SOME OBSERVATIONS UPON ENDOTHELIAL SEPARATION IN THE SMALLER ARTERIES AND VEINS.

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PLATES IX AND X.

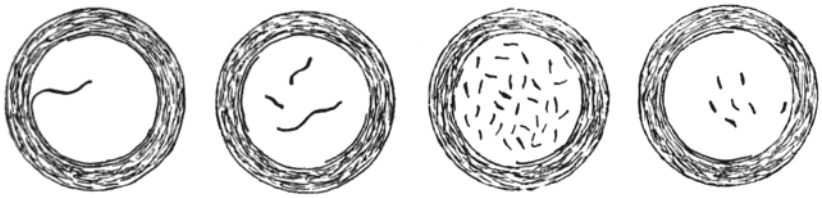
Endothelial separation is a subject which appears to have received very little attention. At the first meeting of the German Pathological Society[1] this subject was discussed by Heller. He described "peculiar findings of endothelial separation" which he had observed in the arterioles and venules, and which he believed to be a vital process because the cells lay embedded among red blood corpuscles. Schmorl stated that he had seen this condition and had formerly believed it an intra-vital one, but now he considers it a post-mortem change, because if intra-vital, emboli of endothelial cells would be found. Several others agreed with the statement of Schmorl, and Chiari remarked that in a gangrenous lung he had once found almost all the endothelium separated from the walls of the vessels.

The following observations are based upon a study of specimens and records of 164 post-mortems in the Pathological Laboratory of Rush Medical College. About half of the specimens were hardened in alcohol and formalin, the others in Zenker's fluid; most of them were embedded in celloidin, stained with eosin and hæmatoxylin, and mounted in Canada balsam.

The endothelial separation observed is not at all uniform, varying from individual cells to large plates of endothelium, and from a few cells to a number almost or quite filling the lumen of the vessel, many cells being free in the lumen, others still attached to the vessel wall. This has made it seem wise to

[1] *Centralblatt für Allgemeine Pathologie und Pathologische Anatomie*, 1899, x, 824.

attempt an arbitrary classification based upon these variations as follows:



1st. Degree. Portions of endothelium separated in entirety, but still attached to the wall of the vessel. (Fig. 1.)

2d Degree. Portions of endothelium separated in entirety and unattached to the vessel wall. (Fig. 2.)

3d Degree. Individual endothelial cells but in large numbers, almost or quite filling the lumen of the vessel. (Fig. 3.)

4th Degree. Individual endothelial cells, few in number and free in the lumen of the vessel. (Fig. 4.)

It was soon discovered that this classification could not be made along hard and fast lines, for while in most instances the degrees were distinct, cases occurred where they merged so indefinitely one into another that it was not easy to draw the line. With one or two minor exceptions, the order of frequency has been the same in all cases: separation of the 4th degree occurring most often, that of the 3d degree next, and that of the 1st degree least often.

The total number of post-mortems from which sections were examined is 164.

The total number of cases showing endothelial separation in one or more parts is 106 (65%).

Of these 106 cases, 34 show endothelial separation of 1st, 38 in the 2d, 45 in the 3d, and 76 in the 4th degree.

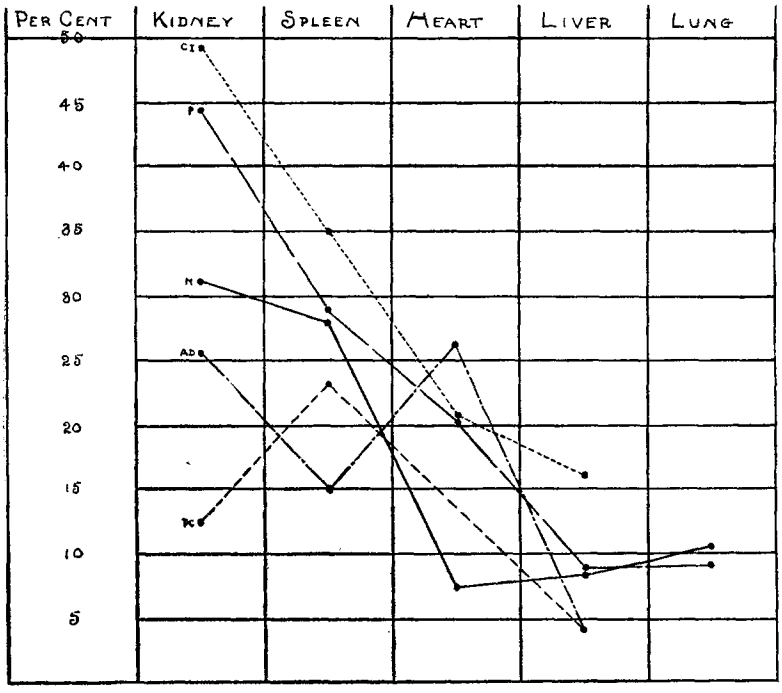
In order to bring out more clearly the frequency of endothelial separation in the different organs, certain of these organs have been studied separately. And in order to ascertain whether or not the condition bears any relation to pathological changes in these organs, they have been divided into groups according to the pathological conditions present in them, and the frequency of all separation and of each degree of separation has been

determined in each case. This form was not carried through for each pathological condition found, but only the most common have been taken and those which represent the greatest diversity of pathological changes. In some cases broad classifications have been adopted to include under one head several conditions, which are but varying degrees of one general process. For example: The term "acute degeneration" is used to include all acute degenerative processes up to an actual necrosis of the part and from whatever cause. In other cases the classification has been more narrow and specific, as brown atrophy of the heart and lobar pneumonia.

	Kidney.	Spleen.	Heart.	Liver.	Lung.
Total number examined	149	125	143	149	139
Endothelial separation	67	36	24	13	19
1st Degree	18	5	2	3	1
2d "	20	6	2	5	1
3d "	21	12	7	2	6
4th "	32	23	16	6	16
Number of normal organs	16	32	40	24	19
Endothelial separation	5	9	3	2	2
1st Degree	2	..	..	..	..
2d "	2	3	1	..	..
3d "	2	4	1	1	1
4th "	3	5	1	1	1
Number showing pathological changes	133	93	103	125	120
Endothelial separation	59	27	21	11	11
1st Degree	14	5	2	3	1
2d "	15	3	1	5	1
3d "	16	8	6	1	5
4th "	29	18	15	5	15
Number showing acute degeneration	59	20	19	44	..
Endothelial separation	25	3	5	2	..
1st Degree	5	..	..	1	..
2d "	6	1	1	..	..
3d "	11	1	1	1	..
4th "	11	1	3	..	..
Number showing chronic interstitial changes	65	37	29	25	..
Endothelial separation	32	13	6	4	..
1st Degree	9	2	1	1	..
2d "	9	3	..	1	..
3d "	4	5	3	..	..
4th "	17	9	4	2	..
Number showing passive congestion	8	21	..	46	..
Endothelial separation	1	5	..	4	..
1st Degree	..	..	..	..	..
2d "	..	..	..	..	..
3d "	1	2	..	..	..
4th "	1	4	..	4	..
Number showing segmentation or fragmentation of heart muscle	..	..	77	..	..
Endothelial separation	..	..	17	..	..
1st Degree	..	..	2	..	..
2d "	..	..	1	..	..
3d "	..	..	4	..	..
4th "	..	..	13	..	..

	Kidney.	Spleen.	Heart.	Liver.	Lung.
Number showing brown atrophy of the heart...	..	..	12	..	..
Endothelial separation.....	..	..	2	..	..
1st Degree.....	..	..	1	..	..
2d "	..	..	..	..	..
3d "	..	..	..	..	..
4th "	..	..	1	..	..
Number showing lobar pneumonia.....	..	..	..	..	30
Endothelial separation.....	..	..	..	..	5
1st Degree.....	..	..	..	..	..
2d "	..	..	..	..	..
3d "	..	..	..	..	1
4th "	..	..	..	..	5
Number showing active tuberculosis of the lungs.	..	..	..	..	28
Endothelial separation.....	..	..	..	..	6
1st Degree.....	..	..	..	..	1
2d "	..	..	..	..	1
3d "	..	..	..	..	2
4th "	..	..	..	..	4

The following chart shows the frequency of endothelial separation in the various conditions of the organs:



CI ..... Represents chronic interstitial inflammations.
P —— —— —— —— " pathological conditions in general.
N ———————— " normal organs.
AD —— - —— - —— - —— " acute degenerations.
PC ---------- " passive congestion.

From the above summary it will be seen that endothelial separation occurs in a large per cent of all post-mortems (65 % in this series), in all organs and in all conditions of the organs, and with but slightly increased frequency in organs showing pathological changes as compared with the normal. In acute degenerations the heart is the first in the order of frequency, showing endothelial separation in 26.3 % of cases, while the spleen shows but 15 %, though normal spleens show this condition in 28.1 % of cases and normal hearts in but 7.5 %. It will also be seen that the frequency of this condition bears a more or less constant relation to the general condition of the part (though no pronounced relation seems to exist between it and specific conditions) and to the organ concerned. For example: In acute degenerations of the organs, the heart excepted, endothelial separation occurs in each one of them less frequently than in normal organs and very much less frequently than in those organs showing chronic inflammatory changes. And, with the exception of the heart, in acute degenerative conditions the kidney and spleen occupy the first places in the order of frequency in each condition, whether normal or pathological. Whether or not this apparent greater frequency of endothelial separation in the kidney and spleen is due to the greater number of arterioles and venules which show in sections of these organs is difficult to say and probably an accurate determination could not be made. It is possible that this may explain a part of this increase. But while this increase in the number of vessels may be a factor in explaining the greater frequency of the condition in some organs and some conditions it does not explain why endothelial separation should occur more frequently in normal organs than it does in those showing acute degeneration. Nor does any explanation which has suggested itself satisfactorily explain this finding, unless it be that the vitality of the endothelial cells has been impaired by the virulence of the toxins which caused the acute degenerative condition, while in chronic inflammatory conditions they have been stimulated to proliferation by the weakness or dilution of the toxins, as suggested by Mallory,[2] thus producing a condition which would

[2] *The Journal of Experimental Medicine*, 1900, v, 1.

favor desquamation during the death agony or immediately after death.

Since the greater number of arterioles and venules offers a possible explanation of the apparent increased frequency of endothelial separation in certain organs and in certain pathological conditions of those organs; since there is no specific condition, with the possible exception of acute myocarditis, in which endothelial separation stands out with marked prominence, though it does seem to bear some relation to general pathological conditions; and since it occurs in so large a per cent of all cases, it seems necessary to look for general explanations of the causes of separation of the endothelium.

In this, as in much work based upon microscopical findings, the question of artefacts must be considered. That a certain amount of endothelial separation might in some cases be produced during the preparation of the sections and especially during the hardening process is not at all unlikely. But this objection cannot be maintained against that very large proportion of cases in which the desquamated endothelium lies embedded among red blood corpuscles; for here it could have occurred only while the blood was fluid. Moreover, if the condition is the result of artefact it should probably be more frequent in this series; for the technique, while by no means faultless, was practically the same in all cases, with the exception of the different hardening fluids used, and there is no essential difference in the frequency of the condition in the first half of the cases when alcohol and formalin were used and the last half when the specimens were hardened in Zenker's fluid. And the hardening process certainly seems the most likely time for endothelial detachment.

In considering Heller's belief that the process is a vital one and his reason for believing so, several things suggest themselves. In the first place, if the process occurs during life we should expect to find in post-mortems showing endothelial separation, numerous minute areas of necrosis caused by emboli of endothelial cells occluding capillaries. Nothing has been found to indicate that minute necroses are more frequent in the cases

with endothelial separation than in those without. The absence of minute necroses seems to justify the classification of those instances in which the blood-vessel was entirely filled with endothelial cells as separation of the third degree rather than to consider them conditions of embolism of endothelial cells.

Moreover, if the condition were an intra-vital one the vessels would be expected to show certain reparative changes, especially in the cases of the large separations of the first and second degrees, and deposits of fibrin upon the wall of the vessel might be looked for. No such changes were observed in this series.

It has been said that the process would seem a vital one because the desquamated portions are intimately mixed with blood corpuscles. But the blood may remain fluid within the vessels for a comparatively long time. Desquamation might take place during this period and still allow the cells to lie among the corpuscles; the intimate mingling of the cells with the blood corpuscles might perhaps be brought about by amœboid movement of the desquamated cells to which Mallory [3] has called special attention in connection with the proliferation of endothelial cells caused by toxines. The question of a possible relationship between toxins and endothelial detachment, due to infection during life or to post-mortem bacterial invasion of the tissues, is an interesting one, but the facts at hand hardly justify its discussion at this time. We know practically nothing of the length of survival of endothelial cells after general death has taken place. The morphological observations recorded in this study are hardly exact enough to determine whether or not the detached endothelial cells had exercised their power of amœboid movement.

Many desquamated cells lie next the wall with no blood corpuscles between them and the vessel wall, desquamation having taken place probably after the coagulation of the blood.

From the findings in this series it would appear that endothelial separation, while in some cases possibly the result of artefact, in many cases cannot be so considered, and in these cases it is probably not a vital process because no evidence of

[3] Loc. cit.

cellular emboli or of reparative changes is present. Neither is it a late post-mortem change since the cells are in many cases embedded among the blood corpuscles. It might occur during the death agony, perhaps produced by irregular contractions in the arterioles similar to those occurring in the heart at that time. But the fact that the condition is found also in the veins might make this seem unlikely.

No doubt observations upon suitable material other than from post-mortems—from surgical operations and similar sources—would shed much light, not only upon the question of the time of production of endothelial separation, but also upon the question of its causes.

EXPLANATION OF PLATES.

PLATE IX.

Fig. 1.—Showing endothelial separation of the 1st degree in a central vein in a congested liver.

Fig. 2.—Showing endothelial separation of the 2d degree in an artery in a fibrous kidney.

PLATE X.

Fig. 3.—Shows endothelial separation of the 3d degree in a somewhat hyaline artery in the spleen.

Fig. 4.—Shows endothelial separation of the 4th degree in a thickened artery in the pancreas.

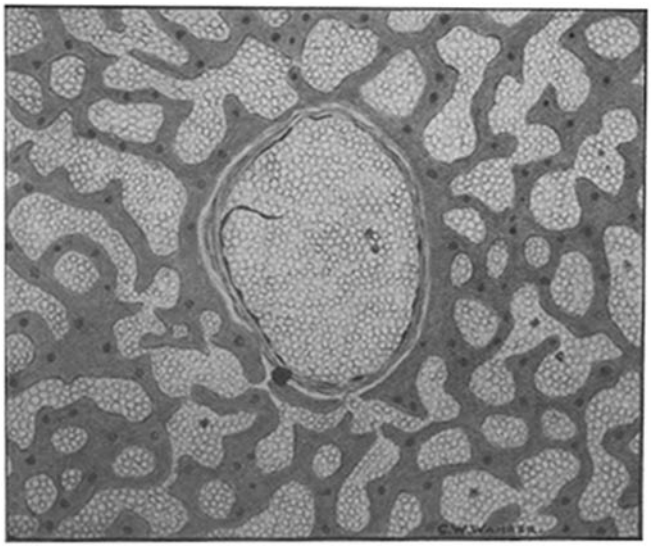


FIG. 1.

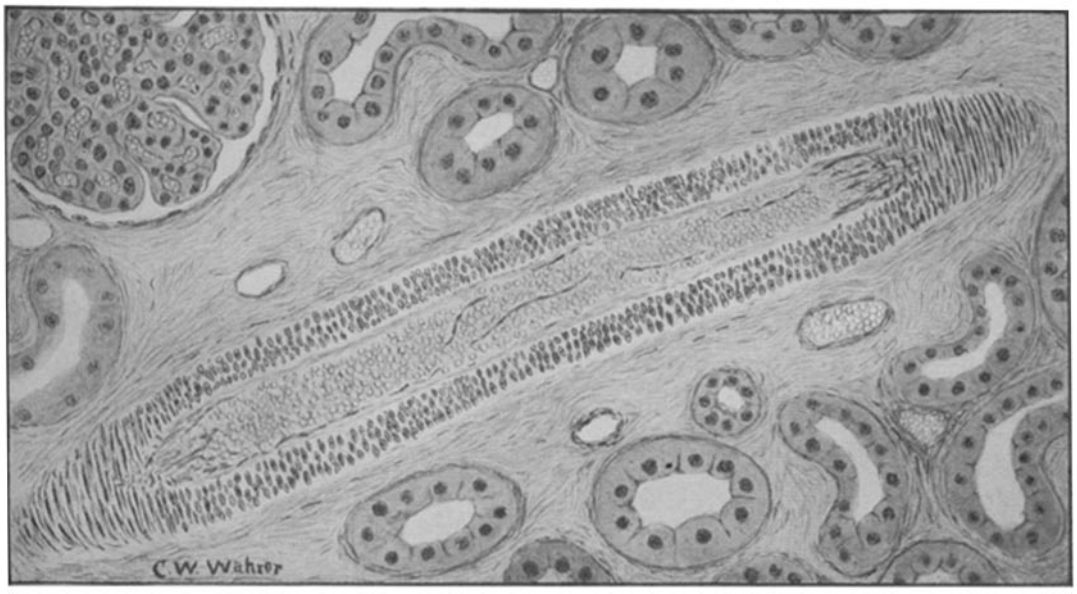


FIG. 2.

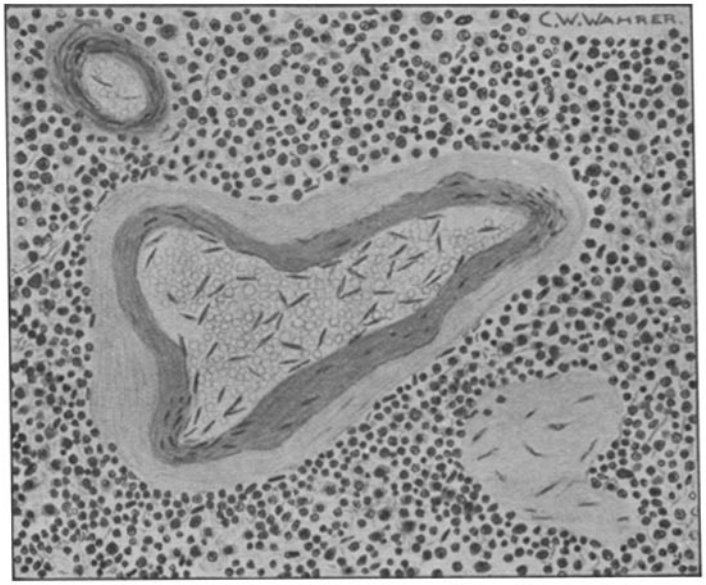


FIG. 3.

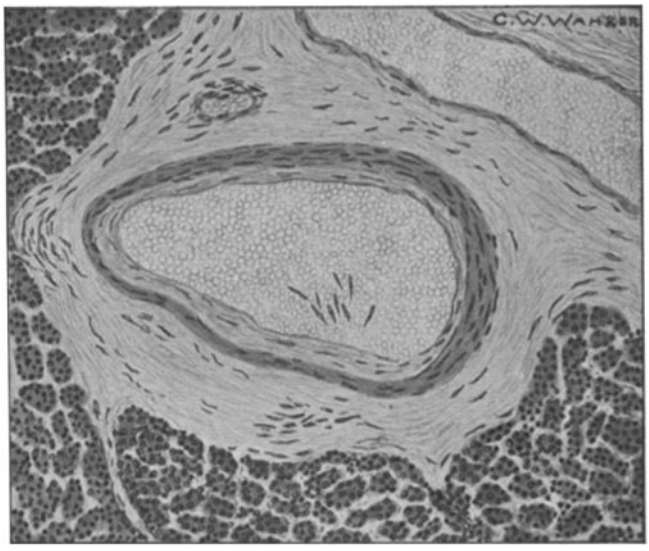


FIG. 4.