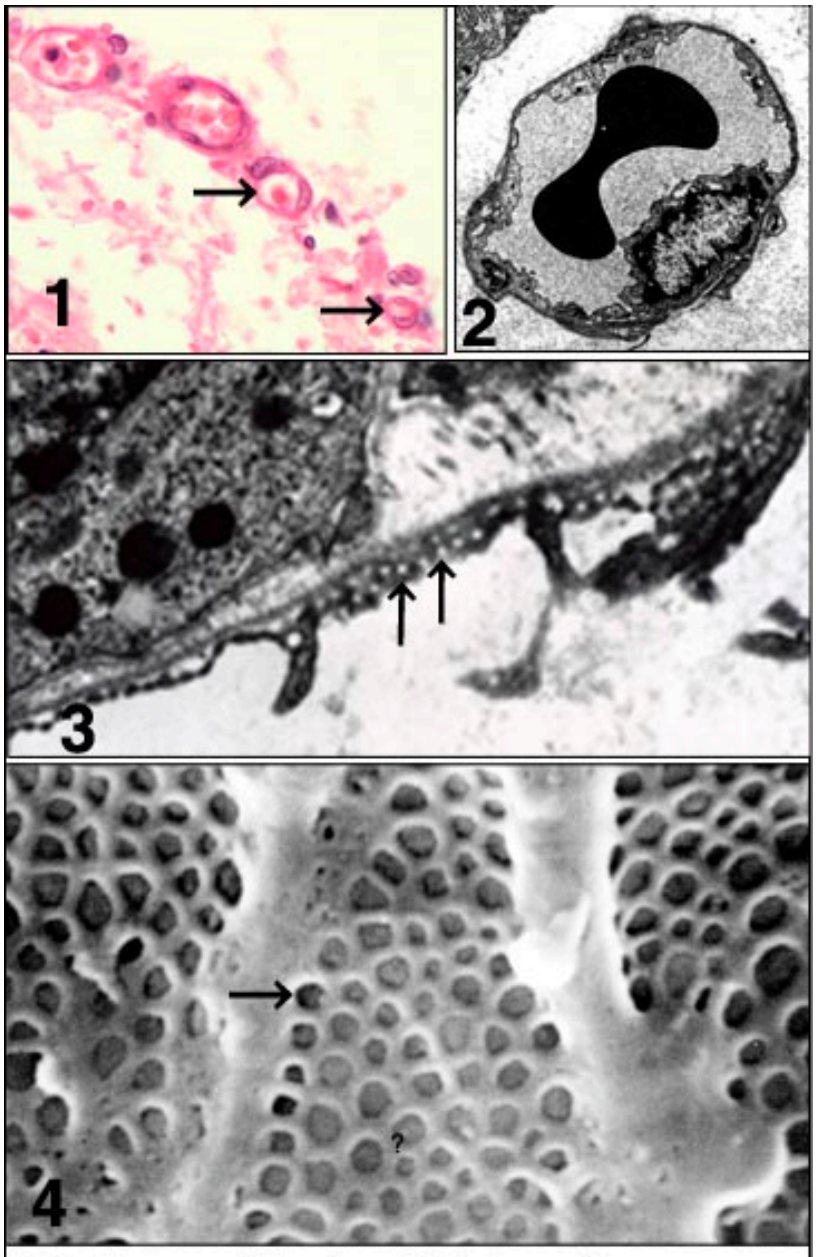
Capillaries



1. Continuous capillaries (arrows) of various caliber.
2. A TEM of a capillary containing a RBC.
3. Fenestrae (arrows) in a tangential section of endothelial cell cytoplasm. TEM
4. Endothelial fenestrae (arrows) as seen from the lumen of a glomerular capillary. (courtesy of P. Andrews)

Capillaries are the smallest functional units of the blood vascular system and are inserted between arterial and venous limbs of the circulation. They branch extensively to form elaborate networks, the extent and type of which reflects the specific organ or tissue with which they are associated. The capillaries associated with some organs are considered tight and function as a barrier between the blood and the organ in question. Others exhibit variable degrees of

“leakiness” and allow materials to pass from the blood into surrounding interstitial tissues. Based on the appearance of the endothelium and the basal lamina in electron micrographs, capillaries are classed as continuous, fenestrated, or as discontinuous. Regardless of the type, the basic structure of capillaries is similar and represents an extreme simplification of the vessel wall. The tunica intima consists of endothelium and a basal lamina; the tunica media is absent and the tunica adventitia is greatly reduced.

Continuous Capillaries

Continuous capillaries are the common type of capillary found throughout the connective tissues, muscle, skin, and central nervous system. Their lumina range from 4 to 10 μm in diameter and in the smaller vessels may be encompassed by a single endothelial cell. In larger capillaries, three or four cells may enclose the lumen. The wall consists of a continuous endothelium and a thin tunica adventitia. The endothelial cells rest on a continuous basal lamina and show the same features as endothelial cells elsewhere in the vascular tree. They contain the usual organelles, caveolae and transcytotic vesicles, a proteoglycan layer covering a few short microvilli on the luminal surfaces, and a variable number of membrane-bound granules. Multivesicular bodies also can be found. Adjacent cells may abut each other or overlap obliquely or show sinuous interdigitations. At intervals, adjacent cell membranes unite in occluding junctions, but it is not certain that these form complete belts as in other epithelia. The tunica adventitia is thin and contains some collagen and elastic fibers embedded in a small amount of ground substance. Fibroblasts, macrophages, and mast cells are present also. Pericytes are irregular, branched, isolated cells that occur at intervals along capillaries, enclosed by the basal lamina of the endothelium. The cells resemble fibroblasts and characteristically contain a few dense bodies and numerous cytoplasmic filaments. Actin and myosin have been demonstrated in the cytoplasm by immunohistochemistry, indicating a contractile function. However, their exact function is unknown.

Fenestrated Capillaries

Fenestrated capillaries have the same structure as the continuous type but differ in that the endothelial cells contain numerous fenestrae (pores) that appear as circular openings 70 to 100 nm in diameter. Fenestrae may be distributed at random or in groups and usually are closed by thin diaphragms that show central, knob like thickenings. Each diaphragm is a single-layered structure thinner than a single-unit membrane - so it would appear unlikely that it is formed by apposition of two cell membranes. The basal lamina is continuous across the fenestrae on the basal side of the endothelium. The fenestrated capillaries of the renal glomerulus differ in that the pores lack diaphragms and the basal lamina is much thicker than in other capillaries. Fenestrated capillaries are generally associated with the kidney, endocrine glands, and the gastrointestinal tract.

Discontinuous capillaries (Sinusoids)

Sinusoids are thin-walled vessels that are much wider and have lumina that are more irregular in outline than those of capillaries. Sinusoids are abundant in the liver, spleen, and bone marrow. Their endothelia are attenuated and may be continuous as in the bone marrow, or the cells may be separated by gaps and rest on a discontinuous basal lamina. Sinusoids often are associated with phagocytes either as a component of the lining, as in the liver, or closely

applied to the exterior of the wall, as in the spleen. The endothelial cells themselves show no greater capacity for phagocytosis than do endothelial cells in other vessels. They do show more active endocytosis and more numerous lysosomes than are found in endothelia elsewhere.

Diffusion

Exchange of nutrients and wastes between tissues and blood occurs across the thin endothelium of capillaries. It has been estimated that no active cell lies more than 30 or 40 μm away from a capillary. The most important way materials cross the endothelium is by diffusion, and the total capillary surface available for exchange has been calculated to be over 100 square meters. Lipid-soluble materials diffuse directly through the endothelial cells; water and water-soluble materials are transmitted by aquaporins, transcytotic vesicles, and fenestrae of fenestrated capillaries.

In the continuous capillaries, caveolae and transcytotic vesicles have been implicated in transepithelial transport of water-soluble materials; pinocytosis also may contribute to transfer of substances of high molecular weight. Subcategories of continuous capillaries found at specific locations are referred to as tight capillaries. The endothelial cells of these capillaries are tightly united by occludens type junctions and the cytoplasm is devoid of caveolae and transcytotic vesicles. The endothelium lining of these capillaries contributes to the blood brain barrier, the blood testis barrier and the blood thymic barrier.

The movement of fluid out of or into capillaries is controlled by pressures within the blood itself and in the surrounding interstitial (connective tissue) compartment. These forces are: capillary hydrostatic pressure, plasma solute osmotic pressure, interstitial hydrostatic pressure and interstitial solute osmotic pressure. If, for example, feeding arterioles dilate the hydrostatic pressure of the capillary blood increases and surpasses the plasma solute osmotic pressure as well as both surrounding interstitial pressures, the movement of fluid will be out of the capillary and into the interstitial tissue. If, on the other hand, arterioles contract thereby reducing the hydrostatic pressure the net effect is to draw fluid into the capillary lumen driven primarily buy the plasma solute osmotic pressure. A similar situation occurs in the distal (venous) portion of the capillary bed as capillaries combine to form venules. Here the plasma solute osmotic pressure is great enough to draw most of the tissue fluid back into the blood except for about 10% which eventually is captured and returned to the blood by the lymphatic system. Albumin, a highly negatively charged protein produced by the liver, plays an essential role in maintaining the oncotic pressure to hold fluid within the vascular system. Fluid exchange also may occur through intercellular clefts between endothelial cells. For example, endothelial cells retract from one another in the presence of histamine. This allows fluid and protein to diffuse out of capillaries into surrounding tissues causing edema. This process is reversible and can occur in minutes.

Endothelial Cell Secretion

Endothelial cells are now known to secrete several substances of the underlying extracellular matrix (types III, IV, and V collagens, fibronectin, laminin), as well as several factors involved with maintenance of vascular tone, blood clotting, and emigration of leukocytes.

Endothelial cells synthesize and release nitric oxide, which causes relaxation of adjacent smooth muscle, thereby decreasing the vascular tone of blood vessels. Nitric oxide is derived from arginine in a reaction catalyzed by nitric oxide synthase to produce nitric oxide and

citrulline. Nitric oxide activates guanylate cyclase in smooth muscle cells causing increased levels of cyclic guanosine monophosphate (cGMP) and vasodilation. The medicinal effects of nitroglycerin and amyl nitrates occurs as a result of the conversion of these compounds to nitric oxide whereas compounds such as Viagra inhibit cGMP phosphodiesterase and thus maintain increased cGMP levels. Endothelial cells also can respond to anoxia by secreting a peptide called endothelin I, a potent vasoconstrictor of long duration that binds to smooth muscle cells of arteries, thereby elevating blood pressure. Endothelial cells at sites of inflammation in response to cytokines are capable of synthesizing and inserting intercellular adhesion molecules into their luminal plasmalemma. These factors bind to circulating leukocytes, allowing them to migrate through the endothelium to the site of inflammation. Endothelial cells also contain prostacyclin, an agent that that causes vasodilation and inhibits platelet adhesion, as well as thrombomodulin and tissue plasminogen activator, which exhibit anticoagulant activity. Under some circumstances endothelial cells can release thromboplastin to promote blood coagulation and other thromboplastic substances such as von Willebrand factor and antihemophilic factor VIII of the blood coagulation system. Von Willebrand factor stored in Weibel-Palade granules of endothelial cells also promotes platelet adhesion to subendothelial collagen at the site of injuries. Thus, endothelial cells also are equipped to initiate clotting and repair minor defects in the lining of vessels to prevent the leakage of blood.