

17 Heart

(a) The heart and its layers

Oxygenated blood for the body leaves the left ventricle of the heart via the aorta (systemic circulation)

Blood leaves via pulmonary artery for the lungs (pulmonary circulation)

Right atrium (receives deoxygenated blood from the body via superior and inferior vena cava, and coronary sinus)

Left atrium receives oxygenated blood from lungs via pulmonary vein

Right ventricle Left ventricle

Tunica intima Tunica media Tunica adventitia

Pericardial cavity

Fibrous pericardium

Epicardium

Myocardium

Endocardium

The wall of the heart, and that of the blood vessels are continuous and contain three layers:
 Inner layer of tunica intima (endocardium in the heart)
 Middle layer of tunica media (myocardium in the heart)
 Outer layer of tunica adventitia (epicardium in the heart)

(b) Ventricular wall (H&E, low magnification)

Myocardium

Endocardium

Epicardium

500µm

(c) Endocardium (low magnification, stained for glycogen: red)

Myocardium

Sub-endocardium

Tunica intima (endocardium)

Endothelial lining

Purkinje fibers in sub-endocardium

Connective tissue

Smooth muscle

200µm

(d) Comparison of Purkinje fibers and cardiomyocytes (high magnification)

Myocardium

Cardiomyocytes (TS) with central nucleus intensely stained due to high numbers of myofibrils

Intercalated disc

Cardiomyocyte (LS)

Capillary

20µm

Sub-endocardium

Purkinje cell (fiber), with few peripheral myofibrils, a large diameter, and abundant glycogen

20µm

(e) Section through myocardium after acute myocardial infarction (H&E, high magnification)

The damaged myocardium has been infiltrated by white blood cells (neutrophils, macrophages)

Degenerating cardiomyocyte

Neutrophil

20µm

(f) Epicardium

Squamous epithelium (mesothelium)

Connective tissue in tunica adventitia

The outer layer of tunica adventitia in the heart also contains blood vessels (vasa vasorum, including the coronary arteries) which provide the blood supply for the heart

Cardiac myocytes in myocardium surrounded by connective tissue, fibroblasts and blood vessels

20µm

The heart is part of the cardiovascular system.

This system is important for:

- pumping blood around the body (systemic circulation) and between the heart and the lungs (pulmonary circulation);
- distributing oxygen, nutrients, hormones, and immune cells around the body;
- removing carbon dioxide and metabolic waste;
- regulating temperature.

Throughout the body, the walls of the heart and the blood vessels (or tubes) that make up the cardiovascular system contain three layers (Fig. 17a):

- **tunica intima:** inner layer that consists of flat endothelial cells supported by a basement membrane and delicate collagenous tissue;
- **tunica media:** intermediate muscular layer;
- **tunica adventitia:** outer supporting tissue layer (sometimes called tunica externa).

The muscular walls of the cardiovascular system only have one layer of muscle, in contrast to two or even three layers of muscle in the gut.

The three layers of the heart (tunica intima, tunica media, and tunica externa) are called the **endocardium**, **myocardium**, and **epicardium**, respectively (Fig. 17b).

Tunica intima/endocardium

The endocardium consists of a simple squamous epithelium (endothelium), which lines the endocardium, and underlying layers of connective tissue, in which the middle layer contains smooth muscle cells.

The innermost connective tissue layer is called the **subendocardium** (Fig. 17c). This layer contains the cells specialized for conduction: Purkinje cells (see below).

The lining epithelial layer is continuous with the epithelium lining all the blood vessels in the circulatory system.

Purkinje fibers are cardiac muscle fibers that are specialized for conduction. They are found in the subendocardium of the ventricles (a connective tissue layer). Purkinje cells differ from normal cardiac cells (Fig. 17d) in the following ways.

- Purkinje fibers do not contain many myofibrils, and those present are found at the cell periphery, which is demonstrated here by the less intense staining compared to cardiac muscle.
- They have higher levels of glycogen than cardiomyocytes.
- There are no intercalated discs between the cells, but desmosomes and gap junctions are present and connect these cells to each other.

- Purkinje fibers are larger than cardiac muscle cells, and do not have T-tubules.

The heart is stimulated to contract rhythmically by impulses generated by the sino-atrial (S-A) node. Impulses from the S-A node are conducted via the internodal pathway to the atrio-ventricular (A-V) node, and then into the ventricles. The left and right bundles of Purkinje fibers are responsible for the spread of the impulse around the ventricles.

Tunica media/myocardium

This 'middle' layer of the heart is called the myocardium.

The myocardium contains cardiac muscle cells (cardiomyocytes), blood vessels, fibroblasts, and small amounts of connective tissue.

Intercalated discs connect the cardiomyocytes to each other (see Chapter 9 and Fig. 17d). Importantly, gap junctions in the intercalated discs are responsible for communication between cardiomyocytes and the spread of electrical conduction around the heart.

The striated appearance of the cardiomyocytes is due to the regular arrangement of muscle sarcomeres in myofibrils that are packed into these cells (see Chapter 9).

A high-magnification image of the myocardium, taken from a patient who has had a heart attack (acute myocardial infarction; Fig. 17e), shows how the cardiomyocytes have become damaged. The tissue around the cardiomyocytes is full of white blood cells (mainly neutrophils and macrophages) that have escaped from the blood vessels, and which are engulfing the damaged tissue.

Tunica adventitia/epicardium

This outermost layer of the heart is called the epicardium (Fig. 17f).

The epicardium consists of a layer of flattened (squamous) epithelial cells and underlying connective tissue.

This layer of epithelium is called the **mesothelium**, as it lines the closed pericardial cavity which surrounds the heart. The mesothelium secretes fluid into the pericardial cavity, which lubricates the movements of the epicardium on the pericardium.

The epicardium contains coronary arteries, veins, vasa vasorum, connective tissue, and autonomic nerves that supply the myocardium.

Vasa vasorum are small blood vessels that supply the heart and the larger blood vessels, such as the aorta.

18 Arteries and arterioles

(a) Schematic diagram of part of the circulatory system (simplified)

(b) Aorta (H&E, low magnification)

(c) High magnification images of the three layers of the aorta

The aorta is an elastic, conducting artery in which the predominant layer is the **tunica media**, which is rich in collagen and elastin

(d) Muscular artery (trichrome, low magnification)

The tunica media layer is the thickest layer of the muscular artery

(e) Muscular artery (trichrome, high magnification)

(f) Internal and external elastic layers of the femoral artery (unknown stain)

(g) Atherosclerosis in the coronary artery

Accumulations of cholesterol

Atheroma core in the tunica intima

Tunica media

Fibrous cap

Lumen

Lesion also contains smooth muscle cells, macrophages, foam cells, lymphocytes and cell debris

In the systemic circulation, oxygenated blood (shown as red in Fig. 18a) leaves the heart and is pumped around the body through a series of blood vessels.

Blood leaving the heart enters large elastic ‘conducting’ arteries, which conduct the flow of blood from the heart into smaller arteries.

Blood then flows into distributing (**muscular**) arteries. These are about the size of a pencil in diameter, and are all named (e.g., femoral artery, brachial artery). The blood is distributed into smaller arteries (**arterioles**) before entering the **capillaries**. (See Chapter 19 and Fig. 19a,b for more on small arteries and arterioles.)

Capillaries are small, thin-walled structures that allow the transport of gases and nutrients between the lumen of the blood vessel and the surrounding tissues. Deoxygenated blood (blue, Fig. 18a) flows out of capillaries into small veins (**venules**), into medium veins and then into large veins before being returned to the heart.

The structure of blood vessels varies throughout the body, mainly by variations in the middle (**tunica media**) layer, and these variations in structure are important for their functions.

Elastic arteries

The elastic arteries (Fig. 18b) receive blood directly from the heart under high pressure. They include the aorta and its largest branches (the common carotid, brachiocephalic, subclavian, and common iliac arteries). These arteries have a diameter greater than 1 cm.

The walls of these arteries need to be able to accommodate the large changes in blood pressure between systole and diastole. When blood is pumped into the arteries during systole, the wall of the artery distends. Collagenous fibers in the tunica media and adventitia layers prevent a large distension.

During diastole (the relaxation phase of the cardiac cycle), blood pressure is maintained by the elastic recoil of the arteries in diastole, which forces blood away from the heart and into the rest of the circulation. The elastic recoil also forces blood back towards the heart, but this blood is prevented from re-entering the heart by the closure of the aortic and pulmonary valves.

The **tunica intima** (Fig. 18c) consists of:

- a simple squamous lining layer of cells (**endothelium**) which is continuous with the endothelium of the heart. This layer is important for forming a selective permeability barrier between the tissues and the blood;
- a **basement membrane**;
- a thin layer of **loose connective tissue** containing elastin and collagen fibers, and contractile smooth muscle cells;
- an **internal elastic layer**, which is continuous with the underlying elastic layer in the tunica media.

The lining endothelial cells can become ‘activated’ in response to external stimuli, and this can lead to vascular diseases such as atherosclerosis.

The **tunica media** (**middle layer**, Fig. 18c) is the most prominent layer. It contains:

- concentric sheets (lamellae) of elastin fibers, and collagen fibers. There are gaps (fenestrations) in these sheets, to allow diffusion of substances within this layer. Adults have about 40–70 lamellae, and the number can increase in hypertension;
- smooth muscle cells (myointimal cells), which synthesize the collagen and elastin in the tunica media layer, and lie between the sheets of elastin.

The **tunica adventitia** (Fig. 18b,c) is a thin outer layer. It contains:

- connective tissue (collagen and elastin);
- fibroblasts and macrophages; and
- small blood vessels (**vasa vasorum**) and nerves.

The vasa vasorum provide the outer regions of these large arteries with nutrients. The inner region is supplied by nutrients from the lumen of the artery. Small arteries do not require vasa vasorum.

Muscular arteries

These are the ‘distributing’ arteries. They have a large diameter of 2–10 mm. While they are smaller than elastic arteries, they are mostly large enough that they are all named (e.g., brachial artery, femoral artery, coronary artery).

They contain a prominent layer of smooth muscle in the tunica media (Fig. 18d–f) and a regular lumen, distinguishing them from muscular veins (Chapter 19).

The **tunica intima** (Fig. 18e) consists of:

- a single outer layer of flattened endothelial cells;
- an underlying basement membrane and subendothelial connective tissue;
- a inner layer of elastic fibers (the inner elastic layer; IEL).

The **tunica media** (Fig. 18e) is the most prominent layer. It consists of:

- a thick layer of smooth muscle cells, arranged circumferentially around the lumen of the artery, and embedded in an elastic matrix.
- an external elastic layer (EEL), the outermost layer of the tunica media (Fig. 18f).

The smooth muscle cells run circumferentially, and can contract (squeeze, or constrict) to reduce the size of the lumen, or relax, to increase (dilate) the size of the lumen. This changes the amount of blood that is allowed to flow through these arteries.

The **tunica adventitia** (Fig. 18e) is fairly broad. It contains:

- collagen and elastin; and
- fibroblasts.

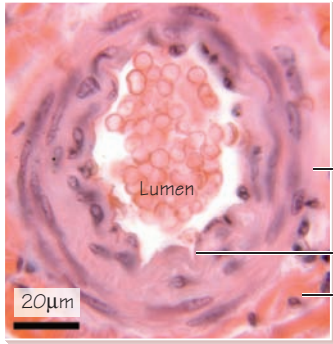
Atherosclerosis

Smooth muscle cells can accumulate lipid and migrate into the subendothelial layer, which can then thicken and atherosclerosis can develop (Fig. 18g). This weakens the arterial wall, and can result in an aneurysm (swelling).

Atherosclerosis can lead to heart disease, stroke, and gangrene.

19 Capillaries, veins, and venules

(a) Small artery (H&E)



In small arteries the tunica media is the predominant layer, but the external elastic layer is absent.
The outer tunica adventitia layer contains connective tissue and is thin

Lumen


Tunica media (with smooth muscle cells)

Tunica intima contains a thin internal elastic lamina (IEL)

Tunica adventitia

20µm

(b) Small arteriole (H&E)



Tunica intima does not contain an IEL

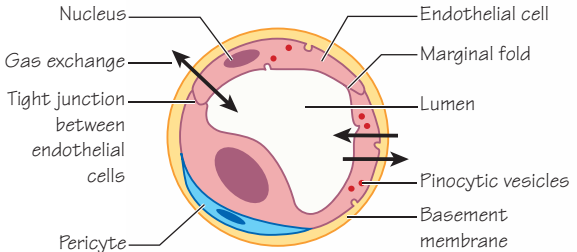
The tunica media only contains 1 layer of smooth muscle cells

Lumen

Tunica adventitia is poorly defined/absent

20µm

(c) Diagram of a continuous capillary



Nucleus

Gas exchange

Tight junction between endothelial cells

Pericyte

Endothelial cell

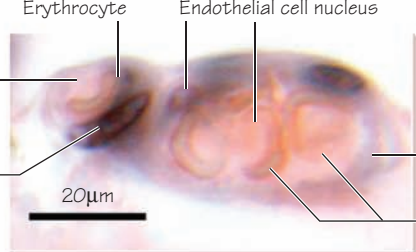
Marginal fold

Lumen

Pinocytotic vesicles

Basement membrane

(d) Small blood vessels (H&E)



Erythrocyte

Capillary (TM and TA layers absent)

Pericyte

Endothelial cell nucleus

Lumen of venule is larger than that of the adjacent capillary

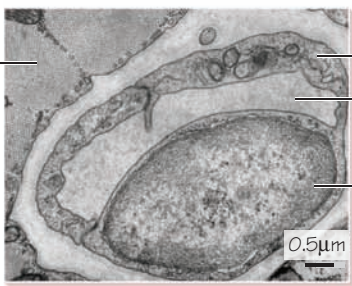
Post-capillary venule (TM and TA layers absent)

Erythrocytes

20µm

(e) Continuous capillary (EM)

Basement membrane is continuous, vesicle transport (arrows) is bi-directional



Muscle cell

Cytoplasm of endothelial cell, filled with vesicles

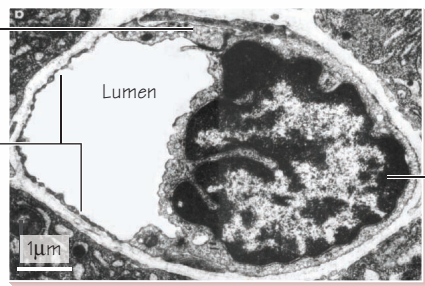
Lumen

Nucleus

0.5µm

From An Atlas of Fine Structure: The cell

(f) Fenestrated capillary (EM)



Lumen

Fenestrations

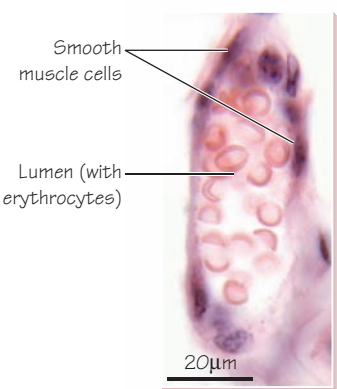
Pores, gaps or 'fenestrae' (~80nm wide)

Nucleus

1µm

Electron micrograph from Cell Structure. EK Carr, Churchill Livingstone

(g) Small vein (H&E)



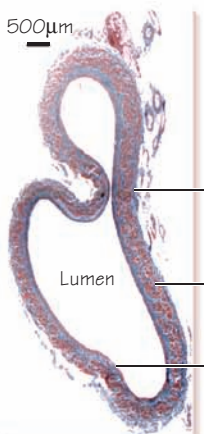
Smooth muscle cells

Lumen (with erythrocytes)

20µm

This small vein has one layer of smooth muscle continuous with the tunica intima

(h) Large vein (trichrome)



500µm

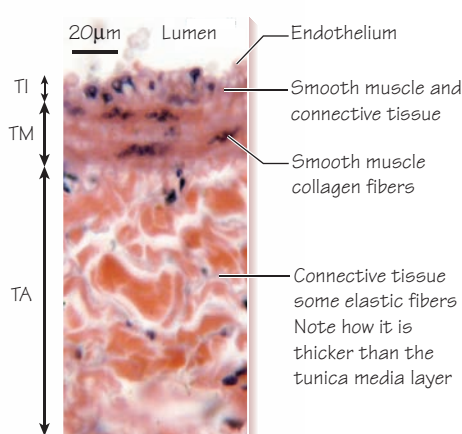
Lumen

Tunica adventitia (TA)

Tunica media (TM)

Tunica intima (TI)

(i) Large vein (high magnification, TS)



20µm

Lumen

Endothelium

TI

TM

TA

Smooth muscle and connective tissue

Smooth muscle collagen fibers

Connective tissue some elastic fibers

Note how it is thicker than the tunica media layer

Small arteries/arterioles

As arteries branch, and reduce in size, the outer elastic layer is lost, and the thickness of the tunica media layer reduces in size.

Small arteries have the following characteristics.

- Diameter is about 0.1–2mm.
- The smooth muscle layer (tunica media) is 5–10 cells thick (Fig. 19a).
- The tunica media contains mostly collagen, but some elastin.
- An internal elastic layer is present in the tunica intima.
- The tunica adventitia layer is thin, and contains connective tissue.

Arterioles have the following characteristics.

- Diameter is about 10–100µm.
- The smooth muscle layer is 1–2 layers thick (Fig. 19b).
- An internal elastic layer is absent from the tunica intima.
- The tunica adventitia layer is thin and poorly defined.

In relation to their small diameter, the arterioles contain the greatest quantity of smooth muscle of any vessel.

This is important, because by contracting (vasoconstriction) and relaxing (vasodilation) their smooth muscle, these blood vessels control the blood supply into the capillary bed.

Constricting their lumens generates resistance to blood flow, and so these small arteries are known as ‘resistance’ blood vessels. They are the major determinants of blood pressure in the systemic circulation.

Capillaries

These are small, around 5–10µm in diameter, just large enough to hold one red blood cell, although some specialized capillaries, such as those found in the liver, can be larger, 30–40µm in diameter (see below).

The wall of the capillary contains flattened endothelial cells connected to each other by tight junctions (fascia occludens).

Capillaries do not have a tunica media or tunica adventitia layer (Fig. 19c–f).

The wall thickness of these vessels is only 0.5µm, which facilitates gas diffusion across the capillary wall between the capillary and its surrounding tissue. Nutrients are exchanged by a mixture of gas exchange and pinocytosis (‘cell drinking’) in which the endothelial cells take up nutrients from the lumen via their apical surface, and secrete them into the surrounding tissue at their basal surfaces (or vice versa).

Types of capillary

There are three types of capillary: continuous, fenestrated, and discontinuous.

Continuous capillaries

In continuous capillaries (Fig. 19c–e, most common), tight junctions connect the endothelial cells to each other, and the underlying basement membrane is continuous. This type of capillary is found in muscle, the lung, and the central nervous system.

Continuous capillaries contain many vesicles, for transport of substances between the lumen and the surrounding tissue (Fig.

19e). They may also be surrounded by a pericyte, which contributes to new smooth muscle cells during development and in wound healing.

Fenestrated capillaries

Fenestrated capillaries are found in endocrine glands, the gut, and the gall bladder. They contain small pores (fenestrae) about 80 nm in diameter in the walls of the endothelial cells (Fig. 19f), which increases permeability between the capillary and the surrounding tissue. This allows exchange of macromolecules such as proteins (hormones) in addition to water and ions.

Discontinuous capillaries

Discontinuous capillaries also contain fenestrae but, in addition, the basement membrane of the endothelium is discontinuous. This type of capillary forms the liver sinusoids, found between liver hepatocytes. They contain particularly wide lumens (up to about 40µm).

Sinusoids are also found in the spleen and bone marrow.

Capillaries drain into postcapillary venules and then into veins of increasing size. Arteriovenous shunts, direct connections between arteries and veins, can divert blood away from the capillary beds in some areas (e.g., the skin).

Veins

Veins are divided up into categories on the basis of size. These include small veins (postcapillary and muscular venules), and medium and large veins.

Postcapillary and muscular venules

These do not have a **tunica media** or **tunica adventitia** layer. They can be distinguished from capillaries because the lumen of these vessels is large compared to their thickness (Fig. 19d; compare the capillary and vein). Muscular venules are similar to postcapillary venules, but are surrounded by a thin layer of smooth muscle (1–2 layers, Fig. 19g).

Medium and large veins

Medium veins (diameter ~10mm or less) mostly have names, and valves are common in these vessels, particularly in the lower limbs. Valves prevent the reversal of blood flow, due to gravity.

Large or muscular veins (diameter greater than 10mm, Fig. 19h,i) are easily distinguished from arteries in sections by the following.

- The lumen of veins tends to be irregular, whereas that of arteries is regular.
- The tunica media is thinner compared to muscular arteries.
- The tunica adventitia is larger relative to the tunica media layer, and is the thickest layer. (Vasa vasorum can be present in this layer.)

The layer of smooth muscle in the tunica media layer is used to regulate the diameter of the veins. However, as blood pressure in the veins is lower, only a relatively thin layer is required.