>pleura.</td>
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<td></td>
<td></td>
<td>peritoneum.</td>
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<tr>
<td>27. Tubercular Ulceration of Bowel</td>
<td>35</td>
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<td>28. Dementia</td>
<td>51</td>
<td>pericardium.</td>
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<tr>
<td>29. Do.</td>
<td>32</td>
<td>pericardium.</td>
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<td></td>
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<tr>
<td></td>
<td></td>
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<tr>
<td>30. Senile Insanity</td>
<td>72</td>
<td>pericardium.</td>
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<tr>
<td></td>
<td></td>
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<td></td>
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<td>peritoneum.</td>
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<td></td>
<td></td>
<td>dura.</td>
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<tr>
<td>31. Do. Do.</td>
<td>86</td>
<td>pericardium.</td>
</tr>
<tr>
<td></td>
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<td>pleura.</td>
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<td></td>
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<td>peritoneum.</td>
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<td>32. Do. Do.</td>
<td></td>
<td>pleura.</td>
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<tr>
<td>Disease.</td>
<td>Age.</td>
<td>Surface Examined.</td>
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<td>33. Dog poisoned by Benzoate of Soda.</td>
<td></td>
<td>pleura.</td>
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<tr>
<td>34. Peritonitis following rupture of the uterus.</td>
<td>34</td>
<td>pleura. peritoneum.</td>
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<td>35. Cirrhotic Kidney.</td>
<td>39</td>
<td>pleura.</td>
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<td>36. Acute Pericarditis and Pleursy with effusion and empyema.</td>
<td>17</td>
<td>peritoneum.</td>
</tr>
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<td>37. Cancer of Omentum with secondary infiltration.</td>
<td>64</td>
<td>peritoneum.</td>
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<tr>
<td>38. Double Aortic and Mitral disease with Ascites and Hydrothorax.</td>
<td></td>
<td>pleura. peritoneum.</td>
</tr>
<tr>
<td>40. Acute Alcoholism.</td>
<td>46</td>
<td>pleura. peritoneum.</td>
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<td>41. Do. with hyperpyrexia.</td>
<td></td>
<td>pleura. peritoneum.</td>
</tr>
<tr>
<td>42. Alcoholic Insanity.</td>
<td>66</td>
<td>pericardium. pleura. peritoneum.</td>
</tr>
<tr>
<td>43. Cancer of pylorus.</td>
<td>49</td>
<td>pleura. peritoneum.</td>
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<tr>
<td>44. Early peritonitis following traumatic rupture of bowel.</td>
<td>21</td>
<td>pleura. peritoneum.</td>
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Surface Examined:
- pleura.
- peritoneum.
- pleura.
<table>
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<th>Age</th>
<th>Surface Examined</th>
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<tbody>
<tr>
<td>45. Empyema following Pneumonia</td>
<td>31</td>
<td>pleura, peritoneum</td>
</tr>
<tr>
<td>46. Septic Peritonitis following operation</td>
<td>39</td>
<td>pleura, peritoneum</td>
</tr>
<tr>
<td>47. Gangrene of Lung</td>
<td></td>
<td>pleura, peritoneum</td>
</tr>
<tr>
<td>48. Sub-acute Nephritis, with Meningitis and chronic Pleurisy</td>
<td>30</td>
<td>pleura, peritoneum</td>
</tr>
<tr>
<td>49. Cancer of Omentum and Stomach</td>
<td>64</td>
<td>pleura, peritoneum</td>
</tr>
<tr>
<td>50. Acute Mania with exhaustion</td>
<td>62</td>
<td>pericardium, pleura, peritoneum</td>
</tr>
<tr>
<td>51. Purpura Haemorrhagica</td>
<td>26</td>
<td>dura</td>
</tr>
</tbody>
</table>
III. THE NORMAL AND PATHOLOGICAL HISTOLOGY OF SURFACE ENDOTHELIUM - WITH A REVIEW OF THE LITERATURE.

The Normal Structure of endothelial cells has already been so fully worked out, that there seems little to be added to the description already given by such authorities as Schäfer, Kölliker, Klein, Rutherford, Stirling, Piersol, etc. in their various textbooks. Certain observations, however, which have been made by other authorities on certain changes in shape which endothelial cells undergo during the performance of certain physiological functions, and which are not described in the ordinary text books, will be referred to here.

Briefly stated, the serous membranes, according to the above mentioned authors, have an endothelial lining, consisting of a single layer of thin transparent irregularly shaped polygonal cells, of variable size and great delicacy. Each cell has a round, oval, or sometimes a kidney-shaped nucleus. The nucleus contains a reticulum of fine threads, arranged in the form of a network and which seems to be connected with the fibres of the cell plate. This fine network has the property of staining readily with basic dyes and is called chromatin or chromoplasm, while the fluid which lies between the meshes does not stain with basic dyes, and hence is called achromatin. Occasionally, there
are one or two nuclei in the meshes.

The cell plate is composed of two substances, one being homogeneous, and the other, according to Klein occurs in the form of a coarse network of minute fibres giving an appearance of granularity to the cell plate.

Between the cells there exist minute apertures which are of two kinds - large and small. The large ones are true apertures and are called stomata. They open into underlying lymph spaces and are surrounded by a ring of cubical cells. The smaller apertures are much more numerous, and are called pseudo stomata by Klein and Burdon Sanderson. They contain according to Schäfer an accumulation of the intercellular substance or processes which are sent up to the surface of the membrane from more deeply lying cells.

Sometimes there are seen in the immediate neighbourhood of, and lining the stomatous openings, numbers of proliferating or germinating cells. Klein states that many of these produce small round lymphoid cells, which pass into the lymphatics, and ultimately form white blood corpuscles.

The endothelial cells are described by the majority of writers as uniting by tortuous and serrated lines of cement substance, which can readily be made out as dark lines after staining with nitrate of silver.
Muscetello\(^6\) however, states that the form of the endothelial cells lining the pleuro-peritoneal cavity, intestines, epicardium, bladder etc. varies according to the degree of retraction or distension of the organs. When the bladder, for example, is distended, the endothelial cells present a regular and straight outline, but when retracted, they appear irregular, sinuous, and indented.

He compares the pleuro-peritoneum to a contractile organ, as the serous membranes are supported on muscular tissue, which is liable to contraction and expansion. Thus, the endothelial cells in them would also become altered in shape and outline.

Soulie\(^7\) made similar observations to those of Muscatello, with the addition, that in the case of the epicardium, the cells were lamellar during diastole and became cubical during systole of the heart; in the case of the pleura the cells were lamellar during inspiration, and pavement shaped during expiration.

He also states that there exists on the surface of the pulmonary pleura, and especially in the epicardium, depressions into which the cells pass during alterations in the volume of the organ.

There is one other point regarding the overlapping of endothelial cells, which has received attention from some observers, but of which no mention is made in most
of the text books, Piersol distinctly states that there is none. Delchuyseen, however, says that endothelial cells may not necessarily be placed in a continuous layer — that is end to end; but may overlap like tiles on a roof; so that the nucleus of one cell may seem to project into another cell.

With regard to the nutrition of endothelial cells, Schäfer says that no blood vessels have ever been discerned penetrating the endothelial tissue, but in all probability the nutrition of the endothelial cells is carried on by the blood plasma, derived from the blood vessels of the subendothelial connective tissue, which passes through the minute channels between the cells.

**Development of Endothelial cells.**

Most embryologists now, I believe, agree that endothelial cells are developed from the mesoblast, instead of from the hypoblast as was formerly supposed. Schäfer includes in his list of structures derived from the mesoblast, the serous membranes; consequently the endothelial cells must be derived from the same blastodermic layer. Balfour and Foster as well as Hertwig and Mark seem to take the same view of the origin of these cells.

As already stated, in my introductory note, the literature on the pathology of endothelial cells is very scanty. Undoubtedly, work on this subject has
been done, but as the investigations have been published in a very fragmentary form, references have been exceedingly difficult to obtain.

W.F. Robertson was probably among the first to describe somewhat fully, the pathological changes which may take place in endothelial cells. He has described both proliferative and degenerative changes.

Proliferative changes, he observed very frequently in the surface endothelium of the dura, and, also, in the pia-arachnoid, in both of which situations they frequently formed minute localized aggregations, which projected above the surface, and constituted one form of granulation. He also observed similar proliferative changes in the perivascular canals of the dura. These usually occurred along with proliferation of the surface endothelium.

He has also observed several degenerative changes. Fatty changes, both in the nucleus and the cell plate are frequent. A condition which he terms "vitreous" degeneration, owing to the microscopic appearances presented by these degenerated cells, he has also met with. This condition he describes as commencing in the nucleus, which becomes vacuolated. The process ultimately extends to the cell plate, until, finally, the whole cell plate is destroyed. When this change affects extensive areas of the endothelium, a silvery appearance can be recognised with the naked eye. He
believes the condition to develop with great rapidity and to arise specially in the moribund state.

A common degenerative process and one characterised by an infiltration of the cell plate, with small yellowish granules, he has described as occurring, in the endothelial cells of the pia-arachnoid. As these granules were lighter in colour, larger and less numerous than those in the normal pigment cells of the pia-arachnoid, he regarded them as being distinctly pathological. The nature of the pigment granules, however, he does not state. Another condition in which the endothelial cells have degenerated to form a homogeneous glassy material, he has also described. This change he has called "hyaline" degeneration; merely using the word as a descriptive term. As a result of proliferative and hyaline degenerative changes taking place, the so called concentric bodies are formed.

J.W. Findlay has made similar observations to W.F. Robertson, as regards the origin of these hyaline concentric bodies, and states that the hyaline material is an exceedingly unstable substance causing considerable variations and anomalies in staining.

Regarding the origin of fibrous tissue, most text books by such authors as Thoma, Ziegler, Coats, etc. describe it as being derived from fixed connective tissue corpuscles. Thoma also says in his text book...
that Thiersch, Waldeyer, Baumgarten, and Raab were the first to demonstrate the origin of connective tissue from the endothelium of blood vessels.

Professor Greenfield describes a marked proliferative change in the endothelial cells of Bowman's capsule, in sub-acute interstitial nephritis, with the subsequent formation of fibrous tissue. He is inclined to regard the fibrous tissue as being probably developed from the endothelial cells.

The relationship which the endothelial cells bear to a serous exudate has given rise to much difference of opinion. Buhl in 1863, held the view that the endothelium lies over the exudation. Neumann supports Buhl's assertion. He could, never, however, demonstrate the cells as a continuous layer, but as islets, the cells of which, however, were not sharply defined from one another, but the nuclei were readily recognisable being large, round, and swollen. Further, he says that the endothelial cells cannot be seen under the fibrin.

Riese, quoted by Neumann, states that the serous exudate is covered by endothelial cells, which are derived from the proliferation of the cells round the margin of the exudation; but Neumann thinks this very improbable. Wagner holds the ordinary view, viz, that the endothelial cells lie underneath the exudation.
Marchand also holds the same view.

Lazarus-Barlow agreed with Neumann that endothelium might be found frequently covering false membranes but he did not think that this change was commonly seen. He asserts that the endothelium usually becomes degenerated to form part of the false membrane, or, if this does not happen, that it can be seen lying beneath the false membrane and not covering it.

IV. AUTHOR'S OBSERVATIONS AND CONCLUSIONS ON THE NORMAL AND THE PATHOLOGICAL HISTOLOGY OF SURFACE ENDOTHELIUM.

(a) Normal Structure.

Personally, I have little to add to the normal histology of endothelial cells as already described.

The endothelial cells of the surface, in haematoxylin and eosin stained preparations, show a larger round or oval shaped nucleus, the chromatin of which is deeply stained with the former dye. The cell plate is usually also faintly stained with haematoxylin.

Endothelial cells are also found lining certain grooves in the subendothelial connective tissue, and in which fine capillary blood vessels run. These grooves are perivascular canals; and are doubtless simply lymph spaces. They were first of all noticed by Obersteiner as existing in the dura, but since then they have been more particularly described by W. F. Robertson, in the same situation. There is, however,
evidence to show that these perivascular canals also occur in the sub-endothelial connective tissue of the other serous membranes (Specimen 1. Fig. 1.)

On superficial horizontal section, endothelial cells, lining the outer walls and floor of these grooves can be distinctly made out.

Delchuyssen's observations on the overlapping of the endothelial cells I have been able to verify in some cases, but I have not been able to see a continuous series of cells overlapping, in the manner described by him; but merely a few cells, here and there, presenting this appearance. I have not been able to corroborate Soulé's observation on the changes in dimension which endothelial cells undergo during the performance of the functions of various organs.

As these changes can only be seen on vertical section, and as I am, at present, not specially concerned with this method, nor have I been able to procure material from cases in which the organs were artificially retracted or distended, I have not been in a position to observe the appearances described by him.

After death, all the organs are usually flaccid and contracted; thus, the endothelium will generally present a cubical shape and a sinuous outline, as some authors have stated.

In many of my sections, e.g. (Specimen 2,) the
outlines of the cells can be seen in a very clear manner, and without the aid of silver nitrate.

The phenomena of overlapping and alteration in the form of the endothelial cells are, in all probability, of a purely physiological character, being a natural process for allowing the cells to adapt themselves to the altered degrees of tension which take place, during the performance of the functions of the various organs. When the organ distends, no overlapping of the cells takes place, but they become straight in outline; while, when the organ becomes contracted, the cells may overlap, and at the same time become tortuous in outline.

The stomatous openings are exceedingly minute, and are, in the vast majority of my sections, invisible with the ordinary powers of the microscope. Indeed, I have only been able to convince myself of their presence in a very few instances.

(b) Development of Endothelium.

Developmentally, as already mentioned, endothelial cells, and connective tissue corpuscles have the same origin, viz, from the mesoblast. Morphologically, the surface endothelial cells, and those lining the peri-vascular canals cannot be clearly distinguished from connective tissue corpuscles; and, they are termed endothelial cells, or connective tissue corpuscles,
according to the situation in which they are found.

Such developmental and morphological facts furnish I think, suitable evidence for supposing that endothelial cells are, most probably, merely modified forms of connective tissue corpuscles, which have taken on a special function, viz, that of diminishing friction between the two opposing surfaces of a serous membrane.

Further, I think these facts are of some importance, as it is quite conceivable that endothelial cells are capable of forming fibroblasts in the organization of fibrinous exudation, much in the same way, as connective tissue arises, as a result of the proliferation of the endothelium which spreads over a thrombus, and penetrates its substance during its organization.

(c) Morbid appearances of Endothelial Surfaces recognisable with the unaided eye.

I made a point of examining carefully the macroscopic appearances of the serous membranes, after their removal from the body, and before placing them in the hardening fluids, and, also of comparing these with the appearances shown afterwards in the microscopical preparations. In the vast majority of these, however, nothing abnormal could be seen, by the naked eye; while in other instances, certain morbid appearances, - such as the presence of granulations, - could be distinctly observed. These were in most cases, very minute, and
were seen with difficulty; while, in one or two instances, they were exceedingly well marked, - the most marked examples occurring, in the serous membranes of cavities which contained a considerable quantity of fluid. Preparations from these granular membranes usually showed, on examination by the microscope, rounded areas of proliferated cells.

To the naked eye, an appearance resembling frosted glass was observed in the dura by W.F. Robertson in cases where there was extensive vitreous like degeneration of the endothelial cells. Although I met with this vitreous like degeneration, as revealed by the microscope, I was unable to detect any glassy appearance by the unaided eye, as the process, in my cases, affected only very minute areas of the endothelium.

Sometimes the pleural surface was so much disorganized by the presence of fibrous adhesions, thick layers of fibrin etc, that it was found useless to examine such tissue, it being impossible, in such a case, to obtain the endothelial surface.

(d) Microscopic Changes.

Many of the serous membranes appeared to me to present very little departure from the normal, except such changes as result post mortem. But, in any case, if the post mortem change was discarded, these furnished me with sufficient normal material from which I
could study and obtain a knowledge of the normal appearances presented by the cells. As in other tissues, as the result of disturbances of tissue nutrition, we may have, on the one hand, the endothelial cells multiplying or proliferating, or, on the other hand, degenerating or dying, — the former condition being due to increased nutrition or function, — the latter to diminished nutrition or diminished function.

The changes which occur in endothelial cells may be classified into two chief groups, viz, proliferative and degenerative, each of which may be either acute or chronic. In acute processes, as a rule, there is very little to be described in connection with endothelium, as, in most cases, it is extensively destroyed.

My observations, therefore, have, to a large extent, been made in the more chronic cases, where destruction of the endothelial cells does not so rapidly take place. In acute conditions, proliferation and desquamation usually take place simultaneously. In the chronic condition, we have also two chief processes, viz, proliferation and degeneration, and these may occur either together or separately.

I propose, therefore, describing the morbid appearances in endothelium under three headings. (1) Simple proliferation without degeneration. (2) Proliferation, with degeneration of the cell elements in the proliferated area.
(3) Degeneration in the cell elements, unaccompanied by proliferation.

This does not pretend to be a scientific classification, because the same degenerative changes may occur in the endothelial cells whether they are in proliferated areas or not. Still the above classification is a convenient one for purposes of description.

(A) Degenerative Changes in Endothelial Cells.

The degenerative changes which I have observed in endothelial cells are as follow; (1) Cloudy Swelling or Albuminous Degeneration, and Fatty Degeneration. (2) Gedematous or Dropsical Degeneration. (3) The formation of a homogeneous clear looking substance, resembling the material in hyaline degeneration. (4) Vacuolation. (5) The formation of an opaque substance, somewhat resembling that in No. 3, but differing from it, in its origin, its appearance, and its property of only staining slightly with haematoxylin and not at all with eosin. (6) Pigmentary Degeneration.

(1) Cloudy Swelling, or Albuminous Degeneration, and Fatty Degeneration.

These are progressive steps in the disintegration of the cell protoplasm, and represent different degrees of the same degenerative process; and are very frequently observed in the endothelial cell elements - chiefly affecting the cell plate.
The first mentioned condition, however, is the one I have most frequently met with; fatty degeneration having only very rarely been seen. An interesting condition and one evidently of the nature of an albuminous degenerative change consists in the formation of somewhat large globules of an albuminous material, and is, by far, the more common of the two processes. It seems to occur, without any accompanying swelling of the cell plate, or any marked granularity of the cell protoplasm; but the nucleus may show a slightly increased granularity. This appears to me, therefore, not to have been an acute process, but a much more gradual one. The most marked examples of this degenerative process have occurred in preparations taken from cases of Senile Insanity, Choreic Insanity, General Paralysis of the Insane, Dementia and Epilepsy.

In ordinary Cloudy Swelling, the protoplasm of the cell plate, usually presents a markedly granular appearance, and is seen to be swollen from the presence of minute granular molecules of an albuminoid substance precipitated in them, and differing entirely from the normal finely granular appearance presented by the cells - the granules of the latter being more translucent.

In the cases in which I have observed this
albuminous change, the process has progressed so far, as to form quite large albuminous globules, resembling those of fat, but which has, as a rule, usually stopped short of actual fatty degeneration.

These globules, as shown in some of the sections, (Specimens 3-7. Figs III. and IV.) are exceedingly numerous. In other cases, only one or two small globules are visible in the cell plate. Occasionally, they seem to destroy and fill almost the entire cell; the nucleus generally escaping. They are of a refractile character, and vary much in size, the largest being slightly smaller than that of a red blood-corpuscle. Where they are numerous in the cell plate they have pushed the nucleus to one side, and caused it to become flattened or irregular in shape.

Sometimes, one may see in a few of the nuclei a single globule in each of these, but in such cases there are always accompanying them corresponding globules in the protoplasm of the cell plate. That these globules are not fat is certain, because the majority of them gave no dark brown or black reaction with osmic acid. In the surrounding tissues, the fat-cells were distinctly blackened so that there could be little doubt as to the process of staining having been properly carried out. Further, when the sections were placed in ether, it was found that the globules were not dissolved, but remained practically unchanged. That these
globules, however, may go on to fatty degeneration, is quite obvious, from the fact that several of the globules have been blackened by the osmic acid.

Here and there, over the sections, are seen somewhat large clear spaces, containing a small quantity of a granular looking material which does not stain with haematoxylin. These are probably the result of the disintegration and subsequent fusion of one or two cells, the precise chemical nature of the granular material formed in these spaces being however uncertain. In all probability, the albuminous globules are produced simply by a precipitation in the cells, of finely granular albumen particles, some of which coalesce to form them, or else they may result from a breaking up of the protoplasm of the cell.

Albuminous degeneration, in the majority of the cases, occurred in persons well advanced in years, (indeed, the highest degree of the change is shown in specimens taken from a case of senile insanity,) or in persons dying from some exhausting disease, and is thus evidently due to the fact that the nutriment which is carried to the endothelial cells is insufficient to maintain their normal functions.

Albuminous degeneration, therefore, appears to differ from Cloudy Swelling, as usually found in other tissues, such as liver, muscle, and kidney cells etc, because the latter change usually takes place in acute
septic conditions, associated with high temperature.

In all the cases I have examined the endothelial cells have been singularly free from fat, and in cases where the appearances presented in the preparations resembled fat it was found, after placing them for 24 hours in osmic acid that no darkening of the cell plate or nucleus was obtained although the surrounding fat was blackened.

(2) Oedematous Serous, or Dropsical Degeneration.

A condition, closely allied to cloudy swelling, apart from fatty degeneration, is that of oedematous serous, or dropsical degeneration. This condition has occurred in one or two of my cases, the most marked example being in the cells of the pleura, from a case of pneumonia, in which there was no formation of fibrin. It has also, however, occurred in cases where there was dropsy of the serous cavities. In Specimen 8, Fig V, the appearances presented are as follow; the protoplasm of the cells has become swollen, and the latter seem to have merged into one another; so that a homogeneous translucent ground substance has been produced. No outline of the individual cells, nor any trace of the intercellular cement substance are visible; neither can any granules be seen in the cell protoplasm.
Owing to this fact, the nucleus is rendered very prominent. The ground substance is stained unequally with the haematoxylin; in some parts of the section, it is scarcely stained at all, while, in others, it has taken on the dye more deeply - being of a pale pinkish blue tint. This difference in its staining properties, is probably due to some of the cells being more swollen than others. The cell protoplasm here and there is seen to contain vacuoles of a spherical shape, and containing a clear fluid. The nuclei are comparatively few in number, are immensely swollen, being four or five times the size of the normal nuclei and are very pale and translucent.

They are also, for the most part, oval in shape, but others are kidney, and horseshoe shaped, and their outline is very sharp. The chromatin network has been ruptured and the scattered threads have arranged themselves chiefly round the periphery. It is owing to this fact and to the watery fluid contained in the nucleus that its peculiar translucent appearance is due. The nucleoli are well seen, in the sections, being stained of a reddish-violet colour with the haematoxylin. I think there is little doubt that this change has been produced by the imbibition of fluid, owing to the damaging of the nutrition of the cell, and, as a result of the inflammation alone, there being no fluid in the pleural cavity. It is in fact a
change analogous to what takes place in the skin when it is blistered.

In the other cases, in which it occurs, it arises simply from the imbibition, by apparently healthy cells, of water from the dropsical fluid contained in the serous cavities.

(3) Another pathological condition to which endothelial cells are liable, is characterized by a tendency they have to disintegrate, and form an apparently homogeneous transparent or translucent substance. As the microscopic appearances and staining reactions presented by this substance, somewhat resemble those seen in hyaline degeneration of the connective tissue and muscle in arteries, we may call it hyaline degeneration, but I merely use it as a convenient term for applying to any substance of a hyaline appearance, without expressing any opinion as to its composition, Bearing this explanation in mind, I will use the word "hyaline" throughout this paper, in the above sense only.

This peculiar degenerative change is of specially frequent occurrence in the dura of the brain where it forms the so called concentric bodies. These bodies I have never observed in the endothelial lining of the pleura, pericardium, or peritoneum, but I have met with them in the dura taken from some of the cases in
which I also examined the other serous surfaces. Whether they only occur in, and are peculiar to the dura, I am unable to say.

In some of my cases, however, I have observed rounded bodies, containing an apparently homogeneous substance, and, as these bear a close resemblance to the concentric bodies in the dura, both in their apparent composition and mode of origin, it is conceivable that they may be very closely related to one another. Usually hyaline material, in haematoxylin and eosin preparations, stains pink with the latter dye. However, while admitting this to be the general rule, I do not believe it to be the invariable one; hyaline material, being so exceedingly unstable a substance, may present considerable variations in its staining properties. In my preparations, (Specimens 10-13, Figs. VII. VIII.) taken from the three large serous surfaces, these bodies have stained violet with the haematoxylin. On the whole, therefore, I am inclined to think that these bodies are of a hyaline character. Virchow and other authorities regarded concentric bodies as being derived, by a process of deposition from the fluids of the tissues. That the process is not so simple as this, has, I think, been conclusively proved by W.F. Robertson, who described their formation as a result of proliferative and hyaline degenerative changes, in the endothelial cell
elements.

Concentric bodies, according to W.F. Robertson, occur frequently in the dura of hospital patients, and in the mentally sound, but he found them to be more numerous in cases of insanity. These concentric bodies, have usually a rounded shape, but they may be of various forms, from several spheres running together. They have usually a well marked capsule, composed of the same hyaline material, or, it may even appear fibrous in character. The concentric rings are frequently well marked and numerous, in some bodies, while they are very indistinct in others. In the centre of the bodies, there may be seen a mass which stains somewhat more deeply than the rest of the substance. This may be due to the shrivelled up nuclei of the degenerated cells. (Specimen 9, Fig VI.)

Briefly stated, the development of these bodies is as follows - the cell plate assumes a homogeneous appearance, and shows a slightly increased affinity for eosin; the nucleus at first staining with haematoxylin in haematoxylin and eosin preparations, later on, taking the eosin dye, as it also gradually assumes a homogeneous appearance. Finally, a homogeneous globule is formed, as a result of the blending of the nucleus and the cell plate.

In this way, a small concentric body may arise from a single endothelial cell; but more usually
several coalesce to form a single body of larger size. The concentric markings appear later and are most likely due to shrinkage. Hyaline Degeneration has not been a frequent change observed, in many of my preparations, except, however, in those derived from the dura, in cases of insanity. Indeed, I have only met with appearances resembling it in two cases - one being from the pericardium; the other from the pleura of a case of acute phthisis; consequently, the development of the rounded bodies has been extremely difficult to follow, and my views, therefore, must be, to some extent problematical, until further evidence is obtained on the subject. Having, however, studied the various degrees of degeneration presented by the cells in the several sections,(Specimen 10, Fig. IX.) I believe the process to be as follows, viz, the cell plate and the nucleus, at first, swell up and assume a homogeneous appearance. During this stage both stain with eosin in haematoxylin and eosin preparations; the nucleus the more deeply of the two. At a later stage, the nucleus and the cell plate blend together. The blended cell plate and nucleus then lose the pink stain of the eosin, and become vacuolated and transparent. The vacuoles now run together and finally a homogeneous mass is produced which takes up the dye of the haematoxylin and appears as the violet coloured and rounded shaped bodies with thin delicate capsules, as seen in
Specimen 10, Fig VII. Several such degenerated cells may run together to form a single large body.

This hyaline material, I believe, may also undergo retrogressive changes presumably of a fatty nature; for, side by side with the hyaline material, in Specimen 11, may be seen a large number of rounded spaces, in which the violet colour of the haematoxylin is gradually disappearing, the contents becoming granular and ultimately, a clear space is left containing a small quantity of finely granular matter.

In Specimen 11, the development of the hyaline material, although probably taking place in the same manner, as that already described, yet presents some peculiar features, in that the cells before undergoing the change, proliferate to a considerable extent and show a great tendency to arrange themselves in the form of circular groups.

I will, however, refer to this again when describing the proliferative changes accompanied by degeneration.

(4) Vacuolation of the cell nucleus, frequently occurs in many of the endothelial cells, and is probably due to some albuminoid transformation of the nuclear protoplasm. The vacuoles may be very numerous in the nuclei of some cases, and may apparently be present, without any other recognisable alteration in the protoplasm of the cell plate. Usually, the process of
vacuolation does not progress to any great extent, it being, as a rule, confined to the nucleus, which however may become almost totally destroyed. (Specimen 14.)

Frequently, the vacuolation is either preceded, or accompanied by a homogeneous change in the nuclear protoplasm, and it may be preceded by slight proliferation of the cells.

(5) Under certain other circumstances, the nature of which, however, I am unable to state, vacuolation may take place to a considerable degree, the vacuoles increasing in size and the cell plate also undergoing the same change. Ultimately, from the fusing of several of these vacuolated cells, homogeneous glass-like masses are produced which somewhat resemble the appearance presented by frosted glass. (Specimens 15-17, Figs X.XI.XII.) The process of degeneration leading to the development of this homogeneous substance would thus appear to commence in the nucleus and extend to the cell plate.

As shown in microscopical preparations, this homogeneous looking substance occurs in the form of irregular masses having a translucent, bright, and highly refractile appearance.

Running through the mass are seen fine, delicate, dark lines resembling cracks in a plate of glass, and which are possibly the outline of the vacuolated cells. Sometimes little thickenings or beads can be seen on
these delicate lines, these lines being also very often closely packed together - a circumstance very possibly due to shrinkage of the cells. Further, this homogeneous looking substance does not blacken with osmic acid nor stain with eosin, and, as a rule, but very faintly with haematoxylin - although it stains sometimes somewhat deeply. At a rather later stage the cells may totally disappear and then large numbers of clear globules are left, which do not stain with either haematoxylin or eosin.

No evidence of fatty degeneration taking place in these globules, has been visible on the application of osmic acid to the sections, and there is reason to believe the contents of the globules are of a semi-fluid character. This degenerative process may affect large areas of the endothelial surface, while, on the other hand, small masses only, with considerable areas of apparently healthy endothelium between them, are present. The former condition is exceedingly well shown in microscopic preparations obtained from the dura of a case of purpura haemorrhagica, and presents a very striking appearance; the latter condition is shown in preparations obtained from the pleura of a case of acute alcoholism with hyperpyrexia, from the peritoneum of a case of general paralysis of the insane, and from the pleura of a case of pneumonia. These are the only four instances in which I have observed this degenerative process.

From the extensive areas that are affected, in
this degenerative process, it is highly probable that the process may develop very rapidly.

(6) Pigmentary Degeneration.

Normal, or physiological pigment occurs in cells in the form of yellow, brownish, or black granules. It is present in the epithelial cells of the retina; the deep layer of the rete Malpighii; also in the pia arachnoid, choroid, etc; but, as far as I am aware, it has not been described as occurring normally, in the endothelial cells of the larger serous membranes. In the one hundred and one endothelial surfaces which I have examined, I have only met with pigment in the cells, in two of the cases – one in the pleura from a case of septic peritonitis following operation for strangulation of the bowel, the other, also in the pleura, in a case of acute alcoholism, both of which I am inclined to believe show a true pigmentary degeneration or pathological pigment, instead of normal pigment.

As already stated, W.F. Robertson has described a pigmentary degenerative process as occurring in the endothelial cells of the pia arachnoid, and I have observed somewhat similar changes in my two cases, (Specimens 18-20, Fig. XIII). With the low power of the microscope, the pigmented cells are seen scattered over the field, being more numerous and more congregated in some parts than in others. All the cells,
however, do not show this pigmentary change. There are comparatively wide areas showing no pigment at all. From the fact, that these pigment cells are so much scattered, with here and there localized collections of them, and also, from the fact, that I have not been able to recognize any pigmentation in the endothelial cells of any of the other specimens I have examined, I am inclined to the opinion that this is a distinct pigmentary degeneration or infiltration.

As shown in specimens, this pigment is finely granular. It is composed of minute brownish yellow granules, mixed with minute blackish granules. It usually distends the cell, the latter either retaining its normal polygonal shape, or, else becoming somewhat oval in form, and its boundary, in each case, can be seen to be limited by the cell envelope. In most cases the cell protoplasm only is infiltrated, the nucleus, as a rule, showing no trace of pigment. The nucleus is usually pushed to one side, sometimes becoming flattened, at other times, preserving its normal shape. In other cases, infiltration of the whole cell takes place, the nucleus sharing in the same process, and becoming totally destroyed and obscured by the pigment. Occasionally, the pigment is seen to be diffused, as if the cell envelope had burst, and liberated the granules. Sometimes the cell plate shows a slight degree of vacuolation.

What the nature of this pigment is, or what is its
origin, I am unable to determine.

Some authors, however, have stated that this pigment may be composed of fatty particles; but that, in my cases, this is not so, is proved by the fact, that the granules are only slightly darkened, but not blackened by immersion for twenty four hours in osmic acid. Neither does it appear to be a derivative from the decomposition of haemoglobin. Blood, when decomposed, breaks up into two pigments - haematoidin, which occurs in the form of prisms, or needles, of a ruby red or orange colour; but perhaps more usually in an amorphous form; and haemosiderin, which occurs in the form of brownish-yellow granules. Haemosiderin contains iron, while haematoidin contains none. I carried out the iron reaction according to Stieda's method, which consists in placing the microscopic preparation for six hours or so, in a two per cent aqueous solution of ferrocyanide of potassium, then transferring it to a one per cent solution of hydrochloric acid in alcohol, for about twelve hours. The section is afterwards washed and stained with lithium carmine.

As a result of this examination, no deep blue colour in the pigmented cells was obtained; hence I concluded that no iron was present and consequently no haemosiderin. The appearance of the pigment also was against the idea of its being haematoidin, no crystals or needles being present. Haematoidin, however, may occur in an amorphous form; so that the absence of
crystals is not a conclusive proof that it may not be present.

The question also arose whether this pigmentation might not be the result of the absorption of bile pigment, (which is a derivative of the blood pigment and is indeed identical with haematoidin,) more especially as in such cases, as acute alcoholism and septic peritonitis, there may be frequently an accompanying degree of jaundice, as a result of the toxic poison injuring the red blood corpuscles, and bringing about an increased formation of the bile pigment.

No very satisfactory method for the detection of bile pigment in sections is however procurable, although Gmelin's test is the one recommended. But it is difficult of application, when such a small quantity of pigment is present and when the amount of tissue at one's disposal is limited. I, however, tried the experiment, by placing a drop of fuming nitric acid close to the edge of a section, covered with a coverglass, and allowed it to flow on to the section by capillarity. No green reaction indicating biliverdin, however, was obtained. I believe, however, I am correct in stating that bile pigment does not infiltrate endothelial cells at all, as in a case of marked jaundice from which I obtained the pleura, pericardium, and peritoneum, and which were intensely bile stained, there was not the slightest trace of pigment in the endothelial cells, in
any of the sections made from them.

The only other explanation that I have to offer, as to its presence, and which I believe may be the correct one is, that it is merely a disintegrative process taking place in the cell protoplasm, possibly induced by the toxic poisons already referred to; or, as an accompaniment of a chronic atrophic process analogous to brown atrophy of the heart, and fuscous degeneration of cells in nerve ganglia. Probably the pigment is of the nature of tissue pigment, e.g., histo-haematin.

(B) Proliferative Changes in Endothelial Cells.

Proliferation of endothelial cells has been an exceedingly common observation in many of my preparations. Indeed I may say that, in the majority of the cases examined, there has been some evidence of it. In some instances it was very slight, occurring only in very minute areas, and at wide intervals, there being only a few cells clustered together. In other instances, however, it was of a very marked description, large clusters being closely set together. Some of the cells occurred in irregular groups, giving rise, however, to no appearance, visible to the naked eye; others formed many layers of cells, piled, one on the top of the other, and projecting above the surface in the form of minute granulations, which could be distinctly seen
with the naked eye.

A slight degree of proliferation is mentioned in most text books on Histology, as being present in sections of normal serous membranes. This is frequently to be seen around the stomata, which lead into the lymph spaces. Marked proliferation, on the other hand, is stated to be the result of some pathological process, such as chronic tuberculosis, cancer etc. The boundary line, however, between such a degree as is normal (if proliferation can be called normal at all), and such as is pathological, is difficult to define. Probably, in all cases there is an irritant of some kind at work of an infective, traumatic, or toxic character, which directly excites and stimulates the cells, and causes them to undergo proliferation. What becomes of all the proliferated cells, it is difficult to say. Some of them, as is well known, take part in the re-generation of new tissue, to replace the physiological shedding, which is continually taking place in the endothelial cells, others may disappear in quite an unknown manner. In a great many cases, many of them undergo degeneration, break down into a granular, probably fatty detritus, and are removed from the tissues in some way. This, for example, is what frequently occurs in cases of chronic inflammation, from the pressure, and loss of blood supply induced by the contracting and newly transformed connective tissue in the inflamed
part.

We may, therefore, recognize two chief groups of proliferative change. Firstly, simple proliferation, where there may be a considerable degree of proliferation of the cells, but which, under the microscope, show no tendency to undergo degenerative change, and Secondly, proliferation where the tendency to undergo degeneration and to break down is very marked. Many cells seem to disappear in this way.

(a) Simple Proliferation.

Simple Proliferation shows in sections, in the form of irregularly shaped groups (Specimens 21 - 23, Fig XIV; in somewhat circularly arranged groups, (Specimen 12, Fig XVIII.), and in groups, in which the cells are piled up, one on the top of the other, forming visible granulations (Specimen 25, Fig XV.)

The nuclei of the proliferated cells are, in some cases, much narrower than the ordinary nuclei, and are somewhat pointed at their extremities, being, in fact, spindle shaped, instead of round or oval, like the surrounding nuclei. In haematoxylin and eosin stained sections, these nuclei, being younger, usually stain of a much deeper colour, with the former dye, than do the rest of the nuclei. The chromatin network is in most cases, perfectly evident, although somewhat compressed;
while, in others, the nuclei appear to be homogeneous, the chromatin fibres being so crowded together, that little room is left for the achromatin. In still other cases, the proliferated nuclei show little or no difference, in shape, or in size, from those that are normal; nor do they stain more deeply than the normal. One feature which proliferating cells have presented, in many of my preparations, is the remarkable tendency shown to become arranged into circularly shaped groups. In certain cases, this is a condition assumed by the cells, previous to their undergoing a degenerative change. It is a condition well seen in Specimens 10 and 12, taken from two different cases of phthisis, in which there was chronic inflammation, with thickening of the pleura and the pericardium. This will, however, be alluded to again, when the degenerative changes are being considered.

Sometimes, the nuclei, in proliferating cells, assume the most varied shapes, these being well seen in Specimens 26 and 27, Fig. XVI. For example, they are rod, dumb-bell, racket, kidney, and horse-shoe shaped, and so on. They are also small, and somewhat thickly crowded together amongst the endothelial cells, the latter, however, not forming a continuous lining, as they usually do. Whether these are degenerated or simply shrunken nuclei it is difficult to say.
As previously mentioned, proliferated endothelial cells occur, in such numbers, that they form quite distinct projections, or granulations, on the surface of the serous membranes. In this respect, they resemble the granulations seen on the floor of the Fourth Ventricle, in cases of general paralysis of the Insane. I observed well marked examples of these granulations, in a case of double aortic and mitral disease, accompanied by hydrothorax, and ascites; and also in a case of cirrhosis of the liver, with ascites and jaundice. On the surface of the pleura, in the former case, and, on the surface of the peritoneum, in the latter, minute projections could be observed by the naked eye; and, on superficial horizontal section, large numbers of cells heaped on one another and forming nodular masses were visible, by the microscope; and this was still more clearly demonstrated by means of vertical section, (Specimen 28, Fig XVII.) In these two cases, it may be remarked, that both the pleural and the peritoneal cavities, in each, contained fluid, and the cells of both surfaces were swollen and paler than usual - this most probably being due to the absorption of water, from the serous fluid - but, in the one case, the endothelial proliferation occurred in the pleura and not in the peritoneum, while, in the other case, it occurred in the peritoneum and not in the pleura. Why the endothelial cells showed such distinct proliferation
in the one membrane and not in the other, considering they appeared to be placed under the same pathological conditions, it is difficult to explain. Perhaps, there may have been at work some special irritant causing chronic inflammation, which was invisible to the naked eye. An anomaly similar to the above has been noticed in other morbid conditions of the endothelium, viz, in pigmentary degeneration. This was observed, in a marked degree, in the pleura of cases of acute alcoholism and of septic peritonitis, while the peritoneum showed no trace whatever of it.

(b) Proliferation with Degeneration.

As already stated, one peculiar feature which proliferating endothelial cells show, is a tendency to arrange themselves into somewhat circular shaped groups. This circular arrangement, in some instances, would appear to be a form, which the cells assume preparatory to their undergoing degeneration. In considering the subject of proliferating endothelial cells on serous surfaces, due consideration must always be given to the view, that they may be simply those cells, which normally occur around stomatous openings.

Proliferating or germinating endothelial cells, previously alluded to, in connection with the normal histology, have been described as occurring in the pleura, the pericardium, and the peritoneum; but, more
especially in the pleura and the peritoneum. In the vast majority of my preparations, they are not at all numerous; neither have I, as already pointed out, been able to demonstrate, in a satisfactory manner, the presence of stomatous openings. I refer to these points, because the question has arisen in my mind, whether certain rounded spaces, I had observed in microscopical preparations of the pericardium from cases of acute phthisis and of senile insanity, are simply dilated stomata, with proliferated cells surrounding them, or whether they are true areas, formed by the degeneration of some of the proliferated endothelial cells. My opinion is (reasons for which, I will state later,) that these spaces are true degenerated areas, and I will now describe what I believe to be the various stages leading to their formation.

In microscopical preparations of the visceral layer of the pericardium taken from a case of acute phthisis, (Specimens 11 and 12,) the several stages can be distinctly traced, and are as follow, viz.

The endothelial cells, at many places undergo division until many young cells are produced, which become heaped upon one another, and at the same time become arranged into somewhat circular shaped groups. Many of the nuclei of these young cells are narrower than normal, and are pointed at their extremities, while others show no difference as regards shape and size from the parent
cells. The appearance presented at this stage is shown in Fig XVIII.

The next change taking place is, that the central cells gradually undergo a process of degeneration, which leads to their breaking down into a homogeneous mass, which stains violet in haematoxylin and eosin preparations, (Fig XIX.) This homogeneous substance may then undergo disintegration, when a fine granular detritus which does not stain with either haematoxylin or eosin is produced, and which may be seen occupying some of the rounded spaces, (Fig XX.) This granular detritus is probably of a fatty nature. The homogeneous material thus produced, as a result of the disintegration of the cells is, in all probability, of the same nature as that produced in the formation of concentric bodies in the dura, and to which I have already referred; but it does not give the same staining reaction as that found in the dura. This, however, I think is due to the unstable character of the homogeneous material, which may become so altered in its composition, as to take on an entirely different staining reaction. While this degenerative change in the centrally placed cells is going on, the excentrically placed ones are left to form a ring around them. The nuclei of the cells then become flattened out and, ultimately, a circular band of fibrous tissue is formed, which I feel sure is derived from the excentrically
placed endothelial cells, (Fig. XXI.) The fibrous tissue would then seem to increase in amount and to contract, after the manner of all fibrous tissues, and to fill up gradually the rounded spaces, but whether it does so completely or not, I cannot say. Neither have I been able to determine whether or not the endothelial cells in the neighbourhood of these denuded areas proliferate and bridge over the gap.

With the view of determining, if possible, whether some of these spaces might not be dilated stomatous openings, I carefully examined the surface of the pericardium in twenty cases, but in only one did I find any appearance resembling that already described. Two others showed rounded spaces without any proliferating cells. These spaces I was inclined to regard as being simply swollen cells, from which the nuclei had disappeared - a feature I have frequently observed e.g., in Specimen 29. The rest of the cases showed no abnormal appearance at all.

The reasons which have induced me to conclude, that these spaces, occurring in the endothelial lining, are the result of a true proliferative and degenerative change, and are not simply dilated stomatous openings, are the following:

(1) The spaces shown in the sections are extremely large; some of them containing a granular material and a few cells, which may have escaped the degenerative
process.

(2) They are exceedingly numerous and closely set together.

(3) The process does not occur uniformly over the surface, because many other sections, from the same piece of tissue, show an apparently normal structure.

(4) It is highly improbable that such minute openings, as stomata, could become so enormously distended as those shown in the sections.

(5) Out of 101 serous membranes examined, only two showed such appearances as have been described.

(6) The various stages in the degeneration of the proliferated cells can be very distinctly traced.

Granulations, consisting of localised aggregations of proliferated endothelial cells, are likewise liable to undergo degenerative changes. One marked example of this change I have observed, in specimens of the peritoneum, taken from a case of cirrhosis of the liver, with jaundice and ascites, (Specimen 30, Fig. XXII.) With the low power of the microscope, there may be seen, in some of the preparations, numerous rounded bodies, etc., scattered over the field, and, in some parts, they are collected into groups. Several of them may be seen to be distinctly encapsulated, apparently with rings of fibrous tissue. Many nuclei may be also seen in the centre of the bodies, and in the capsule. Under the high power, the cells, in the
majority of these rounded bodies are seen to have undergone a considerable degenerative change, while the apparently fibrous character of the capsule can be more distinctly discerned.

What the nature of the degenerative change in these cells is, I am unable to say. The change, however, appears to me, to closely resemble the so called "hyaline" degeneration, which takes place in connection with the formation of concentric bodies, and which I have already described. In the early stages, the granulations stain violet with the haematoxylin, but later, they take on the eosin dye, and stain of a pink hue, the staining reactions being thus analogous to those seen in the hyaline change. Further, the capsule seems to resemble that which surrounds the concentric bodies. It is probable, that were the cells to undergo a still further change, they would ultimately run together and form a homogeneous mass, which would stain pink with the eosin dye.

(C) Formation of Fibrous Tissue
from surface endothelium.

Whether surface endothelial cells can or can not, form fibrous tissue, is a disputed point, and, indeed it is one that is not settled. This interesting question has arisen in connection with the formation of
fibrous tissue around certain rounded areas of proliferated cells, which I have observed in some of my sections. As there was no pre-existing fibrous tissue in these rounded areas, I am inclined to take the view that the endothelial cells here, as well as those in other situations, may play a considerable part in the formation of fibrous tissue.

Ziegler's theory that fibrous tissue is formed from leucocytes, is now almost universally discredited, and has given place to one more generally accepted by pathologists, viz, that it is derived from fibro-blasts, produced by a proliferation of fixed connective tissue corpuscles. Thoma states, that the cells from which new connective tissue is formed, may arise either from the endothelial lining of the blood vessels, or from the cells of pre-existing connective tissue. As far as I can ascertain, however, little or no attention has been given to the subject of surface endothelial cells becoming converted into fibro-blasts, and forming connective tissue.

In describing the development of endothelial cells, I referred to the fact, that they were now regarded as being derived from the mesoblast, having thus the same origin as connective tissue corpuscles. I also referred to endothelial cells and connective tissue corpuscles, as being morphologically alike, and that I considered these cells to be only highly specialised connective tissue corpuscles. From observations I have made in
specimens obtained by the method of superficial horizontal section, I have come to the conclusion, that the endothelial cells of serous membranes are capable, under certain circumstances, of becoming converted into fibroblasts, and ultimately of forming fibrous tissue.

In the process of organisation of a thrombus, it is well known that the endothelium of the vessel wall proliferates, spreads over, and invests the thrombus. A thin layer of connective tissue is then formed beneath this, as a result of the proliferation of the endothelial cells. The cells, on the surface, then divide, and send down, into the thrombus, processes which become converted into capillaries. Connective tissue now grows around the capillaries and forms a coat to them, which gradually increases in thickness. Eventually, according to Thoma, these new capillaries and those derived from the vasa vasorum, unite and then the vascularisation of the thrombus becomes completed. Such, briefly, are the changes which take place.

Again, in the case of sub-acute interstitial nephritis, the endothelial cells, lining Bowman's capsule, proliferate to a marked degree, so as to form stratified layers inside it, (Sp?40, Fig.XXIII). These gradually fill up the whole space between the capsule and the tuft of capillaries. Ultimately, dense laminated layers of fibrous tissue are formed, which contract and compress the tuft. The tuft then becomes converted into a nodular hyaline mass.
Similar examples to these may be found in the changes which follow the ligation of an artery, or those taking place in congenital syphilitic cirrhosis of the liver.

Now, it seems probable, in the two cases just described, that the endothelial cells, at all events, play some part in the formation of fibrous tissue. It has already been stated that Thiersch, Waldeyer, Raab and Baumgarten, demonstrated the origin of connective tissue to be from the endothelium of blood vessels, while Professor Greenfield, in the case of sub-acute interstitial nephritis, regards the fibrous tissue formed inside Bowman's capsule, as being probably derived from the proliferated endothelial cells. These observations, however, do not necessarily imply that fibrous tissue can be formed from surface endothelium. Nevertheless, considering that they have a bearing on the subject, and especially as I have observed, in several of my own preparations, from serous membranes, certain changes in shape, which the endothelial cells undergo, and which I believe to be analogous to the various alterations, in shape, assumed by connective tissue cells, when they are becoming converted into fibroblasts, I am of the opinion, as already stated, that surface endothelial cells can form fibroblasts, and consequently, can form fibrous tissue. I have been able I think to trace
the various stages taking place in the formation of fibroblastic looking cells from endothelium, in the pleura, and in the pericardium of cases of cirrhotic kidney and of senile insanity respectively, and also in the pleura of a case of general paralysis. In these three cases, there were no acute changes to complicate matters.

Concerning the stages alluded to, one can observe in the microscopical preparations I have made, the protoplasm of some endothelial cells becoming granular and increasing in size. At first they are rounded, but later, the protoplasm becomes drawn out, at various points, so that the cells become pear shaped, or spindle shaped, or assume various other irregular forms. The spindle shaped cells gradually increase in length, until long delicate processes are formed. At their extremities, the processes may show a tuft, or they may show a splitting up into short fibrils. Here and there may also be seen large cells (giant cells), containing three or four nuclei, as if the protoplasm of the cell plate had divided much more slowly, than the nucleus. The actual fibrillation of the cells, however, I have been unable to trace, unless one regards, as such, the splitting up of the processes of the spindle shaped ones, which I have observed, and which Thoma describes as taking place, at the poles of the protoplasm of the
spindle shaped fibroblasts. These appearances are shown in Specimens 31 and 32, Figs. XXIV and XXV.

Authorities differ as to the mode in which the fibrillae arise. Some are of opinion that they are formed by a fibrillation of the peripheral parts of the cell protoplasm, while others maintain that the fibroblasts produce an intercellular substance, which subsequently becomes fibrillar. The point is, no doubt, difficult to determine, and I have no opinion to offer on the subject. In connection with the organisation of a fibrinous exudation, such as occurs in the pleura, the point as to whether endothelial cells can form fibroblasts, or not, is a more difficult problem, owing to the marked desquamation of the cells, which takes place as a result of the inflammatory process. In no case, however, have I been able to observe the cells lying over the false membrane, as Buhl and Neumann maintained, but always lying under the exudation, as Marchand, Wagner, and other writers assert.

In acute inflammation of a serous membrane, the endothelial cells, at an early stage, can be seen undergoing marked proliferation,—numerous karyokinetic figures being visible in the cells. As the inflammatory process progresses, the vast majority of the proliferated endothelial cells, no doubt, desquamate and form part of the false membrane, but, even, after a considerable time, many undesquamated cells still remain, mixed
up in the exudation, and can be seen in the meshes of the fibrin, along with leucocytes. This, I have observed in specimens obtained from a case of early peritonitis of ten hours duration, (Specimen 34,) and peritonitis of thirty-six hours duration, (Specimen 36.) I think it highly probable, that those cells which have not degenerated, are capable of organizing the serous exudation, if not entirely, then with the assistance of the fixed connective tissue corpuscles. No doubt, in acute processes, actual confirmation of this is difficult to obtain, owing to the uncertainty as to whether the fibroblasts are derived from the endothelial cells, or from the fixed connective tissue corpuscles. Still, in specimens which I have examined, from a case of pleurisy, as the result of extension from a pneumonic lung, (Specimen 38,) I think I have been able to trace the development of fibroblastic looking cells, similar to those in the cases previously described, and, from the situation of these cells, I am inclined to regard them as being derived from endothelial cells, and not from fixed connective tissue corpuscles. The appearances are shown in Fig. XXVI.

In chronic inflammation, which produces denudation of the endothelium, the origin of fibroblastic looking cells from endothelium can also be observed. In a section, taken from a case of senile insanity, there can be seen a small area where the endothelium appears to
have been denuded; but in which a few endothelial cells still remain. Some fibrinous threads may also be observed in the same area. In this same area, an endothelial cell can be seen becoming converted into a fibroblastic looking cell, which appears to be about to divide. (Specimen 32, Fig. XXV.) It seems probable that this cell is about to form fibrous tissue and fill up the denuded area.

In tubercle of the peritoneum, from which I have obtained specimens, and where the inflammation is of a chronic character, numerous fibroblastic cells becoming converted into fibrous tissue may be observed, and there appears to be little doubt, that they are derived from the surface endothelium. (Specimen 39.)

Now, from the observations just made, I think it will be admitted, that endothelial cells undergo the same alterations in form, as connective tissue corpuscles undergo, when forming fibroblasts. If this fact therefore be taken into consideration, along with the facts that fibrous tissue is known to be formed from the endothelium of blood vessels, and that it is also formed in various situations, where endothelial cells are present; for instance, surrounding the rounded spaces previously described, as a result of proliferative and degenerative changes; surrounding the concentric bodies of the dura; and observed in Bowman's capsule in cases
of sub-acute interstitial nephritis, as well as observed encapsulating granulations, it appears to me that the evidence is conclusive, that surface endothelial cells are capable of producing fibrous tissue.

In conclusion, I may add that I have also observed in the thickened pleura from a case of acute phthisis, a pathological condition, which I cannot at present classify. Under the microscope, this condition appears as a ring of well defined nuclei, some of which are slightly swollen, but no distinct cell outline can be made out. (Specimen 41, Fig. XXVII.)

It is extremely doubtful what the nature of this condition is. Probably it is a large multinucleated giant cell, such as one finds in tubercle, and which may be formed by the confluence of several endothelial cells. This assumption would seem to derive some support from the statements of Brosch, who in one of his conclusions, in regard to the origin of giant cells from endothelial cells, states, "that as Bizzozero and Bozzolo have proved, that connective tissue cells are able to assume an endothelial character, it appears not to be impossible that all giant cells are descendants of endothelium, or of endothelial like connective tissue cells."
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LIST OF MICROSCOPIC SPECIMENS.

1. Perivascular Canal, from the pericardium of a case of Choreic Insanity, H. and E.

2. Endothelial cells overlapping each other, and showing well defined outlines. From the pleura of a case of peritonitis following rupture of the uterus. H. and E.

3. Albuminous degeneration of endothelial cells. From the pericardium of a case of senile insanity, H. and E.

4. Albuminous degeneration of endothelial cells. From the pleura of a case of senile insanity, Os. Ac. and P.C.

5. Albuminous degeneration of endothelial cells. From the pericardium of a case of senile insanity, Os. Ac. and P.C.

6. Albuminous degeneration of endothelial cells. From the pericardium of a case of senile insanity, Os. Ac. and H.

7. Albuminous degeneration of endothelial cells. From the pericardium of a case of senile insanity. Section immersed for 24 hours in Os. Acid, then placed in Ether.

8. Gedematous or Dropsical degeneration of endothelial cells. From the pleura of a case of pleuro-pneumonia. H. and E.
9. "Hyaline" degeneration of endothelial cells, with formation of concentric bodies. From the dura of a case of senile insanity. H. and E.

10. "Hyaline" degeneration of endothelial cells. From the pleura of a case of phthisis. H. and E.

11. "Hyaline" degeneration of endothelial cells. From the pericardium of a case of phthisis. H. and E.

12. "Hyaline" degeneration of endothelial cells. From the pericardium of a case of phthisis. H. and E.

13. "Hyaline" degeneration of endothelial cells. From the pericardium of a case of choreic insanity. H. and E.

14. Vacuolation of nuclei of endothelial cells. From the pleura of a case of fibroma of kidney with pyelitis. H. and E.

15. Advanced degeneration of endothelial cells, resembling the appearance presented by frosted glass. From the dura of a case of purpura haemorrhagica. H. and E.

16. Degeneration of endothelial cells, resembling the appearance presented by frosted glass. From the pleura of a case of acute alcoholism with hyperpyrexia. H. and E.

17. Degeneration of endothelial cells, resembling the appearance presented by frosted glass. From the pleura of a case of acute alcoholism with hyperpyrexia. H. and E.
18. Pigmentary degeneration of endothelial cells. From the pleura of a case of acute alcoholism. H. and E.

19. Pigmentary degeneration of endothelial cells. From the pleura of a case of septic peritonitis. H. and E.

20. Pigmentary degeneration of endothelial cells. From the pleura of a case of septic peritonitis.

21. Endothelial cells, proliferating and forming irregularly shaped groups. From a case of cerebral haemorrhage. H. and E.

22. Endothelial cells, proliferating to a marked degree and forming irregularly shaped groups. From the omentum (with adhesions) of a case of general paralysis. H. and E.

23. Proliferated endothelial cells. From the pericardium of a case of general paralysis. H. and E.

24. Proliferated endothelial cells. From the pericardium of a case of subacute catarrhal nephritis. H. and E.

25. Proliferated endothelial cells forming granulations. From the pleura of a case of double aortic and mitral disease. H. and E.

26. Proliferated endothelial cells with irregularly shaped nuclei. From the pleura (thickened) of a case of phthisis. H. and E.
27. Irregularly shaped nuclei. At marked spot a cell with four fragmental nuclei may also be seen. From the pericardium of a case of subacute catarrhal nephritis. H. and A.

28. Proliferated endothelial cells, forming granulations (vertical section). From the pleura of a case of double aortic and mitral disease. H. and A.

29. Endothelial cells, from which many of the nuclei have disappeared, leaving colourless spaces, which are bounded by the intercellular cement substance. From the pericardium of a case of acute phthisis. H. and A.

30. Large granulations, in which the endothelial cells are undergoing degeneration, probably of a hyaline character. Some of the granulations can be seen to be encapsulated by fibrous tissue. From a case of cirrhosis of the liver with ascites and jaundice. H. and A.

31. Endothelial cells, which have undergone various alterations in shape, so as to assume the form, taken by connective tissue corpuscles, when becoming converted into fibroblasts. From the pleura of a case of cirrhotic kidney. H. and A.

32. Endothelial cell, in a denuded area of the pericardium, which has assumed the form of a fibroblast,
and appears to be about to divide. In the same area a large cell with three nuclei, as well as some fibrous looking threads, may also be seen. From a case of senile insanity. H. and E.

33. Endothelial cells, elongating and assuming the shape of fibroblasts. From the pleura of a case of general paralysis. H. and E.

34. Acute peritonitis of ten hours duration, showing proliferation of endothelial cells, with the formation of numerous karyokinetic figures. Note that large numbers of the endothelial cells are still present. H. and E.

35. Vertical section from same case as 34. H. and E.

36. Acute peritonitis of thirty six hours duration showing a few endothelial cells still present in the exudation. H. and E.

37. Vertical section from same case as 36. H. and E.

38. Endothelial cells, becoming converted into fibroblasts and apparently about to organise the fibrinous exudation. The stages of development of the fibroblasts can be traced in the parts near the marked spots. From the pleura of a case of pleuropneumonia. H. and E.
39. Large numbers of fibroblasts becoming converted into fibrous tissue. From the peritoneum of a case of tubercule of the peritoneum. H. and E.

40. Subacute interstitial nephritis, showing proliferation of endothelial cells in Bowman's capsule, with formation of dense laminated layers of fibrous tissue. The tuft in many cases has become converted into hyaline nodular masses.

41. Pleura (thickened) from a case of acute phthisis showing multinucleated giant cells? H. and E.

42. Normal endothelium. Note well defined outlines of cells. From the pleura of a case of dementia. H. & E.

43. Normal endothelium. From the pericardium of a case of cerebral haemorrhage. H. & E.

44. Endothelium stained with silver nitrate. From the pericardium of a case of cerebral haemorrhage.
DESCRIPTION OF ILLUSTRATIONS.

Fig 1. Normal subendothelial capillary and perivascular canal. From a case of choreic insanity. Patient aet. 61. (X 600.)

Fig 2. Endothelial cells, showing well defined outlines, without the aid of silver nitrate. From the pleura of a case of peritonitis. Patient aet. 34. (X 600.)

Fig 3. Albuminous degeneration of endothelial cells in the pericardium. From a case of senile insanity. Patient aet. 72. (X 600.)

Fig 4. Albuminous degeneration and fatty degeneration of endothelial cells, in the pericardium, From a case of senile insanity. Patient aet. 72. Stained with osmic acid and picro-carmine. (X 600.)

Fig 5. Cedematous degeneration of endothelial cells in the pleura. From a case of pleuro-pneumonia. (X 600.)

Fig 6. Concentric body in the dura, From a case of senile insanity. Patient aet. 72. (X 600.)

Fig 7. "Hyaline" degeneration of endothelial cells in pleura. From a case of phthisis. Patient aet 34. (X 600.)
Fig 8. "Hyaline" degeneration of endothelial cells in the pericardium. From a case of choreic insanity. Patient aet. 61. (X 600.)

Fig 9. Drawing to show probable mode of development of hyaline rounded bodies occurring in the pleura. From a case of phthisis. (X 600.)

Fig 10. Degeneration of endothelial cells in dura to form a homogeneous substance resembling frosted glass in appearance. From a case of purpura haemorrhagica. Patient aet. 26. (X 600.)

Fig 11. Degeneration of endothelial cells in the pleura to form a homogeneous substance resembling frosted glass in appearance. From a case of acute alcoholism with hyperpyrexia. (X 600.)

Fig 12. Degeneration of endothelial cells in pleura to form a homogeneous substance resembling frosted glass. From a case of acute alcoholism with hyperpyrexia. (X 600.)

Fig 13. Pigmentary degeneration in endothelial cells of pleura. From a case of acute alcoholism. Patient aet. 46. (X 600.)

Fig 14. Simple proliferation of endothelial cells of pericardium. From a case of general paralysis. Patient aet. 47. (X 600.)

Fig 15. Simple proliferation of endothelial cells of pleura. From a case of double aortic and mitral
disease with hydrothorax. Note the cells heaped on one another and forming granulations.
(X 600.)

Fig 16. Irregularly shaped nuclei in cells of pleura. From a case of acute phthisis. Patient aet. 48. 
(X 600.)

Fig 17. Vertical section of pleura. From a case of double aortic and mitral disease. Note the 
granulations, composed of masses of proliferated endothelial cells. (X 600.)

Fig 18. Proliferated endothelial cells, arranged in circular groups, previous to their undergoing degeneration. From the pericardium of a case of phthisis. Patient aet. 34. (X 600.)

Fig 19. Proliferated endothelial cells, undergoing degeneration. Note that a few cells still remain in the degenerating area. From the pericardium of a case of phthisis. Patient aet. 34. (X 600.)

Fig 20. Proliferated endothelial cells, undergoing degeneration, so as to form a rounded space. Note that space contains only a little granular debris. From the pericardium of a case of phthisis. Patient aet 34. (X 600.)

Fig 21. Rings of fibrous tissue surrounding rounded spaces. Fibrous tissue contracting and becoming distorted. From the pericardium of a case
of phthisis. Patient aet. 34. (X 600.)

Fig 22. Endothelial granulations, encapsulated by delicate rings of fibrous tissue. From the pleura of a case of cirrhosis of the liver with ascites and jaundice. Patient aet. 27. (X 115.)

Fig 23. Proliferating endothelial cells in Bowman's capsule with formation of dense layers of fibrous tissue. From a case of subacute interstitial nephritis. (X 600.)

Fig 24. Surface endothelial cells, presenting the form assumed by the fibroblasts, which are derived from fixed connective tissue corpuscles. From the pleura of a case of cirrhotic kidney. Patient aet. 39. (X 600.)

Fig 25. Surface endothelial cell, presenting the form of a fibroblast; also a giant cell. From the pericardium of a case of senile insanity. Patient aet. 72. (X 600.)

Fig 26. Fibroblasts of various forms, lying in the meshes of fibrin and apparently about to organize the fibrinous exudation. From the pleura of a case of pleuro-pneumonia. (X 600.)

Fig 27. Multinucleated giant cell, with wreath of nuclei ?. From the thickened pleura of a case of acute phthisis. Patient aet. 34. (X 600.)