RESEARCHES ON THE NORMAL AND PATHOLOGICAL

HISTOLOGY OF SURFACE ENDOTHELIUM AS EXAMINED BY

THE METHOD OF SUPERFICIAL HORIZONTAL SECTION.

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THESIS.

Submitted to the University of Edinburgh, for the

Degree of Doctor of Medicine.

by

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I. 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 be-
lieved 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 sect-
ion 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 advant-
ages, e g,- in studying inflammatory processes, upon
the surface, it is, of course, essential, to make verti-
cal 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 hori-
zontal 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 lay-
ing it on blotting paper. A small fragment of the
tissue is next laid, with the endothelial surface down-
wards, 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 suffi-
ciently thin section is left. The knife is then lower-
ed (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 sect-
ions 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 import-
ant 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 pericard-
ium (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 Ehrlichs' 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 mortems 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 occurr-
ed, 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 endo-
thelial 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 ex-
planation, 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.

Disease.	Age	Surfaces Examined.
1. Choreic Insanity.	61	pericardium.
		pleura.
		peritoneum.
2. Acute Phthisis.	34	pericardium.
3. Do. Do.	48	pleura.
4. Do. Do.		pericardium.
		pleura.
		peritoneum.
5. Do. Do.		pleura.
		peritoneum.
6. Tubercular Pleurisy and		
Tubercular Peritonitis. . .	15	pleura.
7. Chronic Phthisis with empyaema.	20	pleura.
		peritoneum.
8. Pneumonia.	21	pleura.
9. Do.		pleura.
		peritoneum.
10. Do.	52	pleura.
		peritoneum.
11. Cerebral Hemorrhage. . . .	68	pericardium.
		pleura.
		peritoneum.

Disease.	Age.	Surface Examined.
12.Bronchitis with Emphysema. . .	24	pleura.
		peritoneum.
13.Tubercule of Peritoneum. . .		peritoneum.
14.General Paralysis of Insane. .	48	pericardium.
		pleura.
		peritoneum.
15. Do. Do.	47	pericardium.
		pleura.
		peritoneum.
16.Epilepsy.	44	pericardium.
		pleura.
		peritoneum.
17. Do.	33	pericardium.
		pleura.
		peritoneum.
18. Do.	40	pericardium.
		pleura.
		peritoneum.
19.Subacute Catarrhal Nephritis. .	32	pericardium.
		pleura.
		peritoneum.
20.Insanity.(Puerperal)	39	pleura.
		peritoneum.

Disease.	Age.	Surface Examined.
21. Cirrhosis of Liver with Jaundice and Ascites. . . .	27	pericardium. pleura. peritoneum.
22. Melancholia with Phthisis. . .	35	pleura.
23. Senile Insanity.	70	pleura.
24. Do. Do.	70	pericardium.
25. Senility.	71	pleura.
26. Chronic Insanity.	35	pericardium. peritoneum.
27. Tubercular Ulceration of Bowel.	35	peritoneum.
28. Dementia.	51	pericardium.
29. Do.	32	pericardium. pleura. peritoneum.
30. Senile Insanity.	72	pericardium. pleura. peritoneum. dura.
31. Do. Do.	86	pericardium. pleura. peritoneum.
32. Do. Do.		pleura.

Disease.	Age.	Surface Examined.
33. Dog poisoned by Benzoate of Soda.		pleura.
34. Peritonitis following rupture of the uterus.	34	pleura. peritoneum.
35. Cirrhotic Kidney.	39	pleura.
36. Acute Pericarditis and Pleursy with effusion and empyaema.. .	17	peritoneum.
37. Cancer of Omentum with secondary infiltration. . . .	64	peritoneum.
38. Double Aortic and Mitral disease with Ascites and Hydrothorax. .		pleura. peritoneum.
39. Fibroma of Kidney with Pyelitis.	55	pleura. peritoneum.
40. Acute Alcoholism.	46	pleura. peritoneum.
41. Do. with hyperpyrexia .		pleura. peritoneum.
42. Alcoholic Insanity.	66	pericardium. pleura. peritoneum.
43. Cancer of pylorus.	49	pleura. peritoneum.
44. Early peritonitis following traumatic rupture of bowel.. .	21	pleura. peritoneum.

Disease.	Age.	Surface Examined.
45.Empyaema following Pneumonia. .	31	pleura.
		peritoneum.
46.Septic Peritonitis following operation.	39	pleura.
		peritoneum.
47.Gangrene of Lung.		pleura.
		peritoneum.
48.Sub-acute Nephritis, with Meningitis and chronic Pleurisy.	30	pleura.
		peritoneum.
49.Cancer of Omentum and Stomach.	64	pleura.
		peritoneum.
50.Acute Mania with exhaustion. .	62	pericardium.
		pleura.
		peritoneum.
51.Purpura Haemorrhagica. . . .	26	dura.

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 Scháfer,[2] Kölliker,[3] Klein,[1] Rutherford,[4] Stirling,[5] Piersol,[8] etc. in their various text books. 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 min-
ute 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 neigh-
bourhood of, and lining the stomatous openings, num-
bers 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 major-
ity 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.

Muscatello [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.

Soulié [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[8] distinctly states that
there is none. Delchuysen[9], however, says that endoth-
elial cells may not necessarily be placed in a contin-
uous 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[2] says that no blood vessels have ever been dis-
cerned 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 en-
dothelial cells are developed from the mesoblast, in-
stead of from the hypoblast as was formerly supposed.
Schäfer[10] includes in his list of structures derived from
the mesoblast, the serous membranes; consequently the
endothelial cells must be derived from the same blasto-
dermic layer. Balfour and Foster[11] as well as Hertwig
and Mark[12] 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 publish-
ed in a very fragmentary form, references have been
exceedingly difficult to obtain.

W.F.Robertson [13,14] 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 sur-
face 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 ultim-
ately extends to the cell plate, until, finally, the
whole cell plate is destroyed. When this change af-
fects extensive areas of the endothelium, a silvery
appearance can be recognised with the naked eye. He

believes the condition to develope with great rapidity
and to arise specially in the moribund state.

A common degenerative process and one character-
ised 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 numer-
ous 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 homo-
geneous 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[15] 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 consider-
able variations and anomalies in staining.

Regarding the origin of fibrous tissue, most text
books by such authors as Thoma,[16] Ziegler,[17] Coats,[18] 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[19] 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[20] in 1863. held the view that the endothelium lies over the exudation. Neumann[21] 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 recognisible 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[22] holds the ordinary view, viz, that the endothelial cells lie underneath the exudation.

(23)
Marchand also holds the same view.

(24)
Lazarus-Barlow agreed with Neumann that endothel-
ium 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 be-
neath 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 haematox-
ylin and eosin stained preparations, show a largeround
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 (25) 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.

Delchuysen'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 Soulié'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 man-
ner, and without the aid of silver nitrate.

The phenomena of overlapping and alteration in
the form of the endothelial cells are, in all probabil-
ity, of a purely physiological character, being a nat-
ural 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 out-
line.

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 pre-
sence 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 in-
stances, 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 degener-
ation of the endothelial cells. Although I met with
this vitreous like degeneration, as revealed by the
microscope, I was unable to detect any glassy appear-
ance 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 dis-
organized 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 furnish-
ed me with sufficient normal material from which I

could study and obtain a knowledge of the normal ap-
pearances 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 multi-
plying or proliferating, or, on the other hand, degen-
erating or dying, - the former condition being due to
increased nutrition or function,- the latter to dimin-
ished 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 ex-
tent, been made in the more chronic cases, where de-
struction 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 ap-
pearances 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) Oedematous 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 degenera-
tion having only very rarely been seen. An interest-
ing condition and one evidently of the nature of an
albuminous degenerative change consists in the forma-
tion 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 accompany-
ing swelling of the cell plate, or any marked granular-
ity 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 prepara-
tions 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 trans-
lucent.

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 glob-
ules 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 be-
come 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 glob-
ules 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 proper-
ly carried out. Further, when the sections were placed
in ether, it was found that the globules were not dis-
solved, but remained practically unchanged. That these

globules, however, may go on to fatty degeneration, is
quite obvious, from the fact that several of the glob-
ules have been blackened by the osmic acid.

Here and there, over the sections, are seen some-
what 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 uncer-
tain. 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 insuffici-
ent 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 proto-plasm of the cells has become swollen, and the latter seem to have merged into one another; so that a homo-geneous 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 pro-
minent. 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 compar-
atively 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 them-
selves 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 be-
ing 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 endoth-
elial 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 degener-
ation, 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 appar-
ent 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. How-
ever, 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, (Specimens10-13,

Figs. VII. VIII.) taken from the three large ser-
ous surfaces, these bodies have stained violet with
the haematoxylin. On the whole, therefore, I am in-
clined 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 hya-
line 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 like-
ly due to shrinkage. Hyaline Degeneration has not
been a frequent change observed, in many of my prepara-
tions, 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 ex-
tent 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 haema-
toxylin 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 under-
go 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 gran-
ular 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 describ-
ing the proliferative changes accompanied by degenera-
tion.

(4) Vacuolation of the cell nucleus, frequently
occurs in many of the endothelial cells, and is probab-
ly 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 pro-
toplasm 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 how-
ever 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 prolifer-
ation 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 develope very rapidly.

(6) Pigmentary Degeneration.

Normal, or physiological pigment occurs in cells in the
form of yellow, brownish, or black granules. It is pre-
sent 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 hun-
dred 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 be-
lieve show a true pigmentary degeneration or pathologi-
cal 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 ob-
served 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 congregat-
ed 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 total-
ly destroyed and obscured by the pigment. Occasionally,
the pigment is seen to be diffused, as if the cell en-
velope 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 pig-
ment 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 black-
ened by immersion for twenty four hours in osmic acid.
Neither does it appear to be a derivative from the de-
composition 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 con-
sists 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 es-
pecially as in such cases, as acute alcoholism and
septic peritonitis, there may be frequently an accom-
panying 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 ex-
periment, 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 remark- able 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 degenera- tive changes are being considered.

Sometimes, the nuclei, in proliferating cells, as- sume 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 resem-
ble 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, accom-
panied 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, min-
ute 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 en-
dothelial proliferation occurred in the pleura and not
in the peritoneum, while, in the other case, it occurr-
ed 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 alcohol-
ism 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 pre-
sence 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 homogen-
eous material thus produced, as a result of the dis-
integration 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 stain-
ing reaction as that found in the dura. This, however,
I think is due to the unstable character of the homo-
geneous material, which may become so altered in its
composition, as to take on an entirely different stain-
ing 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 form-
ed, 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 en-
dothelial 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 peri-
cardium 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 dis-
appeared - a feature I have frequently observed e g,
in Specimen 29. The rest of the cases showed no abnor-
mal 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 un-
dergone 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, how-
ever, 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 to-
gether 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 quest-
ion has arisen in connection with the formation of

fibrous tissue around certain rounded areas of prolif-
erated cells, which I have observed in some of my sect-
ions. 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 <u>surface endothelial cells</u>
becoming converted into fibro-blasts, and forming con-
nective 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 horiz-
ontal 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 endothel-
ial 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 vas-
cularisation 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 cap-
sule, proliferate to a marked degree, so as to form
stratified layers inside it, (Sp.40, Fig.XXIII). These grad-
ually 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 in-
to a nodular hyaline mass.

Similar examples to these may be found in the changes which follow the ligature of an artery, or those taking place in congenital syphilitic cirrhosis of the liver.

Now, it semms 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 pro-
toplasm 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 spin-
dle shaped, or assume various other irregular forms.
The spindle shaped cells gradually increase in length,
until long delicate processes are formed. At their ex-
tremities, 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 fibro-
blasts produce an intercellular substance, which sub-
sequently 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 en-
dothelial cells, at an early stage, can be seen under-
going marked proliferation,- numerous karyokinetic fig-
ures being visible in the cells. As the inflammatory
process progresses, the vast majority of the prolifer-
ated endothelial cells, no doubt, desquamate and form
part of the false membrane, but, even, after a consider-
able 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 ob-
served in specimens obtained from a case of early per-
itonitis of ten hours duration,(Specimen 34,) and per-
itonitis 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 endothel-
ial cells, or from the fixed connective tissue corpus-
cles. 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 des-
cribed, and, from the situation of these cells, I am
inclined to regard them as being derived from endoth-
elial cells, and not from fixed connective tissue cor-
puscles. 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 ob-
served in the same area. In this same area, an endoth-
elial cell can be seen becoming converted into a fibro-
blastic looking cell, which appears to be about to di-
vide. (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 there-
fore be taken into consideration, along with the facts
that fibrous tissue is known to be formed from the en-
dothelium of blood vessels, and that it is also formed
in various situations, where endothelial cells are pre-
sent; for instance, surrounding the rounded spaces pre-
viously 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 sup-port from the statements of Brosch,[26] 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 show-
    ing 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. Oedematous 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, re-
    sembling 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 hyper-
    pyrexia. 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 hyper-
    pyrexia. 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 A.

20. Pigmentary degeneration of endothelial cells. From
    the pleura of a case of septic peritonitis.
    Os. Acid, and H.

21. Endothelial cells, proliferating and forming irreg-
    ularly 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 pericard-
    ium of a case of general paralysis. H. and E.

24. Proliferated endothelial cells. From the pericard-
    ium 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 E.

28. Proliferated endothelial cells, forming granula-
    tions (vertical section). From the pleura of a
    case of double aortic and mitral disease. H. and E.

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 E.

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 E.

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

32. Endothelial cell, in a denuded area of the peri-
    cardium, 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 form-
ation 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 fibro-
blasts and apparently about to organise the fibrin-
ous 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 pleuro-
pneumonia. 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.   Oedematous 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 heap-
ed 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 prolifer-
ated 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 re-
main in the degenerating area. From the peri-
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(X 600.)

Fig 20. Proliferated endothelial cells, undergoing
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ular debris. From the pericardium of a case of
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Fig 21. Rings of fibrous tissue surrounding rounded
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Fig 22. Endothelial granulations, encapsulated by
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Fig 23. Proliferating endothelial cells in Bowman's
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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
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Patient aet. 72. (X 600.)

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

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