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Histological and Ultrastructural Study of Intracranial Saccular Aneurysmal Wall

By

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With 9 Figures

Summary

The material studied consists of 10 cases of intracranial saccular aneurysms. Four came from autopsies, and in each of the other six aneurysmal wall was obtained at surgery after clipping of the aneurysm. The most significant findings from this pathological study are the almost complete disappearance of the internal elastic lamina at the level of the aneurysmal neck, sclerosis of the muscle coat, and in satellite vessels and vasa vasorum disruption of the internal elastic lamina and partial luminal occlusion.

The importance of ischaemic changes in the aneurysmal wall is discussed. Rupture of the aneurysm at the distal extremity of the sac depends probably on the progressive brittleness of its wall which becomes sclerotic and less resistant to the blood pressure within. Splitting or rupture of the aneurysm appears to be dependent on degenerative ischaemic alterations in its wall.

Key words: Aneurysms; electron microscopy.

Introduction

Many of the problems related to aetiopathogenesis of intracranial saccular aneurysms and to the mechanisms of their rupture are still matters of discussion. While the morphological structure of the aneurysmal wall has been extensively studied by optic microscopy (Padget 1944, Stehbens 1963, Nystrom 1965), its electron microscopy aspect has been described by only a few authors and in a limited number of cases (Nystrom 1965, Lang 1965, Stehbens 1975). Also, most of the

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ultrastructural studies were performed on autopsy material, and only two cases of biopsy study are reported in the literature—by Lang (1965) and by Stehbens (1975). It seemed interesting to us to perform a morphological study on biopsy material obtained intraoperatively as well as on autopsy material in an attempt to improve our knowledge of aneurysm structure. Aneurysms with repeated ruptures and several episodes of SAH, and aneurysms that had never bled were studied, with the aim of correlating the alterations in the aneurysmal wall that are relevant to rupture.

Table 1. *Autopsy Cases*

No.	Sex	Age	No. of S. A. H.'s	Interval (days)	Site	BP (Mx)
1	F	55	3	5	IC	190
2	M	44	1	7	A. com.	140
3	M	49	0	—	A. com.	135
4	M	47	1	1	MC	150

Table 2. *Biopsy Cases*

No.	Sex	Age	No. of S. A. H.'s	Interval (days)	Site	BP (Mx)
1	M	46	2	5	A. com.	145
2	M	44	2	1	IC	120
3	M	33	2	1	A. com.	150
4	M	53	1	28	MC	160
5	M	49	2	2	A. com.	135
6	M	52	0	—	MC	150

Material and Methods

The material studied consists of 10 cases of intracranial saccular aneurysms. Four came from autopsy material which was obtained 12–24 hours after death. Table 1 shows the interval from the last SAH to death. In one case there had been no SAH, and the cause of death was kidney insufficiency. The other six cases were operated on, and the aneurysmal wall was obtained at surgery after clipping of the aneurysm. Table 2 shows the interval between the last SAH and surgery. In one operation case the aneurysm had not bled. It was a giant aneurysm of the middle cerebral artery in a patient with temporal lobe epilepsy. Material for optic microscopy was stained with haematoxylineosin, Weighert-Van Gieson, and PAS.

For electron microscopy, specimens were fixed in 1.5% glutaraldehyde with Sorensen buffer, postfixed in 1% osmium tetroxyde, dehydrated in tragded ethanol, and embedded in Epon 812. Thick sections were cut with

the LKB 4800 ultramicrotome using a diamond knife, and stained with toluidine blue. From selected areas ultrathin sections were cut, and were stained with uranyl acetate in alcohol solution and lead citrate. Microphotographs were obtained with a Siemens Elmiskop 1 A electron microscope.

Results

Optic Microscopy

When the aneurysmal sac could be obtained complete, as in autopsy cases, the neck, the lateral wall, and the fundus could be selectively studied. The lateral wall of the aneurysm is thickened and made up mainly by collagenous tissue which is mostly sclerotic and which has few nuclei (Fig. 1). Muscle fibres are rather scanty and, where present, are scattered and interspersed with collagen fibers. The internal elastic lamina at the level of the neck divides into branches that end in the connective tissue (Fig. 2). The wall and fundus of the aneurysm contain only a few isolated elastic fibres. The endothelium is everywhere well preserved, and is sometimes hypertrophic. The intima is thick in the vicinity of the aneurysmal neck (Fig. 3), where atheromatus material is frequently present.

Vasa vasorum and satellite vessels often contain athero-sclerotic plaques with disturbance of the internal elastic lamina and partial occlusion of the lumen (Fig. 4). The wall of the only autopsy aneurysm that had not bled shows less severe sclerosis of the muscle coat and absence of occlusion of vasa vasorum.

The characteristics of biopsied aneurysms are similar, but only limited examinations of the walls of these could be carried out.

Electron Microscopy

The endothelium of the aneurysm has an irregular surface. It appears partly degenerated near the point of rupture of the wall, and on its internal surface there is heterogenous necrotic material mixed with red cells (Fig. 5). The thickness of this degenerated material is greater at the fundus than on the lateral walls of the aneurysmal sac. Intracytoplasmic vacuoles, empty, or full of dense material, probably lipidic, are seen in the endothelial cells. The endothelium is adherent, usually without interposed elastic fibres, to the external layer, which is made up of mainly collagenous fibres of normal structure (Fig. 6). Fragments of internal elastic lamina were seen at the fundus only in the bipsy case that had not bled. We have never seen granular fragmentation of elastic fibres, as described by Nystrom (1963), in autopsy material, since in our cases the elastic lamina had completely disappeared. Within the

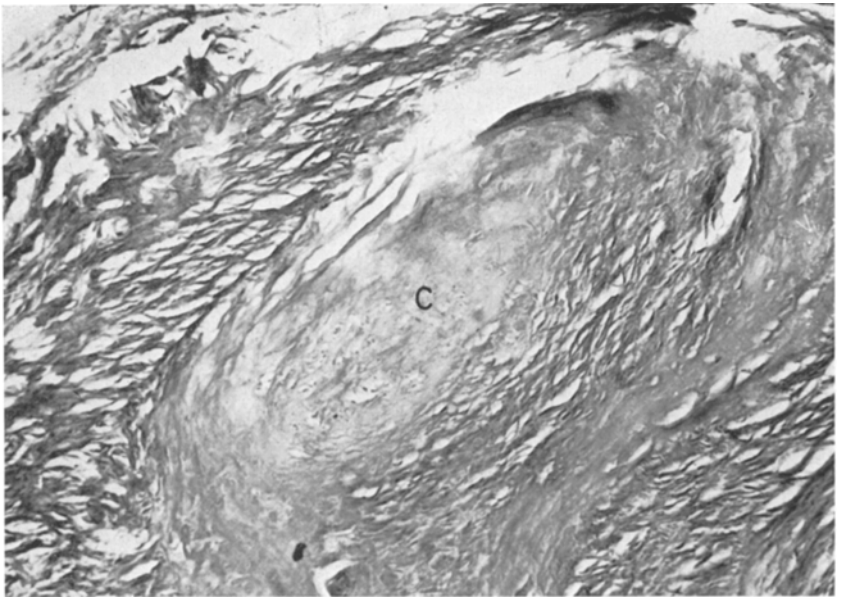

Fig. 1. Aneurysmal wall: (*C*) collagenous tissue, mostly sclerotic and with few nuclei ($\times 340$)

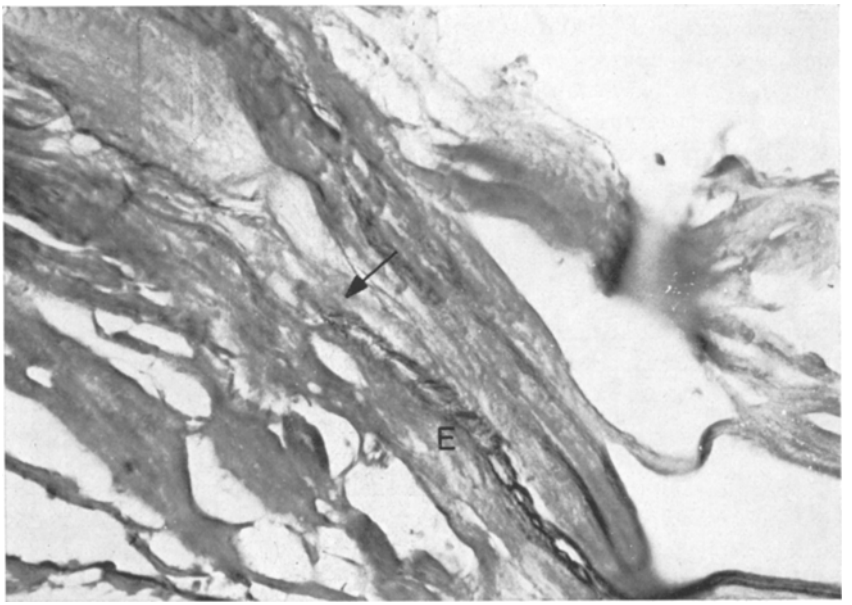

Fig. 2. Aneurysmal neck: (*E*) internal elastic lamina, which divides into many branches that end in connective tissue (arrow). Weighert-Van Gieson staining ($\times 480$)

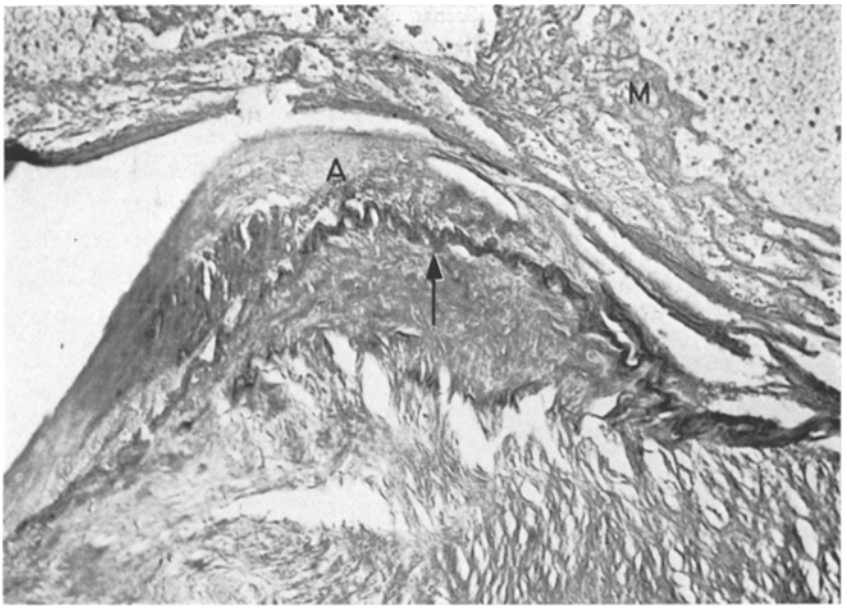

Fig. 3. Aneurysmal neck: (*A*) Thickening of the internal layer. (*M*) Sanguineous material in the lumen. Arrow shows the internal elastic lamina stained black. Weighert-Van Gieson staining (×340)

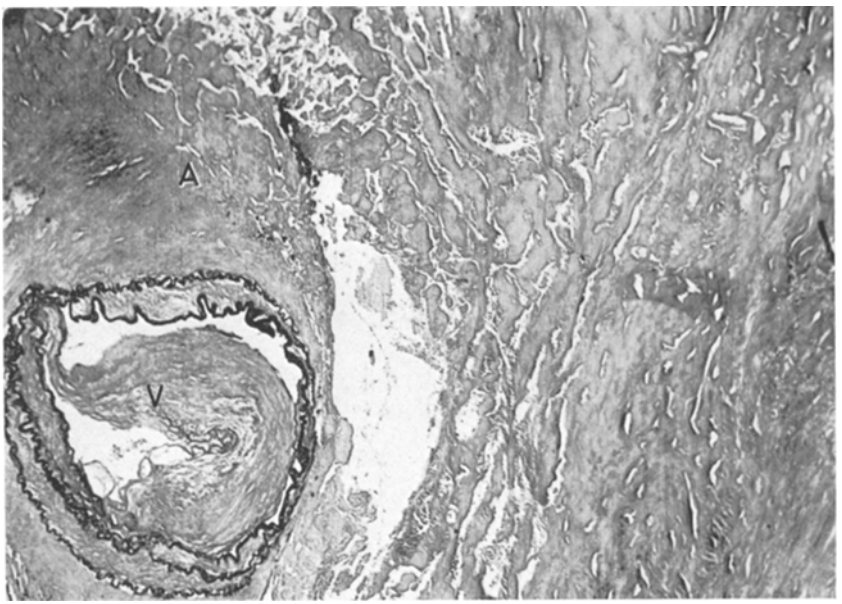

Fig. 4. Aneurysmal adventitia: (*V*) Satellite vessel with disarrangement of the internal elastic lamina and partial occlusion of the lumen (×340)

connective tissue some fibroblast-like cells, well preserved and with star-like prolongations, were seen (Fig. 7). In one case these were directly in contact with the aneurysm cavity where its wall had ruptured. The rare muscular fibres were stretched and torn, and were intermingled with abundant collagenous tissue (Fig. 8). The cytoplasm of these muscular fibres contained swollen mitochondria and dilated endoplasmic

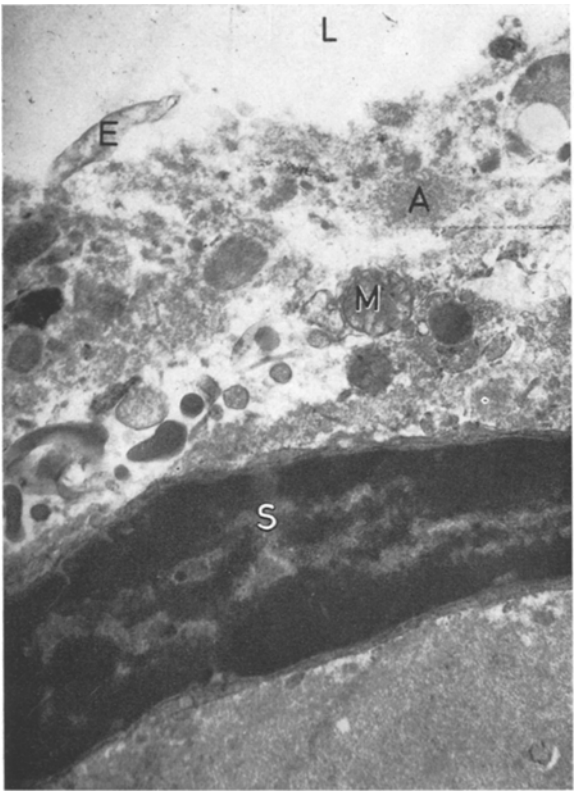

Fig. 5. Aneurysmal wall: (*L*) Lumen. (*A*) Necrotic material on the internal surface. (*E*) Endothelial fragment. (*M*) Swollen mitochondria. (*S*) Subendothelial cell without features of smooth muscle cell ($\times$ 8,000)

reticulum. Within the walls of aneurysms that had bled, particularly the recent ones, free red cells were seen (Fig. 9). The adventitia contained numerous vasa vasorum, whose endothelium was thickened and disrupted. Within the vasa vasorum was amorphic, probably thrombotic, material.

In the only biopsy case that had not bled, the structure of the vasa vasorum was normal, without occlusions.

Discussion

The existence of aneurysms of the circle of Willis has been known since 1761 (Morgagni). However, the mechanism of their formation is still uncertain.

The incidence of cerebral aneurysms in the newborn is rare. Below the age of 20 years it is less than 5% in large series of autopsy material, while above this age the frequency increases considerably (Carmichael 1950, Stehbens 1963). The fact that cerebral aneurysms do not occur

Fig. 6. Aneurysmal wall: The muscle coat is completely lacking and replaced by collagen (*C*). Arrow shows collagen cut longitudinally (×8,000)

in infancy, however, does not exclude the possible occurrence of congenital factors contributory to the development of such vascular malformations. Forbus (1930) emphasises the fundamental importance of original defects in the muscle coats of arteries, especially at the bifurcations. Nystrom (1963) assigns an important role to those factors that produce fragmentation and disappearance of the internal elastic lamina of cerebral arteries, and describes vessels that have ultrastructural aspects of the foetal type, with the internal elastic lamina discontinuous, immature, and thus less resistant. Padget (1944) supposes that cerebral aneurysms originate from the remains of embryonic vessels that have not completely disappeared (*i.e.* the artery of the corpus callosum in

relation to anterior communicating artery aneurysms). Lang (1966) and Stehbens (1973) maintain, on the contrary, the hypothesis that aneurysms originate from a degenerative process, and they bring numerous data, both histological and ultrastructural to support this. The first stage of this degeneration is represented by dysruption of the elastic

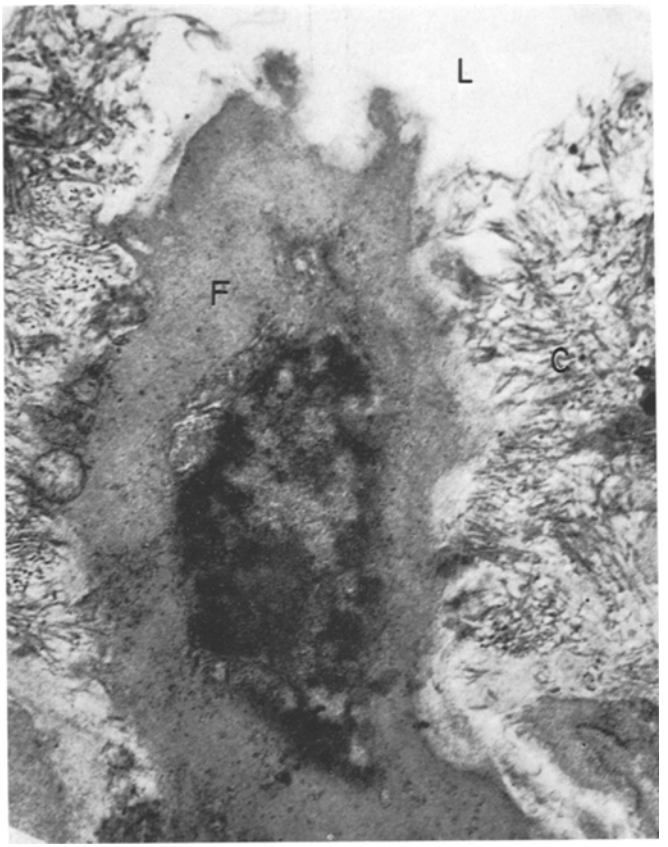

Fig. 7. Aneurysmal wall: (*L*) Lumen, (*F*) fibroblast-like cell in contact with the aneurysm cavity. (*C*) Collagen (× 8,000)

layer, followed by secondary deposition of thickened membranes at the subendothelial site. The alteration of the internal elastic lamina reduces the resistance of the arterial wall to pressure waves, while the thickened membranes endanger the vitality of the aneurysm wall. In fact, alterations in the aneurysm wall most likely play an important contributory part in spontaneous rupture. It is a common observation

that rupture occurs at the distal extremity of the aneurysm, probably because of factors caused by the peculiar heamodynamics within and because of the poor nourishment of this part of the malformation (Frugoni 1958). While the haemodynamic factors have been extensively studied clinically and experimentally (Fry 1968, Fergusson 1972), little

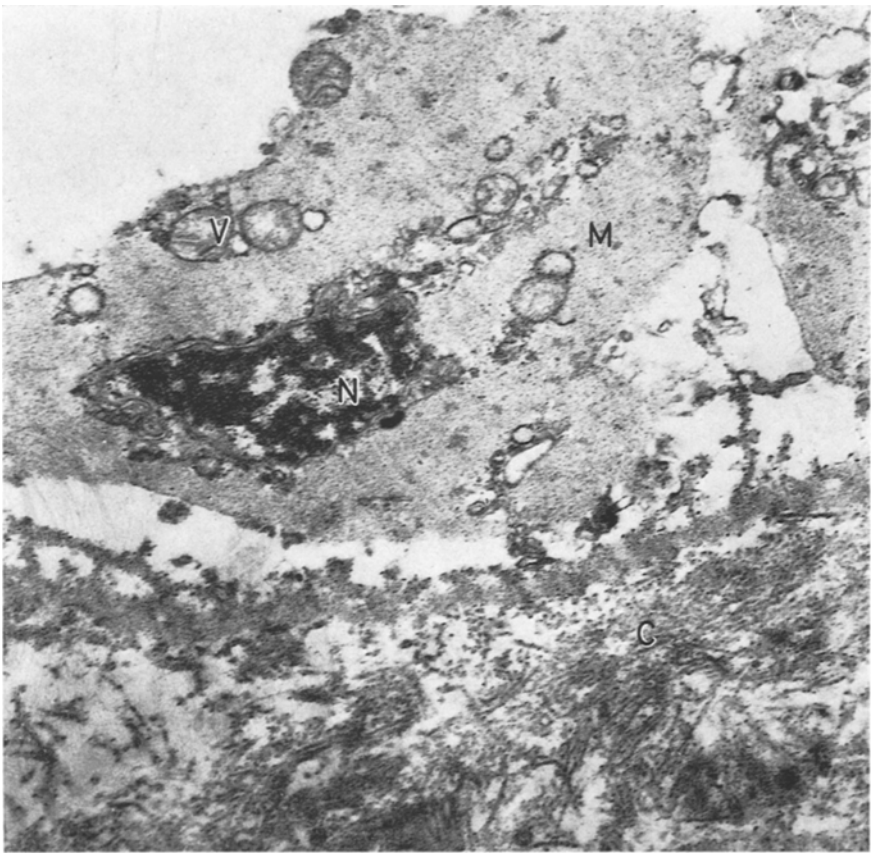

Fig. 8. Aneurysmal wall: (*M*) Smooth muscle cell. (*C*) Collagen. (*V*) Mitochondria. (*N*) nucleus. The cytoplasm contains swollen mitochondria (× 8,000)

has been done to demonstrate the presence of specific structural alteration of the aneurysm wall.

This study shows a correlation between the histological and ultrastructural pictures, and also the similarity between autopsy and biopsy material. The most significant findings of this pathological study are the following:

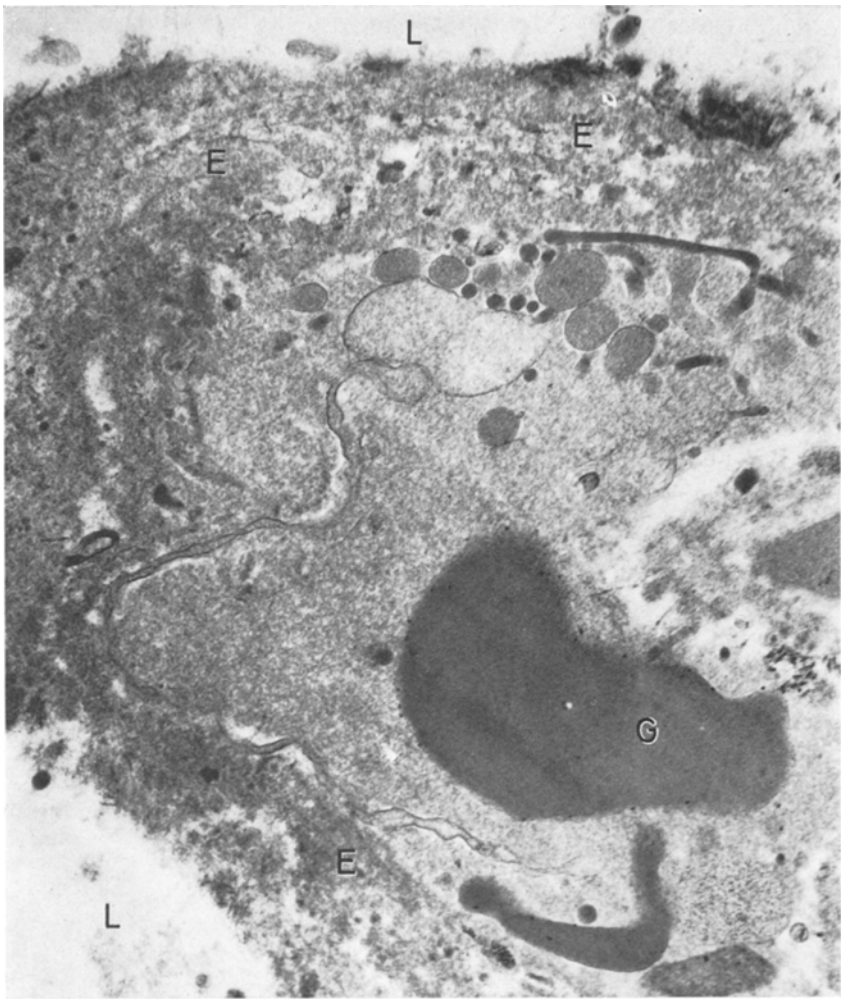

Fig. 9. Aneurysmal wall: (*G*) Red cells enclosed within aneurysmal wall near the lumen. (*E*) Degenerated material on the hypertrophic endothelium ($\times$ 8,000)

a) The endothelium is thin along the wall of the aneurysm, while it is thicker at the neck, with evident degenerative atheromatous appearances.

b) The almost complete disappearance of the internal elastic lamina at level of the neck, with scattered remains in only one case at the fundus.

c) The muscle layer is represented only by connective tissue, rich in collagen, with intermingled scarce muscle fibres.

d) Typical alterations of satellite vessels and vasa vasorum, show disruption of the internal elastic lamina and partial luminal occlusion.

It was possible to observe significant structural differences between aneurysms that had bled and those that had not bled. The non-ruptured aneurysms (two cases) had less severe alterations in the muscle coat and the vasa vasorum, which implied a better degree of resistance of the wall. Aneurysms that had bled once or more had red cells enclosed in the walls as a consequence of the bleeding. There were typical reparative fibroblasts with star-like appearances and production of collagen.

We have never observed the pre-collagenous material, as described by Nystrom (1963), that is an embryonic residue that favours the hypothesis of a congenital origin of saccular aneurysms. The ages of our patients between 33 and 55 years, do not correspond with significant differences in the structure of the wall. No difference was observed in the only hypertensive case, as compared with normotensive cases.

In conclusion, the alterations observed are similar to those typical of atherosclerosis and are, most likely, provoked by the blood streams inside the aneurysms. Our observations, however, neither exclude nor demonstrate congenital alterations of the vessels the importance of which it is impossible to evaluate. Congenital factors in ruptured aneurysms, though important, appear less so than do degenerative alterations, in our opinion. The splitting or rupture of an aneurysm seems to depend on the progressive alteration of its wall, which becomes more sclerotic and less resistant to blood pressure within. Detailed autopsy studies of the circle of Willis have demonstrated a high incidence of congenital alterations (defects of the muscle coat and of the internal elastic lamina) in subjects that have not developed cerebral aneurysms. The topographic distribution of such alterations is different from that of cerebral aneurysms (Lang 1965, Stehbens 1973). On the other hand we must also consider that arteriosclerotic degenerative processes are routine autopsy findings without being associated with aneurysms.

A saccular aneurysm is something different and more complex than a simple degenerative alteration in a vessel. We cannot relate it to a malformation of the arterial wall or to a sclerotic degeneration. The aetiological mechanism of aneurysm formation is still matter of conjecture. However, the hypothesis of a congenital lesion of the vessel seems most likely. Supporting evidence is found, for example, in the correlation between the site of aneurysm and the anatomy of the anterior communicating artery complex (Yaşargil 1975). Also, the arteriosclerotic process is strictly localized to the aneurysm sac, while parent vessels are usually spared. It can be suggested that at the preferential sites of aneurysms there may be more marked alterations of the arterial wall than those found scattered elsewhere in the arterial system by Stehbens

(1963). Also at these sites progressive sclerotic alterations would be associated. Both malformations and degenerative lesions cause aneurysms and lead to their eventual rupture. We have studied the final chances when sclerotic processes prevail, and the congenital malformation is no longer detectable.

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