ANEURYSMS

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This book is dedicated to Margaret, Jane, and Frances.

Preface

Aneurysmal surgery is demanding upon the surgeon for appropriate, safe, perioperative and operative decision making. The purpose of this book is to provide the surgical resident and practicing vascular surgeon a ready reference on the vicissitudes of aneurysmal surgery. The problems in timing and techniques of surgery are unique. The authors hope they have produced a most useful resource for the sophisticated practicing clinician.

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Contents

CHAPTER 1

Pathophysiology of Aneurysm Formation

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Arterial aneurysms are local, irreversible dilatations, outpouchings, or swellings of arterial walls which result in abnormal vessel configurations, alterations in blood flow, and a tendency toward thrombosis and/or rupture. The formation of an aneurysm in a previously normal vessel implies that the arterial wall, at some point in time, was no longer able to maintain its normal configuration or integrity. In more precise terms, the mechanical stress imposed upon the media exceeded its resistance to deformation, disruption, or rupture. In principle, this situation may be due to an abnormal increase in mechanical stress, reduced resistance of the arterial wall to deformation or disruption, or a combination of these influences. Increases in blood pressure or pulse pressure, changes in heart rate or lumen diameter, alterations in branch angles and curvatures, and vibrations distal to critical stenoses may all be associated with long-term increases in medial tensile *stress* (i.e., the tension per unit cross-section of the vessel wall). Reduced medial perfusion, interference with medial cellular metabolism, reduction in medial cellularity, and modifications of matrix composition or mural architecture may all be associated with abnormal increases in medial *strain* (i.e., the deformation associated with a given level of imposed stress). Although there is good evidence to suggest that hemodynamic forces or mechanical displacements may impose greatly increased stresses on arterial walls and result in long-term modifications of vessel wall composition and mechanical properties, most of the findings to date indicate that primary metabolic or structural defects of the media or alterations associated with intimal changes (i.e., atherosclerosis) probably underlie most arterial ectasias and aneurysms. Altered hemodynamic states may, nevertheless, play a significant role. Defects consistent with the preservation of normal arterial wall dimensions and continuity at physiologic levels of medial stress may be sufficiently severe to result in ectasias, aneurysms, and, ultimately, ruptures, when tensile stress is abnormally elevated.

A good deal has been learned in recent years concerning the relationship of structure to function in arterial walls. The aortic media, in particular, has received close attention and data have been forthcoming which indicate that the human abdominal aorta may be especially vulnerable to modifications leading to aneurysmal formation. Findings

relating the pathologic anatomy of aortic aneurysms to intimal changes, which may have repercussions on medial nutrition and metabolism and predispose to thrombus formation, have also been forthcoming. In addition, experimental data that tend to link medial disruption and atrophy directly to hyperlipidemia, rather than to atherosclerotic plaque deposition alone, provide new directions for investigating the pathogenesis and natural history of aneurysmal formation. This chapter reviews the relevant features of arterial functional microarchitecture and indicates, from these and other data, the factors which probably underlie the pathogenesis and natural history of the various forms of aneurysmal disease.

MICROARCHITECTURE OF THE AORTIC WALL

The aortic media is a highly organized, mechanically efficient structure consisting of uniform, alternating layers of cells and matrix fibers. On transverse sections of excised and immersion-fixed samples, the fibrous layers appear to contain more or less continuous elastic fiber sheets that appear as wavy lamellae. The cells in such preparations appear to be arrayed obliquely between successive fiber layers and seem to connect the elastic lamellae; in addition, collagen fibers, although abundant, do not appear to be organized in any consistent manner. If, however, aortas are fixed while distended at increasing intraluminal pressures, a somewhat different picture emerges (46). As vessel diameter increases and wall thickness decreases, the wavy elastin lamellae straighten and cells become aligned, not radially, but increasingly in directions that coincide with the curvature of the vessel wall. In transverse sections of straight segments of the aorta, fixed while distended at physiologic distending pressures, this orientation results in the establishment of continuous layers of overlapping cells lying more or less parallel to the straightened elastic lamellae (8). Meanwhile, collagen fibers are also straightened and drawn taut. There is an abrupt decrease in vessel distensibility at diastolic pressure. Further increases in diameter or decreases in wall thickness are minimal as pressures are raised beyond systolic levels. Thus, during the non-physiologic phase of redistention by pressures ranging from zero to diastolic levels, the relatively large changes in aortic radius and wall thickness merely reflect the restoration of cells and fibers to their normal configurations and orientations. The recoiled elastic fiber lamellae are unbending and stretching, and the collagen fibers are becoming aligned and taut. When diastolic pressures are attained, the taut, inextensible collagen fibers resist further extension until the aorta ruptures when the pressure reaches several times the normal level. Thus, the aorta, functioning physiologically at pressures ranging between diastolic and systolic levels, is normally nearly maximally distended. The relatively high elastic modulus of the media at its normal diameter protects the aorta against excessive dilatation at elevated pressures, while the close association and parallel arrangement of elastin and collagen fibers confer a combination of resiliency and tensile strength. Rapid changes in medial stress tend to be distributed uniformly through the compact wall, for elastic fibers are

focally shared between adjacent groups of cells within the cell layers and the successive elastic fiber layers are also connected. Medial flaws and defects, therefore, tend *not* to be propagated by the normal range of changes in direction or magnitude of medial stresses, and chances of spontaneous rupture are minimal despite the medial irregularities and disruptions that occur with age.

Tensile Stresses and Medial Structure and Composition

The layers that comprise the aortic media of mammals are of similar thickness and architecture, regardless of species, and the number of layers in the aortic media corresponds closely to the tensile stress normally imposed upon it (47). Thus, for adult mammals, there is a nearly linear relationship between aortic radius at mean blood pressure and the number of its transmedial fibrocellular layers. Since, according to the law of Laplace, the tangential tension imposed on the wall of an aorta is a function of its radius and its distending pressure, and mean pressures are similar for most mammals, the average tension per layer would be expected to be nearly constant and independent of species. Estimates made from a study of several species (47) reveal that each increment of 0.017 mm in aortic radius with increasing species size requires an additional fibrocellular layer. The average tension per aortic layer is about 2,000 dynes/cm.

Although the relationship between radius and the number of medial layers appears to be independent of species or location, the relative proportions of elastin and collagen in the aortic media change with distance from the heart. The thoracic aorta normally contains a greater proportion of elastin than collagen, while the abdominal aorta contains more collagen than elastin (9). Yet, the total scleroprotein concentration (i.e., the sum of the collagen and elastin) does not change with distance from the heart. It has also been demonstrated that the anatomic position along the aorta, at which relative proportions of elastin and collagen reverse, differs from species to species, but is consistent for a given species. It would, therefore, appear that the establishment of the fibrocellular layers and total accumulation of fibrous protein in the aortic media are normally governed by the prevailing tensile stress (3). The relative proportions of elastin and collagen at particular locations may be related to other factors, such as the rate of attenuation of the cyclic tensile stresses associated with cardiac output and hemodynamic modifications. The latter, elastin and collagen levels, results from the steady decrease in cross-section as the major branches occur (33).

Although not as prominent as in the aorta, layers can also be enumerated in the walls of the systemic arteries and the pulmonary artery trunk when these are fully distended (12). Thereafter, a close relationship is once more evident between total estimated medial tension and the number of layers, and the tension per layer is nearly constant for homologous mammalian arteries. Both the total tension and average tension per layer are, however, smaller for branch vessels than for the

aorta and correspond to the lower content or fibrous protein compared to smooth muscle in vessels. These vessels may also be expected to undergo considerable changes in diameter in response to neuroendocrine stimulation and changes in peripheral resistance, and during retraction and contraction after injury. Although the static mechanical properties of the aorta outlined above can be demonstrated in vessels devoid of viable smooth muscle, this cannot be assumed to be true of peripheral arteries.

Cohesion and Coordination of Media Structure

In order for an arterial wall to function as a coordinated unit and maintain its integrity in the presence of the varying tensile stresses associated with pressure changes, pulsatile wall motion, and vessel flexion, matrix elements and cells must be closely associated and coordinated. Attachments among the structural components must be sufficiently supple and tenacious to prevent shearing and slippage, which could result in excessive distensibility, aneurysmal dilatation, or rupture. There are at least three modes of interconnection of structural elements in the media (8). Within aortic cell layers, cells are segregated into small groups within which the cells are similarly oriented. Each group is surrounded by a continuous sheath of basal lamina. Running over and into the basal lamina and investing individual cell groups are sheets of interlacing collagen fibrils. Any pull tending to separate the overlapping cells changes the orientation of the surrounding interlacing basketwork of collagen fibrils so that these tighten about the cells, in the fashion of a Chinese finger trap, holding the cell group together and preventing further stretching and slippage. Each cell group is associated with a system of surrounding elastic fibers oriented in the same direction as the cells. Strong focal attachment sites between peripheral dense bodies of the smooth muscle cells and the adjacent elastic fibers form a second mode of bonding. The tenacity of these cell-to-elastin attachment complexes is apparently greater than the cohesiveness of the cell body. Sudden experimental hyperdistention results in focal disruption of cell projections, but preservation of the cell-to-elastin attachments to which they extend. Large collagen fiber bundles are wedged between adjacent elastic fibers and all of the medial structures are embedded in a ubiquitous, fine, and continuous microfibrillar matrix which provides a third means of stress transmission and coordination. Widespread disruption of any of these attachment systems could result in functional inadequacy of the media and yielding, sufficient to form aneurysms.

The structural materials in the walls of major systemic arteries are, in general, organized in a manner similar to that found in the aorta. With the decrease in structural matrix fiber content, however, the prominence of the discrete cell groupings becomes more evident and the component cells in each group are arranged in parallel, which suggests that each group represents a functional subdivision. Preliminary observations reveal that these units are arranged along presumed lines of stress within

the arterial media and the size and orientation of each unit appear to correspond to the directional changes in tension, which correspond to modifications in medial geometry (7). The associated elaboration of collagen and elastin fibers would seem, at least in part, to be governed by the magnitude and distribution of the mechanical stresses on the smooth muscle cell groups.

Adaptive Response of the Media

During early growth, as aortic distending pressures and radii increase from fetal to normal adult levels, collagen and elastin accumulations per medial cell increase in proportion to the increase in medial tension. Comparisons between the pulmonary artery trunk and ascending aorta during growth reveal that this adaptation occurs as the diameters of these vessels increase to a comparable degree, while pressure rises in the aorta and falls in the pulmonary circuit (23). The vessels, nearly identical in wall thickness and morphology at birth, subsequently diverge markedly in thickness, medial architecture, and scleroprotein content in keeping with their developing differences in mechanical stress. Experimental hypertension also results in increased cross-sectional area of the aortic media, due to cell proliferation and accumulation of collagen and elastin, and in proportion to the increased medial tension, although the relative proportions of the two fibrous proteins and the number of medial layers are not altered (44). These data suggest that some ideal level of stress (i.e., force per unit cross-sectional area) is maintained by elaboration of suitable quantities of matrix fibers in a fixed proportion. Although this adaptive potential may persist to some degree when maturation is complete, changes related to growth and hypertension may be due to different mechanisms (45). Once established, however, the number of medial layers appears to be fixed. Whether the greater tension per layer which must then prevail places the hypertensive aorta at some functional disadvantage remains to be investigated. In general, elastin turnover differs in rate from collagen turnover and elastic fibers are known to fix lipids and become calcified (23). There is also experimental evidence that cells obtained from thoracic aortic media proliferate more readily in culture than cells derived from abdominal aorta (25). The consequences of these differences with regard to aortic medial adaptability to mechanical stress or to the tendency to develop aneurysms have not been explored, but merit detailed investigation.

Nutrition of the Media

Maintenance of arterial medial microarchitecture, including the growth and continuing differentiation of its cellular functional units and the elaboration, degradation, and accumulation of suitable proportions of matrix fibers by medial smooth muscle cells, would be expected to depend upon the availability of adequate medial nutrition. Thus, information concerning the manner in which tensile stress and medial architecture are related to medial perfusion and its possible limits could provide

insights into the train of events which may cause an arterial wall to fail mechanically. The aortic media is normally nourished by diffusion from the endothelial surface and by vasa vasorum, which penetrate into the media from the adventitial side. Diffusion from the lumen is apparently sufficient to nourish the inner 0.5 mm of medial thickness. This zone contains no vasa vasorum and encompasses about 30 medial fibrocellular layers (48). Species large enough to have an aortic media composed of more than 30 layers have aortic medial vasa vasorum beyond the 30th aortic layer. Thus, aortas of small mammals (e.g., rats, rabbits, and small breeds of dogs) have fewer than 30 medial layers and are mainly dependent upon perfusion from the intima, while aortas of large mammals (e.g., pigs, sheep, and large breeds of dogs) have more than 30 medial layers and have medial vasa vasorum beyond the inner avascular zone of 30 layers. The distinction between avascular and vascular aortic medias is apparently already drawn at birth, for animals which are destined to have more than 30 aortic medial layers as adults have more than 30 layers at birth and medial vasa are already present (43). Those aortas which have fewer than 30 layers at birth will not exceed 30 layers at full maturity and do not contain medial vasa at birth.

Two additional features are associated with the presence of medial vasa vasorum. First, although the average tension per aortic medial layer is about 2,000 dynes/cm for mammals, the average tension per medial layer for aortas which contain medial vasa tends to be higher than the mean value, which suggests that the presence of medial vasa somehow permits medial layers to function at a higher level of medial stress (50). The second feature is that in very large mammals (e.g., horses and cattle) the avascular inner zone consistently maintains its orderly lamellar arrangement, while the outer vascularized zone may deviate somewhat from the usual architecture as the animal increases in size during growth (49). Elastic fibers become less evident as smooth muscle cells form increasingly prominent bands, suggesting that functional departures from the usual layered architecture, possibly necessary to tether very large and long aortas, may be dependent upon the presence of medial vasa.

Ectasia and Tortuosity

The considerations outlined above suggest that arterial walls are admirably designed to preserve their dimensions and integrity under normal circumstances and to withstand both sudden and long-term variations in tensile stress. Nevertheless, the aorta, as well as several other major systemic arteries, tend to dilate, elongate, and become less supple with age and to undergo deformations with potentially serious clinical consequences. These changes are probably due to metabolic modifications of medial cells and associated alterations in the concentration, mechanical properties, and organization of the matrix components (4, 16, 21, 24, 27). Although frequently associated with atherosclerosis, the precise nature of the corresponding mechanical changes remains to be defined. Abnormal enlargements of vessels usually include increases in both diameter

and length, so that curvatures and configurations are altered and vessels tend to become not only dilated but also tortuous or bowed. With increasing diameters and the establishment of new convexities and concavities, the distribution of tensions is greatly altered, even if blood pressure levels are not greatly changed. Local stresses may, therefore, be augmented at the same time that the aortic wall is becoming less resilient due to changes in compliance. Instead of small defects being bypassed as the result of a well-coordinated distribution of imposed tensions by the structural fibers, flaws are increasingly likely to be propagated and create disruptions. Healing with fibrosis may become the predominant mode of defense rather than the more subtle and mechanically versatile remodeling response which occurs during growth and under normal conditions. A potential vicious circle is, therefore, probable. Chemical and structural alterations in the fibers and the inability of the aortic cells to keep pace and modulate medial fiber composition result both in dilatation and stiffening of the vessel wall. Dilatation results in altered vessel configuration, including tortuosity, with local increases in tensile stress. Since stresses are no longer redistributed and attenuated effectively, due to the associated changes in mechanical properties of the fibers, dilatation and propagation of flaws and disruptions continue. Equilibrium may be reached when sclerosis of the media results in sufficient inextensibility to enable the wall to bear the increased stress without further dilatation, despite the increased radius of curvature and thinning of the wall. Dilatations, whether diffuse or focal, are, however, often not self-limiting. The fibrous reaction which would tend to strengthen the wall appears to lag behind the increased stress in the media associated with dilatation. Concavities of curvatures and obtuse angles at branch points are the sites at which medial tensile stresses are relatively elevated and walls are normally thickest. Stresses are least at acute angle branch points where the media is correspondingly comparatively thin. Depending upon conditions, both locations may be vulnerable to aneurysmal formation—the former because of markedly elevated tension and the latter in relation to its precariously thin wall.

In the sections that follow, we shall attempt to outline the likely pathogenic mechanisms leading to aneurysmal formation in light of the relationships among cell metabolism, medial structure, and composition and the stresses (acute and chronic) that tend to disrupt and distort the vessel wall. In keeping with this approach, arterial aneurysms can be classified according to three principle modes of development. In the most common type, the arterial wall fails to maintain its normal resistance to deformation by the stresses associated with blood flow and pressure. The wall weakens and stretches to form a segmental fusiform or globular enlargement or a focal saccular outpouching. The aneurysmal wall, though it may be attenuated and fibrotic, is continuous with the wall of the adjacent, uninvolved portion of the vessel. Such a lesion is called a true aneurysm. In a second type, overall arterial wall configuration is maintained, but the cohesion among the layers of the media is severely

compromised. Entry of blood into medial disruptions results in extensive separation of medial layers by a hematoma—this is a *dissecting aneurysm*, or acute aortic dissection. Finally, local aneurysmal swellings and deformations may arise as the result of the establishment of a communication between the bloodstream and a local periarterial sac by way of a transmural defect—these are *pseudoaneurysms*, or false aneurysms, for the swellings are not attributable to a deformation of the arterial wall, but to a localized absence of the arterial wall and containment of the bloodstream by extra-arterial tissues.

TRUE ANEURYSMS

Special Vulnerability of the Atherosclerotic Human Abdominal Aorta

The abdominal aortic segment, below the level of the renal outflow, is particularly prone to the formation of both true aneurysms and atherosclerotic occlusive disease. Aneurysmal dilatation of the abdominal aortic segment rarely occurs in aortas which do not already show evidence of dilatation elsewhere. Thus, the tendency to overall aortic enlargement or deformation is usually present in patients with atherosclerotic aortic aneurysms and suggests the presence of some general underlying metabolic compromise of the aortic wall which may be more severe in the distal aorta than elsewhere. Some tendency to dilatation is, however, a normal feature of aging in our population, suggesting that special, local factors in the abdominal segment of certain individuals may be of great importance in predisposing to the development of aneurysmal disease.

Nutrition of the Media

Although the relationship between the number of medial layers and the depth of penetration of vasa into the aortic media applies to both the thoracic and abdominal aortic segments in most mammals, the human abdominal aorta is a notable exception (50). Midway between the renal arteries and aortic bifurcation, the adult human aortic media is about 0.7 mm in thickness. For mammals, in general, this thickness would be expected to correspond to about 40 medial layers and such an aortic wall would be expected to include an outer vascularized zone of about 10 layers. Instead, the adult human abdominal aorta contains about 29 layers and is devoid of medial vasa vasorum; thus, each layer is thicker than expected and sustains an average tension of about 3,200 dynes/cm. This dissociation is reminiscent of the situation which occurs in animals exposed to experimentally induced hypertension (40, 44), inasmuch as the thickness and cross-sectional area of the media correspond to the total medial tension, but the number of medial layers does not. In addition, the tension per layer is elevated to the level usually noted in aortic medias with medial vasa. The degree to which these discrepancies among medial tension, medial structure, and medial vasa at this level in man corresponds to maladjustments in the relative quantities of cells and fibers to altered cell metabolism, or to greater cell turnover, has not been determined. The findings do, however, suggest that the increased