Peripheral Circulation

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EDITOR

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Preface

As in virtually all other areas of science, in recent years there has been a rapid growth of knowledge in the field of peripheral circulation. New information is continuously accumulating from microscopic, total organ, and whole animal studies. These findings have important implications for the traditional concepts of peripheral circulatory function. The information which is now available has reshaped, drastically in some instances, our understanding of the circulation.

The purpose of this book is to present current concepts of peripheral vascular function. It is obviously an impossible task to present up-to-the-moment information in a changing and evolving field. Nor is it our intention to dwell specifically on only the newest ideas. Rather, the goal of this monograph is to synthesize new findings and existing knowledge. Persons who are interested in the peripheral circulation but do not work in the field should find it useful as a guide to current thinking. Individuals who do work in the area may find it a useful summary of information in the field.

The initial chapters examine basic properties of the peripheral circulation which are common to all organs. These are followed by chapters which cover most of the individual organs and tissues. While each chapter on the individual circulations covers certain common topics, each also has a major theme which relates the function of that vascular bed to the specialized role of the organ it serves. In the chapter on coronary circulation, for example, the role of the peripheral circulation in meeting tissue metabolic requirements is emphasized while the chapter on the renal circulation discusses in detail the role of that vascular bed in mediating the exchange of water and solutes. In this way the manner in which the peripheral circulation meets the varied demands which are placed upon it in different circumstances is developed in a systematic fashion. Because of constraints of space, it has not been possible to cover all topics which are potentially important to the reader. In most instances the references at the end of each chapter provide a guide to further reading in the areas covered.

The editor is greatly indebted to the individual contributors who have kindly agreed to preparing chapters in accordance with the philosophy of the book as expressed above. Their flexibility has made the editorial task immeasurably easier.

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Introduction

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The peripheral vasculature is a branching, tapering network of distensible tubes. Blood enters the network from the heart at a pressure of about 100 mm Hg and at a flow rate of 4–6 liters/min in the resting adult human. The blood ejected from the heart during each systole, approximately 70 ml, is received by the aorta and large arteries, which constitute the reservoir and conduit portion of the arterial system. During diastole, the recoil of these elastic reservoirs provides a supply of arterialized blood under pressure to the periphery.

The physical properties of the aorta are well suited to its reservoir function. The aortic wall is composed mostly of collagen and elastin with relatively smaller amounts of smooth muscle. The passive elements provide the elastic recoil that is important to the reservoir function as well as the tensile strength needed to withstand the formidable forces developed by the pressurized blood acting against the wall.

In proceeding from the aorta to the periphery numerous branchings of the arterial vasculature occur. Some of these branching patterns are dichotomous, such as the division of the abdominal aorta into the two iliac arteries. In other instances an orthogonal pattern is seen; typically a small branch arises from a main trunk, with the latter undergoing a modest diminution in diameter beyond the branch point. Examples of such branching patterns may be seen in the microcirculation of the thigh muscle of the rabbit (Figure 1).

The arterial branchings increase the number of parallel and series vessels in geometric progression. The data of Mall (1) on the mesenteric vasculature and those of other workers on the larger vessels have been used by several authors to develop a quantitative description of the angio-architectonics and geometry of the peripheral vascular bed. An example is shown in Table 1 (2). It is evident that the larger vessels in the arterial network have a rather small pressure drop, since intravascular pressure is little reduced from the aorta to the terminal artery branches, despite a linear distance of some 70 mm over which the blood must travel.

RESISTANCE VESSELS

The number of small branches increases prodigiously with successive branchings. It is estimated that there are of the order of 400 million arterioles and about

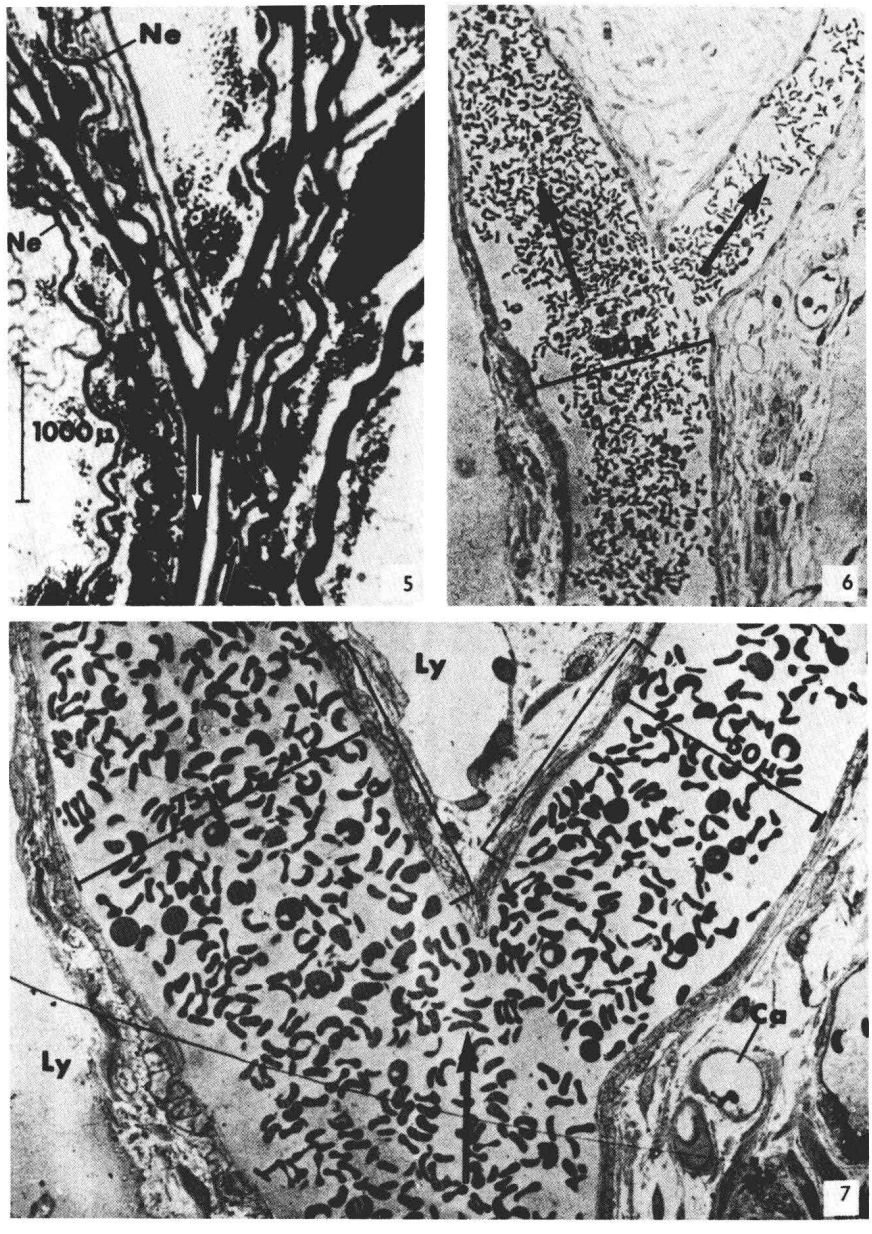


Figure 1. Branching pattern in the arterial network of rabbit thigh muscle. Upper left panel: low-power photograph of small arteries and veins in rabbit thigh. Upper right panel: phase-contrast micrograph of arteriolar branches. Arrow indicate direction of blood flow. Lower panel: electron micrograph of branching site showing morphological details. Symbols are as follows: Ca = blood capillary; Ly = lymphatic channel; Ne = nerve. (*From (4), reproduced by permission.*)

Table 1.

Type of Vessel	*Diameter (mm)*	*Number*	*Total Cross-sectional Area (mm^2)*	*Length (mm)*	*Fraction of Total Volume (%)*	*Intravascular Pressure (mm Hg)*	*Pressure Gradient ΔP/length (mm Hg/mm)*
Aorta	10	1	0.8×10^2	4×10^2	2.0	100	0.0075
Large arteries	3	40	3×10^2	2×10^2	4.0	97	0.0215
Main artery branches	1	600	5×10^2	10^2	3.4	92.7	0.129
Terminal branches	0.6	1800	5×10^2	10	1.7	79.8	0.330
Small arteries	0.019	4×10^7	1.1×10^4	3.5	2.7	76.5	5.97
Arterioles	0.007	4×10^8	1.5×10^4	0.9	1.0	55.6	32.1
Capillaries	0.0037	1.8×10^9	1.8×10^4	0.2	0.3	25.1	89.6
Postcapillary venules	0.0073	5.8×10^9	2.5×10^5	0.2	3.6	4.5	1.90
Venules	0.021	1.2×10^9	3.7×10^5	0.1	25.6	4.1	0.3
Small veins	0.037	8×10^7	8×10^4	3.4	18.6	3.8	0.5
Main venous branches	2.4	600	2.7×10^3	10^2	18.6	2.1	0.004
Large veins	6.0	40	1.1×10^3	2×10^2	15.2	1.7	0.002
Vena cava	12.5	1	1.2×10^2	4×10^2	3.4	1.3	0.003

Data from Schmid-Schonbein (2).

2 billion capillaries in the peripheral circulation, as shown in Table 1. Although total cross-sectional area increases in the smaller vessels, the pressure gradient also increases, because the total area is divided among many vessels. This has the effect of increasing resistance to flow, since by Poiseuille's law resistance is proportional to the fourth power of the radius (Chapter 3). Thus, the fact that total cross-sectional area increases by two orders of magnitude from the aorta to the arterioles fails to offset the concomitant decrease of about three orders of magnitude in diameter of individual vessels.

The small branches of the arterial network (small arteries, arterioles, and precapillary sphincters where the latter are present) constitute the resistance section of the vascular network. Most of the pressure drop occurs in this section (Table 1). The resistance function may, however, be shared; there may be an appreciable resistance to flow in large artery networks of certain vascular beds, for example, in the cerebral circulation and in subcutaneous tissue of the bat wing (Chapter 3).

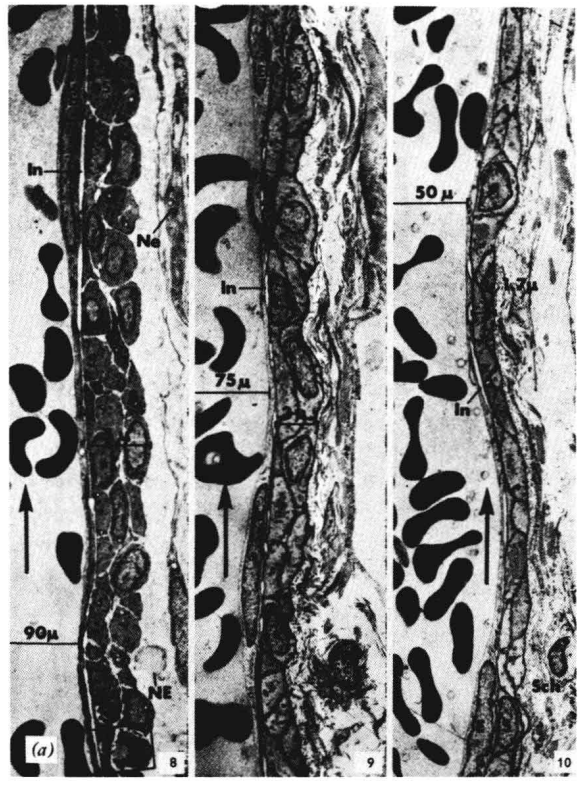
Resistance to flow through an organ or tissue can be expressed in terms of pressure and flow as follows:

$$\text{resistance} = \frac{\text{arterial pressure} - \text{venous pressure}}{\text{flow}}$$

Variations in organ flow may thus be attributed to changes in vascular resistance, arterial pressure, or venous pressure, or a combination of the three factors. Under conditions where blood viscosity remains constant (Chapter 3), it can be assumed that a change in vascular resistance is due to an alteration in vascular geometry, most likely to a change in arterial vessel diameter or number of flowing vessels. The validity of these assumptions may be better appreciated from consideration of blood rheology in Chapter 3.

Alteration of vascular resistance can be attributed to an active or passive change in vascular geometry. The latter is related to the viscoelastic properties of the tissue and the former to a change in the state of the vascular smooth muscle. Vascular smooth muscle is distributed throughout the arterial tree but is more abundant, relative to other wall elements, in small arteries and arterioles. In frog mesentery the composition of the arteriolar wall is 20% endothelium, 4% internal elastic membrane, 55% smooth muscle, and 21% collagen (3). In muscle tissue (rabbit thigh) the smooth muscle layer is of variable thickness in the arterioles, decreasing from several layers of cells arranged concentrically in 100μ arterioles (i.d.) to a single muscle layer in arterioles 50μ or less (i.d.) (Figure 2).

Figure 2. Wall structure in arteriolar network. (*a*) Examples of electron micrographs of 50μ to 90μ arterioles in rabbit thigh muscle. Note decrease in thickness of smooth muscle layer, from three cells wide in 90μ vessel to one cell wide in 50μ vessel. (*b*) Electron micrograph of terminal portion of arteriolar network. Areas marked with asterisk (*) indicate regions of membrane-to-membrane contact between smooth muscle and endothelial cells. Symbols are as follows: E = endothelial cell; Fib = fibroblast; In = elastica interna; Ne = nerve; S = smooth muscle cell; Sch = Schwann cell nuclei; Sp = sphincter. (*From (4), reproduced by permission.*)


In
Ne
90µ
NE
(a)
8
In
75µ
9
50 µ
In
Scl
10


Pig
2 µ
Ne
SP
4 µ
(b)
23

The role of the smooth muscle obviously is to affect diameter changes of the vessels. Smooth muscle is unique in that it is to some extent autonomous while at the same time being subject also to external influences such as the vascular nerves, circulating humoral influences, and tissue metabolites. Rhythmic contraction or vasomotion is often seen in the arteriolar network and is generally considered to be a manifestation of the intrinsic spontaneous activity of the smooth muscle cells in the wall. The smooth muscle cells are also thought to be sensitive to intravascular pressure, responding by contracting when this pressure is increased (Chapter 4). The degree of local versus central (i.e., nervous control) varies considerably among vascular beds. Some are richly innervated (skin), while others, such as the cerebral vessels, are poorly innervated.

Under normal circumstances most resistance vessels are partially contracted and expand in response to local needs, as expressed, for example, by a change in tissue metabolic requirements. Local vascular resistance may also change due to altered sympathetic nervous activity as well. The smooth muscle layer is thus set at a midpoint from which it can either increase or decrease flow to the tissue, depending upon signals received from the tissue, from the nervous system, or from the blood itself.

EXCHANGE VESSELS

The capillaries constitute the exchange network in which the principal transfer of substances between the tissues and the bloodstream takes place. The capillaries consist of a single layer of endothelial cells surrounded by a more or less continuous basement membrane. The structure of the capillary wall varies from one vascular bed to another, and apparently the rate at which substances exchange across the wall is related to this structure. Capillary beds have been classified into several types based upon histological appearance. Illustrated in Figure 3 are examples of continuous, fenestrated, and discontinuous capillaries (5). The capillaries may also be classified on the basis of the type of organ in which they are found, i.e., somatic or visceral. Continuous capillaries are found in muscular, subcutaneous, connective, nervous, and lung tissue. Fenestrated capillaries are found in glandular tissues and regions of rapid fluid exchange (i.e., kidney and intestinal mucosa). Discontinuous capillaries are found in liver, spleen, and bone marrow. The continuous capillary wall may have a thin or a thick endothelial layer (low or high as shown in Figure 3). These capillaries are less permeable than either of the other types. The fenestrated capillaries have circular openings in the cell wall with or without a thin diaphragm, and these are generally more permeable to larger molecules than are the continuous capillary membranes. The most permeable capillary membranes are the discontinuous types, in which large openings are apparent in the wall between adjacent endothelial cells. In addition, there may be holes in the cell itself. The mechanism by which materials exchange across the capillary walls is discussed in detail in Chapter 5.

The geometry of the capillary network varies from one organ to another, and it is difficult to generalize as regards features that may be common to all. A vascular bed that is often considered as a model for such networks is the mesentery, which is shown in Figure 4(*a*). This bed is characterized by a thoroughfare channel that is somewhat larger than the true capillaries but otherwise is similar to them. This channel has an internal diameter somewhat greater than the red cell diameter. In contrast, the diameter of the true capillaries is often less than the maximal red cell diameter and the latter are deformed somewhat in passage through the capillary.

It has been suggested that thoroughfare channels or arterio-venous shunts may limit the exchange of diffusible materials between blood and tissue. There is evidence that diffusible materials injected into the bloodstream do not equilibrate with the tissues in a single passage through the vascular bed. Alternatively, high-flow capillaries could be involved. Anatomical evidence for arterio-venous shunts is extremely limited except in a few areas such as skin.

In skeletal muscle the capillary network is most typically a parallel arrange-

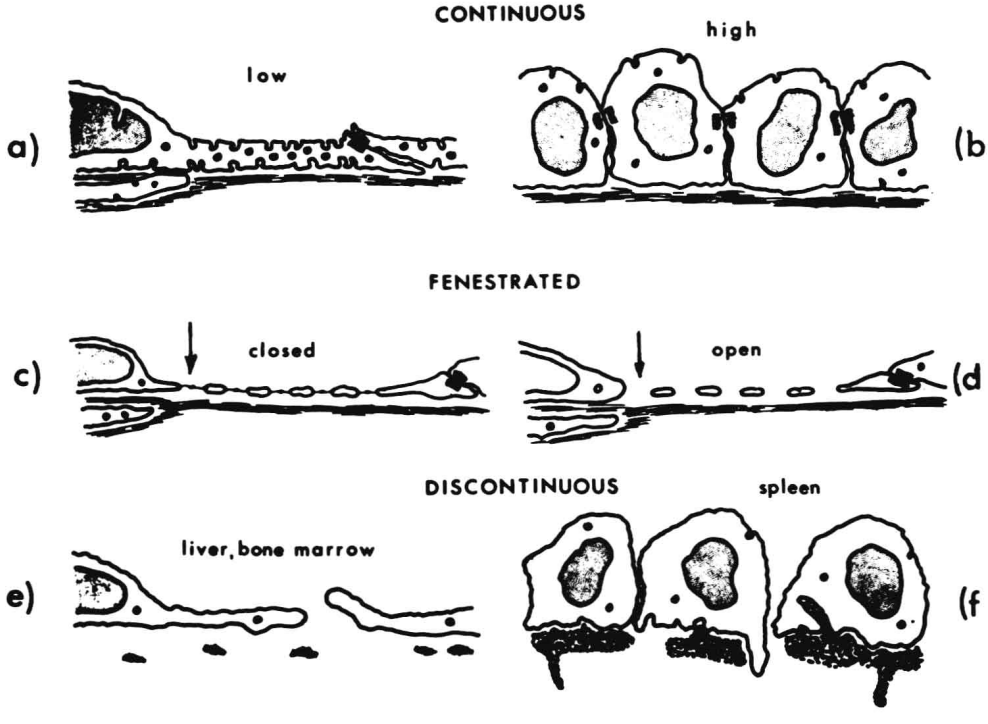
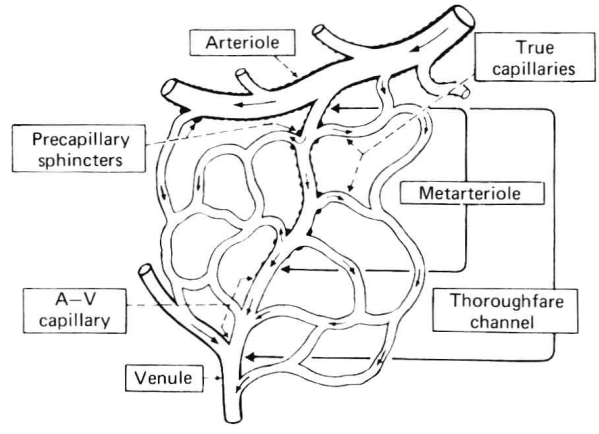
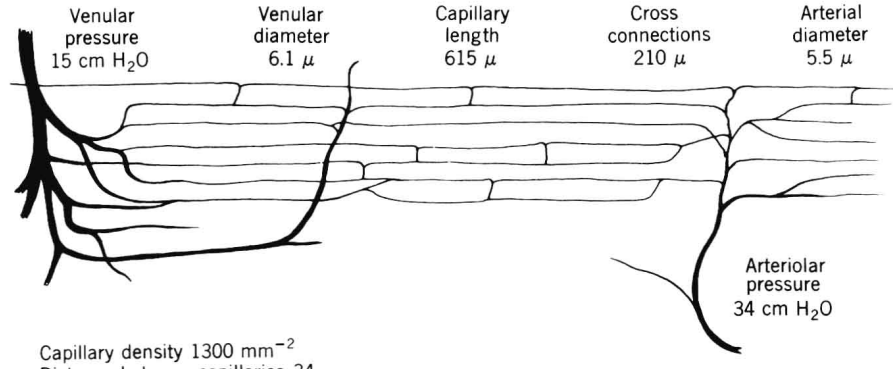


Figure 3. Schematic diagram of continuous, fenestrated, and discontinuous blood capillary membranes. In each diagram, the endothelial cell is shown above. The basement membrane is shown as the darkened region immediately below. The routes by which materials cross capillary membranes is discussed in detail in Chapter 5. (*From (5), reproduced by permission.*)



(*a*)



Capillary density 1300 mm^{-2}
Distance between capillaries 34
Capillary surface area 244 cm^2 cm^{-3} muscle

Micro-occlusion pressure data
Arterial end 32 cm H_2O
Venular end 22 cm H_2O

Capillary filtration coefficient 0.001 μ^3/μ^2 sec cm H_2O difference.

Red cell velocity 700 μ/sec

(*b*)

Figure 4. Examples of capillary networks in peripheral circulation. (*a*) An idealized diagram of the capillary network in mesentery. The arteriole branches into a metarteriole and a capillary network. At the entrance to each capillary is a smooth muscle cell, the precapillary sphincter. The metarteriole loses its muscular coat and continues as a somewhat enlarged thoroughfare channel, which is distinguished from the true capillaries by a somewhat larger internal diameter. (*b*) Idealized diagram of the capillary network in rat cremaster muscle showing the parallel arrangement of the capillaries as well as dimensions and internal pressures. (*From (6) and (7), reproduced by permission.*)

ment of what appear to be identical capillaries (Figure 4(*b*)). The flow through adjacent vessels is rather similar, and it is likely that they are controlled as a group rather than individually as seems to be the case in mesentery, for example.

The exchange process is a function of the available surface areas as well as the

structure of the capillary wall. As is apparent in Table 1, the cross-sectional area of the capillary bed is greater than that of any other section of the circulation. Since the average vessel diameter is lowest here, it also follows that capillary surface area is greater than that of any other section.

The area of the capillary bed that is actually available for exchange is variable, since not all capillaries flow continuously. Flow in some vessels is continuous, but in others it is erratic or periodic. The absence of flow through a capillary essentially removes that vessel from the circulation and decreases the available capillary surface area for exchange by that amount. Some evidence suggests that capillary surface area is a controlled variable in the peripheral circulation. It appears that precapillary sphincters or terminal arterioles may behave somewhat differently from the rest of the arterial network under some circumstances, thus providing relatively independent control of capillary surface area from that of vascular resistance.

The exchange process between blood and tissue is not entirely limited to the capillary network. The postcapillary venules are virtually devoid of smooth muscle and in other ways resemble capillaries but are somewhat larger in diameter. There is reason to believe that they are functionally similar to the capillaries. There is also evidence that their permeability to large molecules is greater.

The exchange of lipid-soluble substances is even less restricted. There is, for example, good evidence that a substantial amount of oxygen diffuses across the walls of the arteriole (Chapter 5).

The permeability characteristics of the capillary are usually considered to be static, although it has been known for some time that certain humoral agents such as histamine can alter capillary permeability. As noted in Chapter 11, there is also growing evidence that the permeability of capillaries in adipose tissue can be altered (increased) by sympathetic stimulation. This apparently involves an increase in permeability to large molecules.

The rate at which water moves across the capillary bed is an important indication of capillary function and is often used as a measure of the exchange network. Most commonly this is determined by measuring the rate of weight or volume gain of an organ following a step increase in venous pressure. It is usually assumed that 60% to 80% of the venous pressure increment is transmitted to the capillaries. Also, an initial rapid increase in blood volume in the venous network must be allowed for in making this measurement. This measure, called the CFC (capillary filtration coefficient) of the organ, is expressed as ml/min·100 g tissue·mm Hg capillary pressure. The CFC increases during hyperemia and, in general, follows the same directional changes as the vascular resistance of the organ, with certain exceptions.

LYMPHATIC SYSTEM

The lymphatic system is a very low-pressure, low-flow system that returns tissue fluid to the circulatory system. Because of the capillary hydrostatic pressure, an ultrafiltrate of blood plasma is continuously filtered across the arterial side of the capillary network. The amount of fluid filtered is perhaps 20 liters per day,