Observations on the Pathology of Saccular Aneurysms

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Embryology

Very little has been added to the classical descriptions of the circle of Willis by Padget '44, '48. The circle of Willis is recognizable in a ventral view of the brain at an ovulation age of 52 ± 1 days. “Like vascular development elsewhere, that of the head arteries is characterized by a gradual dwindling or elimination of certain vessels, originally prominent, which serve temporary needs, paralleled by the elaboration of others.”

Bassett '49 indicated that as early as the 3 mm. stage in the development of the fetus, vascular channels are well defined as such. They contain primitive nucleated erythrocytes. A single endothelial layer forms the walls of the vessels. “Vascularization occurs in response to metabolic demands from centers of proliferation. Early the primordial endothelial channels give rise to innumerable buds forming a plexiform germinal circulatory bed. This gradually differentiates into efferent and afferent structures forming a fine capillary mantle. Cleavage of vessel layers for skull, dura and brain next occurs, beginning in the basilar regions with multiple intricate anastomoses followed by adaptation to developmental alterations in form, size and rate of growth of the brain.”

Evolution to the various components such as artery, vein, capillary and sinus types represents the final step in development, according to Bassett '49. Not until mural structure is well developed are the arteries physiologically and anatomically fixed as such, since there is much shifting about of arterial channels in young embryos. Realignment has progressed to identifiable anterior and posterior portions of the circle of Willis by the 9 mm. stage (4 weeks).

Large Arteries of the Base of the Brain

The subject of the large arteries of the circle of Willis has been reviewed in detail by Baker and Iannone '59, and the dimensions and dynamics by Murray '64. There are certain differences between the cerebral arteries and those of other portions of the body. In general, the cerebral arteries have a much thinner intima and media and a much more conspicuous internal elastic lamina than equivalent-sized vessels in other parts of the body. External to the media is a thin, loose adventitial layer. The adventitia and the intima apparently contribute very little to the strength of the vessel wall (Hassler '61).

The media is often thin or absent at bifurcations. These medial defects can be demonstrated with regularity in carefully-prepared specimens. As long as the elastic layer remains intact the medial defect is tolerated, and apparently nothing unusual takes place.

Variations in the Circle of Willis

Wilson et al. '54 in a study of 143 autopsyed cases reported that an anomalous formation of the circle of Willis was noted in 118 of the 124 cases in which a complete description was available. Essentially, the anomalous formation resulted from hypoplasia of one or more of the component vessels, persistence of an embryonic stem of origin, or a combination of these factors. No absolute correlation of aneurysms of a particular location with specific anomalous formation was found although 85 per cent of the 40 aneurysms of the anterior communicating artery were associated with hypoplasia of the first portion of one anterior cerebral, and the great majority of the aneurysms present lay in locations where circulation would be influenced by focal increase of resistance or altered field of supply.

Alpers et al. '59 reported comprehensively on the anatomical structure and variations in the circle of Willis. Eight hundred and thirty-seven brains were examined. Three hundred and fifty were selected for their survey. “Normal” circles of Willis were found in 52.3 per cent. The most striking anomaly was a filiform or string-like caliber of one of the component vessels in 27.5 per cent of the

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circles. This most frequently involved one or both posterior communicating arteries.

Alpers and Berry '63 reported that a comparative study of the circle of Willis in 91 cases of cerebral aneurysm revealed a high incidence of anomalies involving the posterior communicating arteries, the embryonic derivation of the posterior cerebral artery, and absent arteries.

Riggs and Rupp '63 reported that the configuration of the circle of Willis generally considered "typical" was found in only 192 of 994 cases (21 per cent) while "deformity" of the circle occurred in 802, or 79 per cent. Such structural defects would generally result in greater restriction of collateral flow than in the circle of Willis with the "typical" configuration.

Because of the possible importance of this area in the overall consideration of cerebrovascular disease, Pallie and Samarasinghe '62 have attempted to quantitate the various components of the circle of Willis.

Theories of Formation of Saccular Aneurysms

Hassler '61 reviewed the many theories of the etiology of intracranial arterial aneurysms. At the present time the etiological factors center around two causes, or combinations:

1. The concept of congenital defects. This theory was suggested by Eppinger, 1887 who indicated that certain aneurysms occurred at the site of defects of the elastic layer of arteries, and that these breaches were inborn or congenital defects. He did, however, mention complicating degenerative or atheromatous processes in some instances. It remained for Forbus '30 to elaborate the concept of medial defects. Forbus believed that the intima bulged into the weak medial defect and that the elastica then underwent degeneration secondary to the strain produced by overdistention. Glynn '40, however, was unable to demonstrate evidence of bulging of the medial defect under a greatly increased pressure.

Forster and Alpers '45 stated that their observations conformed with the prevailing opinion that the defect in the media was congenital in type, and that the changes in the elastic membrane varied widely and were independent of degenerative changes elsewhere. These authors felt that the changes in the elastica were secondary to the formation of the aneurysm and minute classification on the basis of a variable anatomical feature did not seem warranted.

Bremer '43 favored the concept of an embryological defect as the cause of intracranial aneurysms by virtue of persistence of remnants of the embryonic vascular system. Bassett '49 also favored the idea that congenital aneurysms probably exist as unresolved vestiges of a primitively normal circulatory system. He stated that, "This primitive system has erred in its response to the evolutionary stimulus of resorption or modification for the pattern of normality as seen in the embryologically mature organism."

2. The concept of postnatal changes in the arterial wall. Progressive fragmentation of the elastic layer was described in detail by Hackel '28. He described the internal elastic lamella as one of exceptional thickness and consisting, during the first two years of life, of a poorly stained middle layer with heavily stained borders. With increasing age there is a tendency for the inner layer to become raised. The space between it and the main lamella becomes occupied by collagen and fine elastic fibrils. During infancy this splitting and increase of elastic tissue is slight, is confined to the larger of the cerebral vessels and is most marked at points of branching and bifurcation. In older subjects these changes become exaggerated and begin to appear in the smaller vessels, but, as in the larger vessels, the condition is always more marked at the points of branching and bifurcation. These intimal hyperplasias are said to be independent of atheromatous degeneration. No fat is demonstrable within them by the usual staining methods.

Glynn '40 called attention to the fact that true saccular aneurysms of noninflammatory origin occurred more frequently upon the cerebral vessels than upon any other of the muscular arteries. He found medial defects in 80 per cent of the bifurcations examined. He proved that the unsupported elastic elements of the vessel wall could normally withstand pressures of 600 mm. Hg, without bulging. Glynn '40 concluded that, "the medial defect did not constitute a locus minoris resistentiae and could play no part as
such in the development of an aneurysm." Schmidt '30 insisted on the importance of atheroma in the etiology of cerebral aneurysms. Strauss, et al. '32 concluded that arteriosclerosis of the cerebral vessels was the commonest pathological condition responsible for aneurysm formation irrespective of the age of the patient.

Recently, Rubinstein and Cohen '64 reported an instance of Ehlers-Danlos syndrome in association with multiple intracranial aneurysms and suggested that aneurysms can, at least in part, be attributed to the generalized mesodermal abnormality in this condition, namely a defective collage-
nous support surrounding the blood vessels.

(3) Combination of the two factors listed above. Carmichael '45 reported developmental defects in the muscular coat in 27 of the 40 sets of cerebral vessels examined. He indicated that where the muscular coat was deficient the intima was lightly fused with the adventitia, but neither the inner nor outer coat showed any constant deviation from its normal structure. In most of the specimens the intima showed one or more patches of fibro-elastic hyperplasia, formed by the splitting of the elastic membrane into several layers separated by a small amount of collagen. Carmichael '45 concluded that circumscribed areas of complete deficiency in the muscular coats of the larger cere-
bral arteries were of frequent occurrence and might be due to defective development, to degeneration and fibrosis of the media or to the effects of advanced atheroma. Similar lesions in the internal elastic lamina might result from focal erosion or from atheromatous degeneration.

Carmichael '50 indicated that the results of a histological study of 13 small aneurysms showed that they all owed their origin to the combined effects of developmental deficiency and arterial degeneration. The aneu-
rysms always arose at the site of substantial breaches in the muscular and elastic coats and these coats were breached in different ways. The gap in the muscular layer was usually a focus of medial aplasia, which might be substantially enlarged by superimposed degenerative changes; but the de-
fect was sometimes an area of hypoplasia in which the underdeveloped media had been destroyed by primary degeneration and fi-
brosis. So far as this medial layer was concerned, developmental deficiency was the dominant factor, and degeneration played only a subordinate part. Yet, the gap in the elastic membrane was due to degenerative changes alone, chiefly to implication of the membrane in an ordinary atheromatous pro-
cess, although other types of focal degeneration might help to widen the breach. The precise combination of lesions varied greatly from case to case, but both developmental and degenerative factors were concerned in the genesis of all these aneurysms and no valid distinction could be made between the so-called congenital (i.e., developmental) and arteriosclerotic types.

Walker and Allègre '54 raised the ques-
tion as to whether the intimal proliferations which involved the elastic layers secondarily were early evidence of arteriosclerosis, of some other disease of the vessel wall or a reaction to the lesion. They concluded that the existence of atheromatous lesions at the site of the aneurysm in a very high percent-
age of saccular and fusiform aneurysms could be regarded as evidence for the view that such lesions play an important role in the pathogenesis of aneurysm. They indicated that the current concepts of the congenital origin of cerebral aneurysms may be recon-
ced with the thesis that degenerative vas-
cular changes precipitate the vascular dilata-
tion.

Crawford '59 indicated that the three main factors, developmental faults in the media, atherosclerosis and hypertension played roles of varying importance according to the age at which the aneurysms de-
velop.

Experimental Production of Aneurysms

White et al. '61 reported on a method previously used in the production of aneurysmal dilatation of the aorta in dogs by McCune and associates '53 and concluded that it was feasible to produce experimental lesions in the intracranial arteries in dogs, resembling congenital berry aneurysms, by the injec-
tion of noxious agents into the walls of these vessels.

Black and German '60 grafted an excised segment of external jugular vein, closed at one end, about an opening in the common carotid artery of the dog. This method was
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previously described by German and Black '54. Twenty-one experimental "berry aneurysms" were observed for clotting and continued patency. The characteristics of the orifice were found to have a definite relation to the quantity and velocity of blood flowing into and out of the sac. Within the aneurysmal chamber the velocity is inversely proportional to the volume. Thus, the larger the volume in proportion to the orifice, the more sluggish will be the flow and the longer the blood will remain in the chamber. It is likely that these factors favor intra-aneurysmal clotting.

Aneurysms in Animals

According to Walton '56 subarachnoid hemorrhage is a very rare condition in animals. He stated there was no evidence that congenital defects in the media occur in the cerebral arteries of animals, but few detailed pathological observations have been made.

Köppen '27 mentioned one aneurysm in a colt, Ask-Upmark and Ingvar '50 described one in a llama, and Hassler '61 reported one in a cow. Stenhens '63 reported in detail the findings of a ruptured aneurysm of the circle of Willis of a chimpanzee.

Hassler '63 reported on the effects of carotid ligation in rabbits. Following carotid ligation exceptionally large defects of the media were found, especially at the anterior end of the basilar artery, but also at the distal end of the junction between the internal carotid and the posterior communicating arteries on both sides. Six of the large defects found in these rabbits showed a considerable bulging of the arterial wall and a defective internal elastic lamina, as in a saccular aneurysm.

Experimental Flow Studies

Discussion of the flow of fluids through tubes can be found in the publication of Forbus '30. He concluded that the point of maximum pressure always corresponded to the point in the vessel wall where the longitudinal axis of the impinging column intersected the vessel wall. Furthermore, the difference between the pressure at different points increased as the velocity of the stream increased, and as the size of the angle of bifurcation increased. Where the differences between pressure at any given points were very small (1 or 0.5 cm. water), side currents or eddies might cause a reversal of the expected relationship.

Rodbard '59 indicated that the energy of a stream is divided into two complementary forces: (1) the pressure distending the wall, and (2) the forward motion or velocity. When there is no flow, the entire energy is manifest as pressure and the wall is fully distended in accordance with the elastic properties of the vessel. When flow begins, some of the energy becomes manifest as velocity. The pressure on the wall is reduced thereby, and the vessel is less distended. As the velocity increases, the distending pressure falls rapidly. Rodbard '59 indicated that it is not generally appreciated that the pressure acting on the wall of a blood vessel will differ strikingly at immediately adjacent sites. Thus, the compressive force at one site in a vessel might be very high, while a much lower pressure may be in evidence nearby.

Hassler '61 constructed models made of grooves in plexiglass plates, and lined them with silicone rubber. Water was then made to flow through models representing various types of bifurcations. Hassler stated, "As is obvious from the results obtained from the experiments with models, pits were formed regularly at those sites which are assumed to correspond to media defects at the points of branching of arteries. The formation of cushions occurred at those sites which are thought to correspond to intima cushions. The results seem to indicate that media defects occur at the points of greatest strain of the arterial wall. The results tend to agree with the assumption that media defects and intima cushions are the products of a passive remodelling of the arterial wall caused by the flowing blood. The results do not seem to lend much foundation to the assumption of Rotter et al. '55 that intima cushions have an active function as blood flow regulators. Nevertheless, the predilection for atheromatosis which these authors believe to exist at the cushions agrees with my findings."

Further Studies

Stenhens '59 reported on the subject of medial defects in the cerebral arteries and indicated that the adventitia extends through the media but comes into contact with the internal elastic lamina at only a very
narrow zone. The defects are thus wedge-shaped, with the apex touching the elastica. The medial defect is occupied by adventitia in which the collagen fibers tend to run longitudinally along the distal sides of the branches. He summarized by stating that medial defects at sites of arterial branching are of common occurrence in man and have been seen in other mammals. In the cerebral arteries of man the defects increase in frequency with age, and cannot, therefore, be regarded as entirely congenital developmental errors. Their anatomical distribution is not similar to that of aneurysms. Their cause is unknown. According to Stehbens '59 the defects may be dependent on a mechanical factor. He indicated that there is no evidence to support the contention that the medial defects are areas of weakness. Furthermore, he stated that such defects play no direct part in the development of intracranial aneurysms.

Brolin and Hassler '58 indicated that the presence of small aneurysms is often overlooked, and this factor will influence reports on their incidence. They immersed various circles of Willis in 2 per cent solution of potassium hydroxide for three weeks. This process of digestion removed most of the muscular and collagenous components, leaving the elastic tissue. The vessels were then washed in water and placed in glycerin. By means of a slit lamp, optical sections of the transparent arterial walls were produced and examined by a stereoscopic microscope. The vessels presenting aneurysms could then be embedded and stained in the usual fashion. By this technique they were able to find four small aneurysms, overlooked on macroscopic examination, in a series of vessels from the cerebral arterial circle from 35 human brains.

Hassler '61 published a monograph on the subject of the morphological studies on the larger cerebral arteries with reference to the etiology of subarachnoid hemorrhage. He indicated that a number of authors have expressed suspicions about the existence of small aneurysms, the presence of which is overlooked clinically and at post-mortem examination. He found 29 small aneurysms in 25 individuals among a "normal" series of 140. This was an incidence of 17 per cent. In a later publication Hassler '65 reiterated that minute aneurysms with a diameter of 2 mm. or less were found to occur in about 17 per cent of the subjects in routine autopsy material. All but two were situated in or very near the distal carina between two branches, the part of the presumed congenitally weak junction between the main trunk and the branch that probably is most exposed to hemodynamic stress.

Hassler '61 studied 15 major-sized aneurysms taken from a series of 250 brains. All aneurysms were situated at the distal carina (the arterial fork between two major branches). He found eight instances of ectasia or diffuse dilatations. He reviewed the subjects of medial defects, intimal cushions, Reuterwell's tears with connective tissue healing and total rupture of the internal elastic layer, other elastic tissue defects, and intravascular bridges.

Stehbens '63 indicated that funnel-shaped dilatations, areas of thinning, and small evaginations probably represented the early stages of aneurysm formation. They were associated with severe degenerative changes in the internal elastic lamina, which was usually deficient in the area of thinning or evagination. The area of thinning or evagination sometimes appeared to affect the medial defect and sometimes the neighboring distal wall of the daughter branch. The defects appeared to be involved in, rather than to have caused, the thinning or evagination. These early changes appeared to be intimately related to degenerative changes, particularly of the elastic tissue, usually occurring about the fork.

Nyström '63 studied the material from seven patients with arterial aneurysms by electron microscopy. Defects of the medial layers and splitting of the elastic lamina were frequent. The elastic lamina generally was fragmented and had lost its normal fibrillar structure. At the sites of the rupture of the aneurysmal sac the elastica was totally lacking. In the walls of some aneurysms the elastica was thickened and its fine structure differed from the normal elastica. The elastica was partly granulated and very electron-dense in relation to what generally might be observed in a normal elastic layer. This unusual elastica occurred especially in the
neighborhood of the ruptures, and consisted of a mass of irregular particles which were electron-dense at their margins and varied from 500 Å to 0.5 μ in diameter.

Hassler '61 reported on histochemical study of the arterial elastic lamella at the edge of intracranial berry aneurysms. He used a micromethod for elastase digestion of the elastin and applied such technique to the pathologically changed elastic lamella at the margin of cerebral aneurysms. The elastase had no effect on the fine, pathological granulation which stained deep black with resorcin-fuchsin or aldehyde-fuchsin, and dark brown with orcein. The elastic lamella in an aneurysm was divided into two or more thin lamellae. The elastin of the various lamellae showed a marked difference in solubility in dilute elastase solutions.

Stehbens '60 indicated that the earliest possible stage of the lesion of atherosclerosis has not yet been carefully defined. Intimal thickenings were found in relation to the sites of branching of the arterial tree. Elastic tissue alterations at branchings were detected before the appearance of intimal proliferation. The changes in the elastic lamina consisted of loss in the depth and uniformity of staining. If the elastic tissue changes are degenerative, it followed that even at an early stage there was some damaging factor in operation.

Most of the present controversy, therefore, revolves around the degenerative changes in the internal elastic lamella. Whether the changes in this layer should be considered a part of the atherosclerotic process is still somewhat in doubt. Moon '57 reported the results of his examinations of coronary arteries in fetuses, infants and juveniles. He found rupture and fragmentation of the internal elastic membrane in newborn infants. This process was associated with a deposition of acid mucopolysaccharide, fibroblastic proliferation, and occasionally, endothelial proliferation. Moon noted that the absence of the later phases of hyalinization of plaques, accumulation of large amounts of lipid and calcification is noteworthy in young individuals.

More recently, experimental data presented by Friedman '63 would suggest that the initial factor in atherosclerosis is a de-
rangement and fragmentation of discrete segments of the internal elastic lamina. Friedman indicated that the initial disintegration of internal elastic laminae initiated or intensified the multiplication of foam cells, the accumulation of which was observed to coincide with the earliest visible plaque.

Initial proliferations in the brain vessels were studied in detail by Rotter et al. '55. These proliferations were described as consisting of elastic fibers and muscle, usually of the mixed elastic-muscular type. As factors in the localization of bifurcation cushions, thickness of the wall, mechanical stresses and the functional activity of the wall of the vessel would have to be considered. Rotter et al. indicated that all three of these components operated primarily at the bifurcation, and that this explained the predisposition of bifurcation cushions for the development of arteriosclerosis. These authors indicated that sclerosis of cushions corresponded to the initial phase of cerebral sclerosis. However, the more severe forms of cerebral sclerosis were not limited to the cushions.

Hassler and Saltzman '59 studied the histologic changes in infundibular widening of the posterior communicating artery. Seven specimens formed the basis of their report, and pathologic changes were found in five. These lesions consisted mainly of long defects in the muscular media embracing in some instances the entire wall in the widened area. In most of the specimens the wall was much thinner than normal and consisted of connective tissue of the intima and adventitia type. The internal elastic lamina was entirely absent in one instance; here the vessel wall had the characteristic appearance of arterial aneurysm. In the other four cases the internal elastic lamina was split up into lamellae. In two cases with funnel-shaped widening of the infundibulum no pathologic changes were observed in the vessels. Fox et al. '64 reviewed the subject and noted the difficulties in differentiating aneurysm from infundibulum of the posterior communicating artery.

The following section represents the results of studies of normal bifurcations and bifurcation defects by the author.
Aneurysm Study

Bifurcations of Arteries of Circle of Willis; Defects and Aneurysms

Meticulous preparation and staining of sections are necessary for the demonstration of satisfactory bifurcations and for study of the details of the structure of saccular aneurysms. In general, celloidin sections are preferable to paraffin sections, because the latter are much more likely to fragment. Various staining methods can be utilized, but the hematoxylin and eosin, Weigert’s elastic stain and Masson’s trichrome stains yield very satisfactory results. Adjacent sections can be stained alternately.

Fig. 1. Schematic diagram of the bifurcation of a vessel of circle of Willis. A. Apex of fork. D. Distal side of branches. P. Proximal side of branches. L. A. Lateral angle. (Modified, after Stehbens.)

Fig. 2. Bifurcation of artery of circle of Willis, showing a typical medial defect (arrows). The adventitia and intima are in loose approximation at A, the apex of the fork. The elastic layer is preserved. (Weigert’s elastic stain.)

Fig. 3. A representative lateral angle defect, showing defective media underneath an intimal cushion. The lumen of the vessel is to the left. The medial gap extends from M to M’, and the cushion is at C. This is an area in which saccular aneurysms do not develop. (Masson’s trichrome stain.)
The material to be presented here was accumulated from 50 saccular aneurysms and 130 bifurcations, mostly from adults, many of whom had one or more saccular aneurysms of the circle of Willis.

Briefly, the normal arteries of the circle of Willis consist of a thinly dispersed adventitial layer; a media which is practically or completely devoid of elastic fibers; and an intima consisting of an elastic lamella and a thin collagenous layer with an endothelial lining. At the apex of the fork of bifurcations (Fig. 1) one often finds the media absent or thin, so that the adventitia and intima are in approximation (Figs. 2 and 21). These medial defects occur with such regularity that they can scarcely be considered abnormal. Yet, they have been the source of much discussion, since medial gaps have been considered areas of weakness and the possible sites of aneurysmal formation. The area devoid of media may be a conspicuous one, yet no aneurysm is in evidence in the majority of instances. When this area was bridged by an intact elastic membrane, no bulge was found. Medial defects at the lateral angles can be found with regularity, particularly beneath zones of intimal pro-

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Fig. 4. Minimal zone of intimal thickening at the apex of a fork. (Masson's trichrome stain.)
Fig. 5. Matching section corresponding to Fig. 4. (Weigert's elastic stain.)
Fig. 6. Well-developed intimal cushion. (Masson's trichrome stain.)
Fig. 7. Matching section corresponding to Fig. 6. (Weigert's elastic stain.)
liferations or cushions, but aneurysms rarely, if ever, appear in these zones (Figs. 3 and 22).

The subject of intimal thickenings, cushions or pads is an important one, because these projections can be found uniformly at the lateral angles of forks and to a lesser degree at the apex of forks in specimens which contain saccular aneurysms. These tufts have been studied extensively. They
have been found in infancy. One of the most consistent changes is fragmentation of the elastic layer together with an increase in the collagenous elements (Figs. 4 to 7, inclusive). Accumulations of macrophages and cholesterol can be found occasionally, particularly in older subjects (Figs. 8 and 9). Presumably these intimal cushions are the sites of focal degeneration of the vessel wall, and may be representative of atherosclerosis.

**SMALL OUTPOUCHINGS**

These form an interesting group of lesions because they may be the precursors of saccu-
Fig. 14. Bifurcation defect of elastica (arrow) apparently circumventing an intimal cushion. (Wiegert's elastic stain.)
Fig. 15. Small area of hyperplasia of intima at the point of the bulge (arrow). This is made up mostly of collagenous tissue and frayed elastica. (Masson's trichrome stain.)
Fig. 16. Elastic defect and more fully developed outpouching at bifurcation (arrow). The elastic layer appears to terminate rather abruptly as it enters the defect. (Weigert's elastic stain.)
Fig. 17. Small unruptured aneurysm of anterior cerebral-anterior communicating junction (arrow).
Fig. 18. Small unruptured aneurysm. The elastica can be traced into the defect but becomes very fragmented. The aneurysm wall is made up chiefly of collagenous tissue. It should be noted that diseased elastica is also proximal to the "neck" of the aneurysm (arrows). (Weigert's elastic stain.)
Fig. 19. Unruptured infundibular aneurysm (arrows). I. C. Internal carotid artery. P. C. Posterior communicating artery. (Weigert's elastic stain.)
Fig. 20. Enlargement of abrupt change in elastic layer is aneurysm shown in Fig. 18. A few elastic fibers can be seen in the thin-walled sac to the right. (Weigert's elastic stain.)
lar aneurysms. Some of the earliest protrusions can be demonstrated as small outpouchings of the elastic layer through defects in the media (Figs. 10, 23 and 24). At times the indentation appears to present at right angles to the wall from which it arises (Fig. 11). There can be little doubt that the elastic layer has undergone conspicuous fragmentation at this point (Fig. 12). Sometimes the defect assumes a bifid appearance (Fig. 13). Occasionally a bulging in the elastica appears to circumvent an intimal tuft at the fork (Fig. 14). Without exception, hyperplastic changes can be demonstrated in the zone beneath the elastic defect (Fig. 15). One might assume logically that as the process of fragmentation of the elastic layer continues, the defect will tend to widen and a full-blown saccular aneurysm may form. However, from the examination of the small defects one cannot predict which are destined to expand further.

LARGER OUTPOUCHINGS

The transitional zone from vessel wall to aneurysm is readily identified. The media usually breaks sharply, although in some instances it may taper gradually. The elastic layer becomes progressively more fragmented as it enters the sac (Fig. 16). Rarely filamentous strands of elastic tissue can be followed throughout the entire aneurysm, but in most instances the fibrils are either absent or stain so poorly as to be seen only with difficulty. The wall of the aneurysm consists for the most part of collagenous tissue, continuous with the adventitia and intima. In some instances a few round cells or polymorphonuclear leukocytes can be seen in the wall of the aneurysm. Fibroblasts and fibrocytes can be seen in abundance. Here and there one finds macrophages.

Despite prominent sacculcation an aneurysm may not rupture (Fig. 17). In some instances there appears to be a reparative process sufficient to protect the dome of the aneurysm (Fig. 18), the point at which rupture usually takes place. There is considerable variability in this respect. In many instances the dome of the aneurysm will become very attenuated, and eventually rupture will take place.

It should be pointed out that in the usual case, the "neck" of the aneurysm is also composed of diseased tissue, in the form of a fragmented elastic lamella. The connective tissue comprising the wall of the aneurysm at this point may (Fig. 25) or may not (Fig. 26) be attenuated.

LARGE ANEURYSMS

It is not the purpose of this study to review in detail the changes in the large aneurysms because there are many excellent publications in this field. The large aneurysms show apparent progression of the defects demonstrated previously. The media usually ends abruptly at the neck of the aneurysm. The elastic layer ceases to exist, for practical purposes. Occasionally a few fine fibrils can be found in the aneurysm proper.

The wall of the aneurysm usually consists of a variable-thickness layer of connective tissue fibers, usually continuous with the adventitia and intima. A few chronic inflammatory cells can usually be seen within the wall of the aneurysm. The larger (and probably older) sacs consist of dense hyaline fibrous tissue often containing flecks of calcium.

INFUNDIBULAR DILATATIONS

These are referred to as funnel-shaped dilatations or infundibular dilatations, and are found most frequently at the junction of the internal carotid and posterior communicating arteries. They are unusual in that they consist of a wide gap between the edges of the media. Bridging the gap is a very thin wall consisting mainly of connective tissue and elastic tissue. Absence or severe fragmentation of the elastic lamella would classify the defect as an arterial aneurysm. However, only one of our specimens fulfills the criteria of an aneurysmal dilatation. The elastic layer is very fragmentary throughout the extent of the dilatation (Figs. 19 and 20).

CONCLUSIONS

Much more needs to be learned about bifurcation defects before definitive statements can be made concerning the cause of saccular aneurysms. In all probability, the defects in the media which are observed with such regularity at the apex of bifurcations, while contributory, are not the major etiologic factors in such aneurysms. Further-
Fig. 21. Bifurcation of artery of circle of Willis, showing typical medial defect. There are minimal changes in the intima and elastica at the apex of the fork. (Masson's trichrome stain.)

Fig. 22. Representative lateral angle defect of the media. An intimal cushion is demonstrated. (Masson's trichrome stain.)

Fig. 23. Tiny outpouching at apex of bifurcation. This might be considered an incipient aneurysm. (Masson's trichrome stain.)

Fig. 24. Small outpouching through medial defect at bifurcation. (Masson's trichrome stain.)

Fig. 25. Unruptured bifurcation aneurysm. There is considerable proliferation of connective tissue in the dome of the aneurysm, but a portion of the “neck,” to the right, is attenuated.

Fig. 26. Unruptured bifurcation aneurysm. The “neck” is made up of connective tissue, for the most part.
more, definite medial defects can be found at lateral angles, where aneurysms do not develop.

The changes in the elastic lamella are particularly striking, even in the smallest identifiable outpouchings. Such protrusions do not appear to take place directly through intimal cushions.

The theory that peculiar hemodynamic factors affect bifurcations in such a way as to exert unusual stress on certain apical regions while providing for the proliferation of intimal pads in a proximal location, is a plausible one, and should be investigated further.

The possible role of atherosclerosis, though undoubtedly of secondary importance, is still not clearly defined. Until the early changes of atherosclerosis are more clearly delineated, other possible causes should be sought.