265e Basic Biology of the Cardiovascular System

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THE BLOOD VESSEL

VASCULAR ULTRASTRUCTURE

Blood vessels participate in homeostasis on a moment-to-moment basis and contribute to the pathophysiology of diseases of virtually every organ system. Hence, an understanding of the fundamentals of vascular biology furnishes a foundation for understanding the normal function of all organ systems and many diseases. The smallest blood vessels—capillaries—consist of a monolayer of endothelial cells apposed to a basement membrane, adjacent to occasional smooth-muscle-like cells known as *pericytes* (Fig. 265e-1*A*). Unlike larger vessels, pericytes do not invest the entire microvessel to form a continuous sheath. Arteries typically have a trilaminar structure (Fig. 265e-1*B–E*). The *intima* consists of a monolayer of endothelial cells continuous with those of the capillaries. The middle layer, or *tunica media*, consists of layers of smooth-muscle cells; in veins, the media can contain just a few layers of smooth-muscle cells (Fig. 265e-1*B*). The outer layer, the *adventitia*, consists of looser extracellular matrix with occasional fibroblasts, mast cells, and nerve terminals. Larger arteries have their own vasculature, the *vasa vasorum*, which nourishes the outer aspects of the tunica media. The adventitia of many veins surpasses the intima in thickness.

The tone of muscular arterioles regulates blood pressure and flow through various arterial beds. These smaller arteries have a relatively thick tunica media in relation to the adventitia (Fig. 265e-1*C*). Medium-size muscular arteries similarly contain a prominent tunica media (Fig. 265e-1*D*); atherosclerosis commonly affects this type of muscular artery. The larger elastic arteries have a much more structured tunica media consisting of concentric bands of smooth-muscle cells, interspersed with strata of elastin-rich extracellular matrix sandwiched between layers of smooth-muscle cells (Fig. 265e-1*E*). Larger arteries have a clearly demarcated internal elastic lamina that forms the barrier between the intima and the media. An external elastic lamina demarcates the media of arteries from the surrounding adventitia.

ORIGIN OF VASCULAR CELLS

The intima in human arteries often contains occasional resident smooth-muscle cells beneath the monolayer of vascular endothelial cells. The embryonic origin of smooth-muscle cells in various types of artery differs. Some upper-body arterial smooth-muscle cells derive from the neural crest, whereas lower-body arteries generally recruit smooth-muscle cells from neighboring mesodermal structures during development. Derivatives of the proepicardial organ, which gives rise to the epicardial layer of the heart, contribute to the vascular smooth-muscle cells of the coronary arteries. Bone marrow–derived endothelial progenitors may aid repair of damaged or aging arteries. In addition, multipotent vascular stem cells resident in vessel walls may give rise to the smooth-muscle cells that accumulate in injured or atheromatous arteries (Chaps. 88, 89e, and 90e).

VASCULAR CELL BIOLOGY

Endothelial Cell The key cell of the vascular intima, the endothelial cell, has manifold functions in health and disease. The endothelium forms the interface between tissues and the blood compartment. It therefore must regulate the entry of molecules and cells into tissues in a selective manner. The ability of endothelial cells to serve as a selectively permeable barrier fails in many vascular disorders, including atherosclerosis, hypertension, and renal disease. This dysregulation of permeability also occurs in pulmonary edema and other situations of "capillary leak."

The endothelium also participates in the local regulation of blood flow and vascular caliber. Endogenous substances produced by endothelial cells such as prostacyclin, endothelium-derived hyperpolarizing factor, nitric oxide (NO), and hydrogen peroxide (H_2O_2) provide tonic vasodilatory stimuli under physiologic conditions in vivo (Table 265e-1). Impaired production or excess catabolism of NO

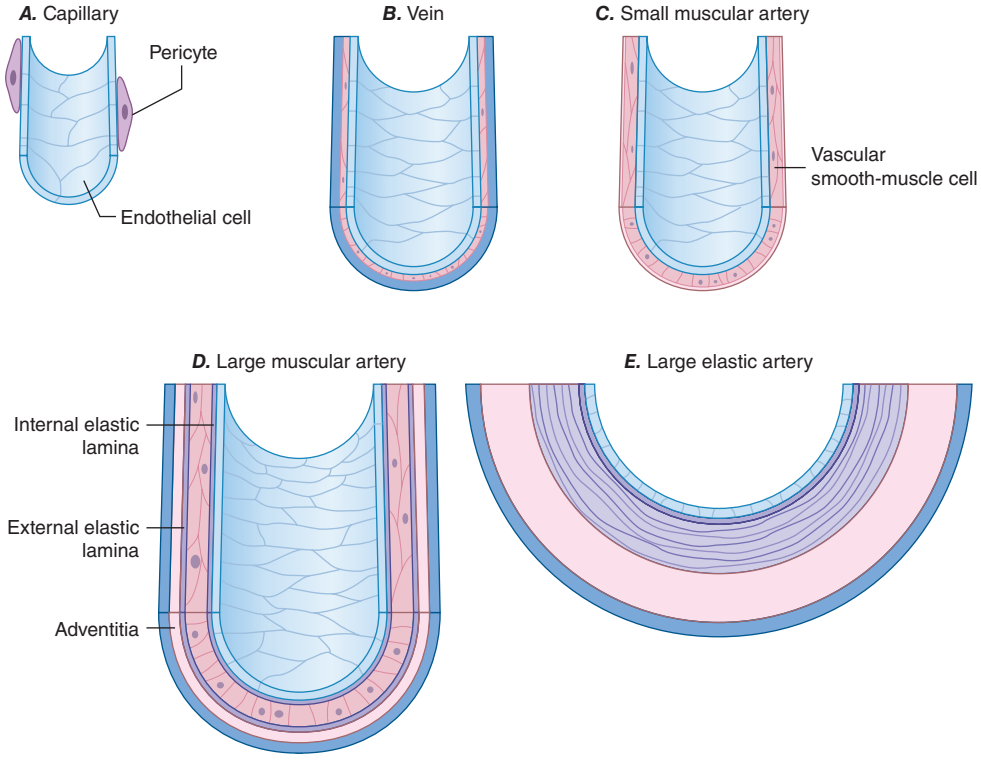

FIGURE 265e-1 **Schematics of the structures of various types of blood vessels.** ***A.*** Capillaries consist of an endothelial tube in contact with a discontinuous population of pericytes. ***B.*** Veins typically have thin medias and thicker adventitias. ***C.*** A small muscular artery features a prominent tunica media. ***D.*** Larger muscular arteries have a prominent media with smooth-muscle cells embedded in a complex extracellular matrix. ***E.*** Larger elastic arteries have cylindrical layers of elastic tissue alternating with concentric rings of smooth-muscle cells.