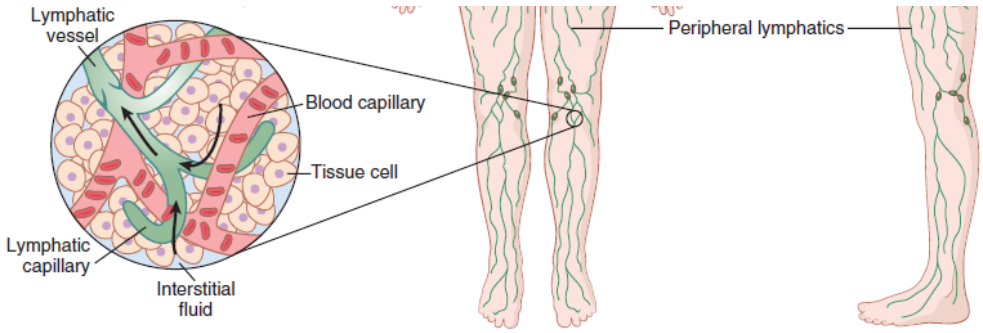
LYMPHATIC SYSTEM

The lymphatic system represents an accessory route through which fluid can flow from the interstitial spaces into the blood. Most important, the lymphatic can carry proteins and large particulate matter away from the tissue spaces, neither of which can be removed by absorption directly into the blood capillaries. This return of proteins to the blood from the interstitial spaces is an essential function without which we would die within about 24 hours.

LYMPH CHANNELS OF THE BODY

Almost all tissues of the body have special lymph channels that drain excess fluid directly from the interstitial spaces. The exceptions include the superficial portions of the skin, the central nervous system, the endomysium of muscles, and the bones. However, even these tissues have minute interstitial channels called *prelymphatics* through which interstitial fluid can flow; this fluid eventually empties either into lymphatic vessels or, in the case of the brain, into the cerebrospinal fluid and then directly back into the blood.

Essentially all the lymph vessels from the lower part of the body eventually empty into the *thoracic duct,* which in turn empties into the blood venous system .



Terminal Lymphatic Capillaries and Their Permeability

Most of the fluid filtering from the *arterial ends* of *blood capillaries* flows among the cells and finally is reabsorbed back into the *venous ends* of the *blood capillaries,* but on average, about one tenth of the fluid

instead enters the *lymphatic capillaries* and returns to the blood through the lymphatic system rather than through the venous capillaries.The total quantity of all this lymph is normally only 2 to 3 liters each day.

The fluid that returns to the circulation by way of the lymphatic is extremely important because substances of high molecular weight, such as proteins, cannot be absorbed from the tissues in any other way, although they can enter the lymphatic capillaries almost unimpeded. The reason for this mechanism is a special structure of the lymphatic capillaries. the endothelial cells of the lymphatic capillary attached by *anchoring filaments* to the surrounding connective tissue. At the junctions of adjacent endothelial cells, the edge of one endothelial cell overlaps the edge of the adjacent cell in such a way that the overlapping edge is free to flap inward, thus forming a minute valve that opens to the interior of the lymphatic capillary. Interstitial fluid, along with its suspended particles, can push the valve open and flow directly into the lymphatic capillary. However, this fluid has difficulty leaving the capillary once it has entered because any backflow closes the flap valve. Thus, the lymphatics have valves at the very tips of the terminal lymphatic capillaries, as well as valves along their larger vessels up to the point where they empty into the blood circulation.

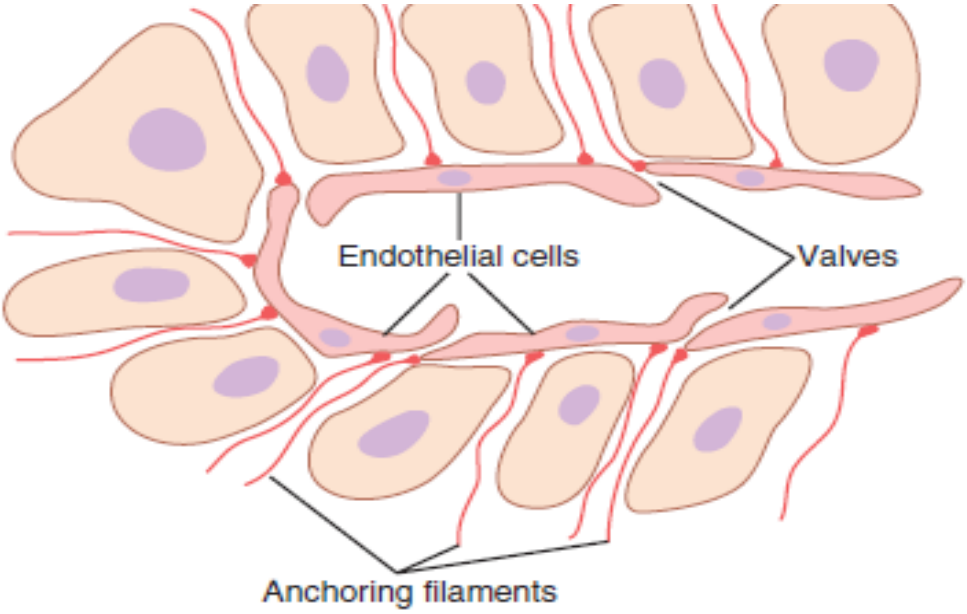


Figure 16-8. Special structure of the lymphatic capillaries that permits passage of substances of high molecular weight into the lymph.

FORMATION OF LYMPH

Lymph is derived from interstitial fluid that flows into the lymphatic. Therefore, lymph as it first enters the terminal lymphatic has almost the same composition as the interstitial fluid. The protein concentration in the interstitial fluid of most tissues averages about 2 g/dl, and the protein concentration of lymph flowing from these tissues is near this value. Lymph formed in the liver has a protein concentration as high as 6 g/dl, and lymph formed in the intestines has a protein concentration as high as 3 to 4 g/dl. Because about two thirds of all lymph normally is derived from the liver and intestines, the thoracic duct lymph, which is a mixture of lymph from all areas of the body, usually has a protein concentration of 3 to 5 g/dl.

The lymphatic system is also one of the major routes for absorption of nutrients from the gastrointestinal tract, especially for absorption of virtually all fats in food. Indeed, after a fatty meal, thoracic duct lymph sometimes contains as much as 1 to 2 percent fat.

Finally, even large particles, such as bacteria, can push their way between the endothelial cells of the lymphatic capillaries and in this way enter the lymph. As the lymph passes through the lymph nodes, these particles are almost entirely removed and destroyed.

CLASSIFICATION OF HYPERTENTION

Hypertension in the Upper Part of the Body Caused by Coarctation of the Aorta. One out of every few thousand babies is born with pathological constriction or blockage of the aorta at a point beyond the aortic arterial branches to the head and arms but proximal to the renal arteries, a condition called *coarctation of the aorta*. When this occurs, blood flow to the lower body is carried by multiple, small collateral arteries in the body wall, with much vascular resistance between the upper aorta and the lower aorta. As a consequence, the arterial pressure in the upper part of the body may be 40 to 50 percent higher than that in the lower body.

Hypertension in Preeclampsia (Toxemia of Pregnancy)

A syndrome called *preeclampsia* (also called *toxemia of pregnancy*) develops in approximately 5 to 10 percent of expectant mothers. One of the manifestations of preeclampsia is hypertension that usually subsides after delivery of the baby. Although the precise causes of preeclampsia are not completely understood, ischemia of the placenta and subsequent release by the placenta of toxic factors are believed to play a role in causing many of the manifestations including hypertension in the mother. Substances released by the ischemic placenta, in turn, cause dysfunction of vascular endothelial cells throughout the body, including the blood vessels of the kidneys. This *endothelial dysfunction decreases release of nitric oxide* and other vasodilator substances, causing vasoconstriction, decreased rate of fluid filtration from the glomeruli into the renal tubules, impaired renal-pressure natriuresis, and the development of hypertension.

Another pathological abnormality that may contribute to hypertension in preeclampsia is thickening of the kidney glomerular membranes (perhaps caused by an autoimmune process), which also reduces the rate of glomerular fluid filtration.

Neurogenic Hypertension

Acute neurogenic hypertension can be caused by strong *stimulation of the sympathetic nervous system.* For instance, when a person becomes excited for any reason or at times during states of anxiety, the sympathetic system becomes excessively stimulated, peripheral vasoconstriction occurs everywhere in the body, and *acute* hypertension ensues.

Genetic causes of hypertension

In humans, several different gene mutations have been identified that can cause hypertension. These forms of hypertension are called *monogenic hypertension* because they are caused by mutation of a single gene. An interesting feature of these genetic disorders is that they all cause excessive salt and water reabsorption by the renal tubules .In some cases the increased reabsorption is due to gene mutations that directly increase transport of sodium or chloride in the renal tubular epithelial cells. In other instances, the gene mutations cause increased synthesis or activity of hormones that stimulate renal tubular salt and water reabsorption. Thus, in all monogenic hypertensive disorders discovered the final common pathway to hypertension appears to be increased salt reabsorption and expansion of extracellular fluid volume. Monogenic hypertension, however, is rare, and all of the known forms together account for less than 1% of human hypertension.

PRIMARY (ESSENTIAL) HYPERTENSION

About 90 to 95 percent of all people who have hypertension are said to have “primary hypertension,” also widely known as “essential hypertension” by many clinicians. These terms mean simply that *the hypertension is of unknown origin,* in contrast to the forms of hypertension that are *secondary* to known causes, such as renal artery stenosis or monogenic forms of hypertension.

In most patients, *excess weight gain* and *a sedentary lifestyle* appear to play a major role in causing hypertension. The majority of patients

with hypertension are overweight, and studies of different populations suggest that excess weight gain and obesity may account for as much as 65 to 75 percent of the risk for developing primary hypertension. Clinical studies have clearly shown the value of weight loss for reducing blood pressure in most patients with hypertension. In fact, clinical guidelines for treating hypertension recommend increased physical activity and weight loss as a first step in treating most patients with hypertension.
The following characteristics of primary hypertension, among others, are caused by excess weight gain and obesity:

1. *Cardiac output is increased* in part because of the additional blood flow required for the extra adipose tissue. However, blood flow in the heart, kidneys, gastrointestinal tract, and skeletal muscle also increases with weight gain because of increased metabolic rate and growth of the organs and tissues in response to their increased metabolic demands. As the hypertension is sustained for many months and years, total peripheral vascular resistance may be increased.

   2. *Sympathetic nerve activity, especially in the kidneys*, *is increased in overweight patients.* The causes of increased sympathetic activity in obese persons are not fully understood, but recent studies suggest that hormones such as *leptin* that are released from fat cells may directly stimulate multiple regions of the hypothalamus, which in turn have an excitatory influence on the vasomotor centers of the brain medulla. There is also evidence for reduced sensitivity of the arterial baroreceptors in buffering increases in blood pressure in obese subjects.

   3. *Angiotensin II and aldosterone levels are increased twofold to threefold in many obese patients.* This increase may be caused partly by increased sympathetic nerve stimulation, which increases renin release by the kidneys and therefore formation of angiotensin II, which in turn stimulates the adrenal gland to secrete aldosterone.

4. *The renal-pressure natriuresis mechanism is impaired, and the kidneys will not excrete adequate amounts of salt and water unless the arterial pressure is high or kidney function is somehow improved.*

in people who have a genetic predisposition to atherosclerosis, who are overweight or obese and have a sedentary lifestyle, or who have high blood pressure and damage to the endothelial cells of the coronary blood vessels, large quantities of cholesterol gradually become deposited beneath the endothelium at many points in arteries throughout the body. Gradually, these areas of deposit are invaded by fibrous tissue and frequently become calcified. The net result is the development of atherosclerotic plaques that actually protrude into the vessel lumens and either block or partially block blood flow. A common site for development of atherosclerotic plaques is the first few centimeters of the major coronary arteries.

Acute Coronary Occlusion

Acute occlusion of a coronary artery most frequently occurs in a person who already has underlying atherosclerotic coronary heart disease but almost never in a person with a normal coronary circulation. Acute occlusion can result from any one of several effects, two of which are the following:

1. The atherosclerotic plaque can cause a local blood clot called a *thrombus* that occludes the artery. The thrombus usually occurs where the arteriosclerotic plaque has broken through the endothelium, thus coming in direct contact with the flowing blood. Because the plaque presents an unsmooth surface, blood platelets adhere to it, fibrin is deposited, and red blood cells become entrapped to form a blood clot that grows until it occludes the vessel. Or, occasionally, the clot breaks away from its attachment on the atherosclerotic plaque and flows to a more peripheral branch of the coronary arterial tree, where it blocks the artery at that point. A thrombus that flows along the artery in this way and occludes the vessel more distally is called a *coronary embolus.*

2. Many clinicians believe that local muscular spasm of a coronary artery also can occur. The spasm might result from direct irritation of the smooth muscle of the arterial wall by the edges of an arteriosclerotic plaque, or it might result from local nervous reflexes that cause excess

coronary vascular wall contraction. The spasm may then lead to *secondary thrombosis* of the vessel.

Angina Pectoris (Cardiac Pain)

In most people who sustain progressive constriction of their coronary arteries, cardiac pain, called *angina pectoris,* begins to appear whenever the load on the heart becomes too great in relation to the available coronary blood flow. This pain is usually felt beneath the upper sternum over the heart, and in addition it is often referred to distant surface areas of the body, most commonly to the left arm and left shoulder but also frequently to the neck and even to the side of the face. The reason for this distribution of pain is that during embryonic life the heart originates in the neck, as do the arms. Therefore, both the heart and these surface areas of the body receive pain nerve fibers from the same spinal cord segments.

Most people who have chronic angina pectoris feel pain when they exercise or when they experience emotions that increase metabolism of the heart or temporarily constrict the coronary vessels because of sympathetic vasoconstrictor nerve signals. Anginal pain is also exacerbated by cold temperatures or by having a full stomach, both of which increase the workload of the heart.

Myocardial Infarction

Immediately after an acute coronary occlusion, blood flow ceases in the coronary vessels beyond the occlusion except for small amounts of collateral flow from surrounding vessels. The area of muscle that has either zero flow or so little flow that it cannot sustain cardiac muscle function is said to be *infarcted.* The overall process is called a *myocardial infarction.*

Soon after the onset of the infarction, small amounts of collateral blood begin to seep into the infarcted area, which, combined with progressive dilation of local blood vessels, causes the area to become overfilled with stagnant blood. Simultaneously the muscle fibers use the last vestiges of the oxygen in the blood, causing the hemoglobin to

become totally deoxygenated. Therefore, the infarcted area takes on a bluish-brown hue, and the blood vessels of the area appear to be engorged despite lack of blood flow. In later stages, the vessel walls become highly permeable and leak fluid; the local muscle tissue becomes edematous, and the cardiac muscle cells begin to swell because of diminished cellular metabolism. Within a few hours of almost no blood supply, the cardiac muscle cells die.

The most common causes of death after acute myocardial infarction are (1) decreased cardiac output, (2) damming of blood in the pulmonary blood vessels and then death resulting from pulmonary edema, (3) fibrillation of the heart, and, occasionally, (4) rupture of the heart