Microscopic Anatomy

CARDIOVASCULAR SYSTEM

I. Introduction

The cardiovascular system is a closed system consisting of a pump, the heart, and a series of tubular blood vessels that interconnect all body tissues and organs. It is subdivided into the pulmonary and systemic circulations that are linked together, as the output of one becomes the input of the other. The different types of vessels (arteries, capillaries, and veins) display structural specializations correlating with their distinct functional roles.

The circulatory system is pervasive; there are thousands of miles of vessels in a typical human body containing about 6 liters of blood. Damage to, or failure of, the cardiovascular system is the major source of human disease and death in this country.

The primary functions of the cardiovascular system include:

1. Supplying oxygen and nutrients to all tissues and organs.
2. Providing communication between endocrine glands and their target organs.
3. Transporting leukocytes to sites of injury and inflammation and providing pathways for lymphocytes to enter lymph nodes for activation of humoral immune response.
4. Carrying waste products of metabolism to the lungs and kidneys for elimination.

You should be aware that the circulatory system also provides a highway for invaders of the body, such as bacteria, viruses, and parasites. The system demonstrates structural and functional adaptations to this challenge.

II. The Heart

The heart acts as two pumps in series, each with an atrium that collects blood before it enters the ventricle, the main pump. Deoxygenated blood from the systemic circulation enters the right atrium, and moves to the right ventricle where it is pumped through the pulmonary artery to the lung where hemoglobin exchanges CO_2 for O_2. The oxygenated blood returns to the left atrium where it passes into the left ventricle and is then propelled through the systemic circulation.

Layers of the heart

The walls of the atria and ventricles are similar in organization, although the walls are thicker in the ventricles. The heart walls contain three distinct layers, the inner **endocardium**, the middle **myocardium**, and the outer **epicardium**.

The **endocardium**, which surrounds the lumen of the heart, is itself composed of three layers: a simple squamous **endothelium** that covers the luminal surface; a thin subendothelial layer of loose collagenous tissue; and a subendocardium, a thicker layer of more dense connective tissue, which, in certain areas of the ventricles, also contains specialized conducting cells called Purkinje fibers.

The thickest layer of the heart is the **myocardium**, which is composed of **cardiac muscle** fibers (also known as cardiomyocytes), surrounded by capillaries and a reticular network of elastic fibers and connective tissue. Arteries and veins are also present.

The third and outer layer of the heart is the **epicardium**, which contains connective tissue with elastic fibers, adipose tissue, and nerves, as well as large coronary arteries and veins. Obstruction of coronary arteries can result in myocardial infarction, a fairly common clinical condition. The epicardium is covered by a **mesothelium**, the visceral pericardium.

Although it is not considered a separate layer, the heart lies in the **pericardium**, a fluid filled cavity surrounded by a simple squamous epithelium. (The visceral side of the pericardium is the mesothelium covering the epicardium.) The fluid within pericardial sac allows the heart to move without excessive friction as it pumps.

Cardiac Muscle Fibers (Myocytes)

There are two basic types of cardiac myocytes, those specialized for contraction and those specialized for impulse conduction.

1. Contractile Cardiomyocytes

Contractile **cardiac muscle cells** contain similar arrangements of contractile filaments (actin and myosin) as skeletal muscle cells, demonstrating regular cross striations with a 2.5 μm repeating unit (Figure 1). However, compared to skeletal muscle cells, cardiac muscle cells can be readily distinguished by their centrally located nuclei, smaller length (50 to 100 μm), smaller diameter (15 to 25 μm), branched organization, and distinctive **intercalated discs**. All of these features are evident in the lab exercises. The branching structure of cardiac muscle fibers establishes a three-dimensional network for the transmission of force and action potentials. At the end of each fiber, cardiomyocytes connect to each other through a multifunctional complex known as the **intercalated disc**. With the microscope the length of cardiac fibers can be measured as the distance between consecutive intercalated discs, which appear as densely stained transverse bands at the level of the Z line. Intercalated discs contain 3 functionally important structures: (1) fascia adherens, a ribbon-like structure where thin filaments insert into the cell membrane, (2) desmosomes, "spot welds" that act to establish cell-to-cell contacts to enable force transmission between cells, and (3) gap junctions that allow action potentials to be transmitted between cardiac muscle cells, making the heart an electrical syncytium. In addition to being a key part of the intercalated disc complex, gap junctions are also present at the lateral surfaces of the fibers.

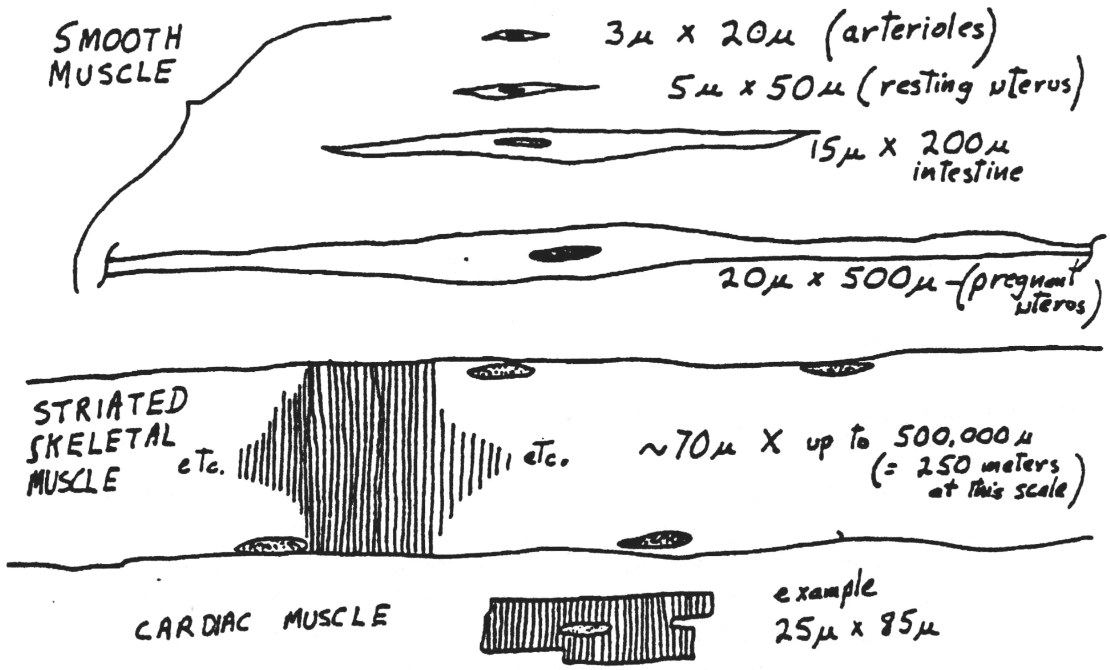

Figure 1: Diagram of typical smooth, skeletal, and cardiac muscle fibers.

Atrial contractile fibers differ from **ventricular** contractile fibers in two major ways. First, atrial muscle fibers are somewhat smaller in diameter and length and therefore generate less force. During diastole, most filling of the ventricle occurs passively with only ~20% due to the contraction of the atria. Second, atrial muscle fibers have an **endocrine** function. In response to volume overload (increased stretch), atrial muscle fibers secrete **atrial natriuretic factor (ANF)**, a hormone involved in the homeostatic control of body fluid compartment size by action in the kidney.

2. Impulse Conducting Cardiomyocytes

The **impulse conducting system** of the heart is composed of two nodes, the **sinoatrial (SA) node** and the **atrioventricular (AV) node**, and a series of **conducting fibers**. The speed and pathways of action potential transmission are regulated by specializations of these cells, including fiber diameter (the larger the diameter the faster the conduction velocity), the number and distribution of gap junctions, and the character of the surrounding extracellular matrix. Electrical impulses are generated at the SA node, which is located near the junction of the superior vena cava and the right atrium (Figure 2). SA node cells reach threshold faster than other cardiomyocyes, therefore the SA node is referred to as the pacemaker of the heart. The SA node initiates an impulse that is transmitted through atrial cardiomyocytes and internodal tracts to the AV node, where it is carried across the connective tissue cardiac skeleton (see below) into the ventricles by the AV bundle of His. This bundle divides into left and right branches entering the two ventricles, and distally turns into specialized conducting fibers called **Purkinje** fibers (see Figure 2).

The cells of the SA and AV nodes are smaller than ordinary cardiac muscle fibers and are embedded in dense connective tissue. The SA node is innervated by sympathetic and parasympathetic fibers. Due to the cardiac skeleton (see below), the cells of the AV node and associated cells of the AV bundle of His normally comprise the sole conduction pathway between atria and ventricles. The conducting fibers of the AV bundle of His are similar in structure to those of the nodes. However, the distal Purkinje fibers, which are bundled together in the subendocardium, are much larger in diameter than ordinary cardiac muscle, which, due to increased conduction velocity, permits the excitatory wave to reach ventricular cardiomyocytes rapidly. Purkinje fibers have one or two central nuclei in a cytoplasm that is rich in glycogen and mitochondria. Although Purkinje fibers are modified for conduction, they retain a minimal contractile capability so that some myofibrils (with cross striations) are present, as well as numerous gap junctions and desmosomes at cell boundaries. These specialized fibers, seen in your Webslide 0033, can be distinguished from other cardiomyocytes by their large diameter and pale staining.

The cardiac skeleton and cardiac valves

The cardiac skeleton consists of dense connective tissue that serves to isolate atria from ventricles, restricting the spread of electrical activity to the specialized conducting system described above. The cardiac skeleton is also an insertion base for cardiac muscle and the four cardiac valves, the semilunar valves of the aorta and pulmonary artery, and the cuspid (AV) valves between the atria and ventricles (tricuspid and mitral valves on right and left sides, respectively). The cardiac valves are thin plates of connective tissue covered on both sides by endothelium. The cuspid valves prevent backflow from the ventricles to the atria during systole. Unlike venous valves, these valves are linked by tendons (chordeae tendineae) to bundles of cardiac muscle fibers, the **papillary muscles** that extend from the ventricle. Contraction of these muscles fibers prevents eversion of the cuspid valves during systole. Regions of the inner surfaces of ventricles are also thrown into muscular folds (trabeculae carneae) that can be observed near the bottom right of Figure 2 and in your Webslide 0024.

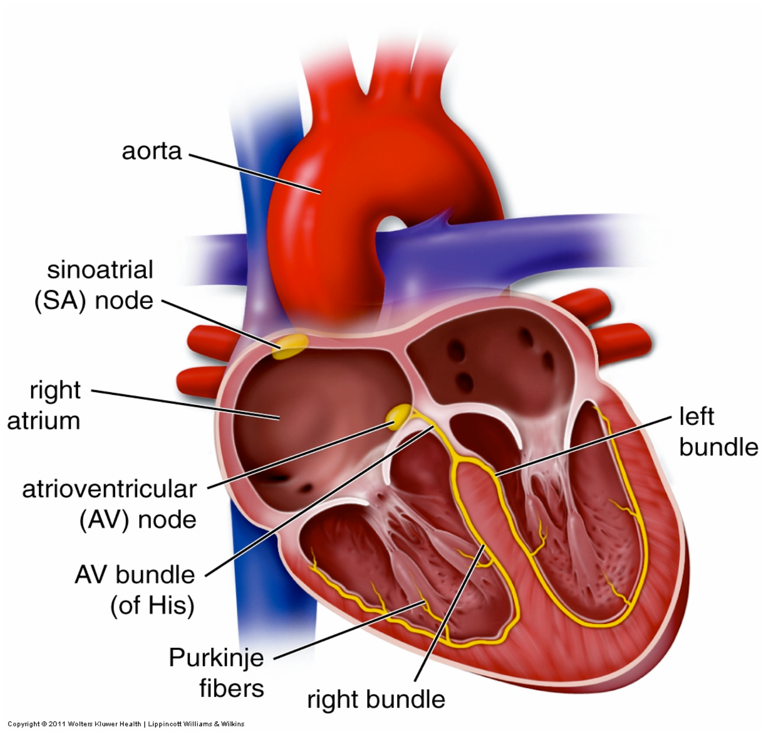

Figure 2: Drawing showing the impulse conducting system of the heart. Note the locations of the SA node, the AV node, the main (AV) bundle of His, the left and right branches of the bundle of His, and Purkinje fibers in both ventricles. Also in both ventricles papillary muscles can be seen connecting to the cuspid valves. (From Histology: A Text and Atlas by Ross and Pawlina)

III. The Blood Vasculature

From the heart the blood first enters large **elastic arteries,** then passes in order through **muscular (distributing) arteries**, **arterioles**, **capillaries**, **venules** (**small veins**), **medium size veins**, and finally **large veins** before returning to the heart. As described below and detailed in Table 1 at the end of the notes, each of these vessel types has a characteristic structure closely related to its distinctive functions.

Typically blood flows from arteries to capillaries directly to veins. However, in some places in the body there are **portal systems**, where two capillary beds are connected by either a vein or an artery. Examples of portal systems include: (1) veins between capillary beds in the small intestine and the capillary network in the liver, (2) arterioles between specific capillary beds within the kidney, and (3) veins between capillary beds in the hypothalamus and pituitary glands. The functional importance of each of these portal systems will be described later in this course.

Some general features of the vasculature

1. The major components of all blood vessels are cells (epithelial, fibroblasts, smooth muscle) and fibers (collagen, elastic). The distribution and orientation of these components vary among the specific types of blood vessels, depending on the functional roles of that vessel.

2. The walls of all arteries (as well as medium and large veins) contain three layers: the **tunica intima** (inner), **tunica media** (middle), and **tunica adventitia** (outer), which are continuous with the endocardium, myocardium and epicardium of the heart, respectively. The connective tissue of the adventitia blends into the surrounding connective tissue of body. The media and adventitia are essentially absent in capillaries and small veins.
3. The luminal lining of all blood vessels (inner layer of the intima) is an endothelium. The endothelium is a simple squamous epithelium in almost all vessels except for a few notable exceptions in the spleen and lymph node, which will be discussed later in the course.
4. For a given lumen diameter, arteries generally have thicker walls than veins. Specifically, arteries have thicker media than do veins.
5. The orientation of smooth muscle cells in the media is primarily circumferential, whereas in the adventitia the muscle cells primarily have a longitudinal orientation.
6. Veins are the lowest pressure vessels of the vascular tree.
7. The velocity of blood flow is smallest in the capillaries, maximizing trans-epithelial movement of gases, nutrients, or waste products.

Structural details of the vessels

Let us now consider the structural features, as related to functional roles, for all the major vessels in the body, starting with the large arteries leaving the heart and ending with the large veins returning to the heart.

1. Arteries

The arteries are the distribution tubes of the cardiovascular system. They branch into vessels of smaller and smaller diameter, but with their total cross-sectional area constantly increasing. Therefore the flow rate decreases as one goes from large to small arteries and then to the capillaries.

Elastic arteries

The largest diameter arteries coming directly from the heart (aorta and pulmonary artery) are termed **elastic arteries**. Blood pressure is not constant as it enters the vasculature; it is higher during systole, when the ventricles contract, and drops during diastole as the ventricles relax and are refilled. In the vasculature the pressure is evened out by expansion of the walls of elastic arteries during systole and release of that stored energy by elastic recoil during diastole.

Elastic arteries contain a well-defined intima containing an endothelium with underlying fibrous connective tissue. The specialization of elastic arteries is most evident in the organization of the media, which consists of alternating layers of smooth muscle and fenestrated layers of elastin, with as many as 60 interdigitating layers of smooth muscle and fenestrated elastic tissue found in the largest elastic arteries. The elastic connective tissue layers of the media are primarily secreted by these smooth muscle cells, which are therefore critical to normal repair of the arterial wall. The adventitia of elastic arteries is relatively thin, with loose connective tissue containing small arteries that break up into capillary plexuses in the outer layer of the media. This vascular supply is termed the **vasa vasorum** (blood vessels of the blood vessels).

Muscular arteries

Muscular arteries act to control the distribution of blood among the organs. They also modulate blood pressure by changing their luminal diameters by actively contracting or relaxing the smooth muscle in their walls.

Muscular arteries have an intima consisting of an endothelium and underling connective tissue, a media containing primarily circumferentially oriented smooth muscle cells, and a rather thick adventitia with fibroblast and elastic and collagen fibers. A key and distinctive structural feature of muscular arteries is the presence of both an **internal elastic lamina** (**IEL**), located between the intima and media, and an **external elastic lamina** (**EEL**), located between the media and adventitia. These elastic laminae (sometimes called membranes) are compact layers of fenestrated elastic sheets that appear as dense wavy lines in cross section and can be clearly seen in your webslides.

Arterioles (small arteries)

Arterioles, which distribute blood flow within specific regions of the organs, vary considerably in size and structure. In large arterioles a distinct internal elastic lamina can be observed between the intima and media, and several layers of concentric smooth muscle cells are present in the media. For small arterioles no IEL is present, the media can consist of only a few layers of smooth muscle cells, and the adventitia consists of loose connective tissue that is indistinguishable from the surrounding CT.

2. Capillaries

Capillaries are the smallest diameter vessels, with diameters frequently so small (3.5 to 5 μm) that erythrocytes moving within them stack and deform. Other capillaries can be 6 to 9 μm in diameter, with the size of capillaries in a given section depending on how the tissue was processed. While there is no media or adventitia in capillaries, pluripotent cells known as **pericytes** are occasionally found underneath the endothelial basal lamina. These pericytes are able to proliferate and differentiate into endothelial or smooth muscle cells. The thin wall of capillaries is designed to permit nutrients to pass from the blood stream to cells, and also enable the products of cell metabolism and endocrine hormones to pass to the blood stream.

Basic types of capillaries include **continuous** and **fenestrated**. Continuous capillaries, which have an uninterrupted endothelium with a continuous basal lamina, are found in smooth, skeletal, and cardiac muscle, lung, and skin. Fenestrated capillaries, which contain permanent pores about 100 nm in diameter passing through the cell, are found in renal glomeruli and endocrine glands where, as you will learn later, there is trans-endothelial passage of renal filtrate and hormones, respectively.

3. Veins

In general, veins have less organized walls than do arteries. Usually the media of veins are considerably thinner than the media of corresponding arteries with similar diameters.

Venules (small veins)

Venules drain capillary networks and are distinguished from capillaries by their larger luminal diameters. These vessels simply have an intima lined by endothelium surrounded by loose connective tissue.

Most veins have a continuous endothelium. However, as you will learn later in this course, specialized sinusoids in the spleen and liver have a **discontinuous endothelium**, characterized by gaps between adjacent epithelial cells.

Medium veins

The **medium veins** also contain an endothelium surrounded by a thin layer of connective tissue. The media consists mostly of smooth muscle and some collagenous fibers and fibroblasts. The adventitia is often as thick or thicker than the media and is composed of loose connective tissue.

Large Veins

Large veins have a relatively well-developed intima due to a heavy subendothelial connective tissue layer, and can contain an internal elastic lamina. The media, consisting mainly of smooth muscle, is usually thinner than the adventitia. The muscularity of the media of large veins varies with hydrostatic load; head veins, which drain by gravity, are nearly devoid of smooth muscle, whereas propulsive veins can exhibit some concentric smooth muscle in the media. Considerable longitudinally oriented smooth muscle can be found in the adventitia, particularly in large veins stressed by pressure, stretch or flexion, such as the inferior vena cava, as seen in your Webslide 23A. **Valves** are found in many medium and large veins and serve to maintain blood flow towards the heart. These valves, which point towards the heart, are semilunar infoldings of the intima that contain elastic and collagenous fibers.

IV. The Lymphatic System

The lymphatic system drains excess interstitial fluid (lymph), which is not reabsorbed at the venous ends of capillaries, and transports it to the systemic circulation. The lymphatic circulation begins at blind-ended capillaries and ends at the thoracic and the right lymphatic ducts that drain into the subclavian and internal jugular veins, respectively.

In addition to beginning as open blind-ended tubes, lymphatic capillaries differ from blood capillaries in several aspects. In general, they exhibit larger diameters, have an incomplete basal lamina (so that the diffusion of large macromolecules and leukocytes is not severely inhibited), and lack associated pericytes. These thin-walled vessels do not collapse because of a set of anchoring filaments that extend from the outer surface to the surrounding connective tissue. In normal histological sections, larger lymph vessels are not easily distinguished from veins. However, in non-perfused and well-fixed sections, lymph vessels can be distinguished from blood vessels by the absence of erythrocytes, higher frequency of valves, and thinner coats of smooth muscle.

The role of the lymphatic system and lymph nodes in the immune response will be covered in detail in the Lymphatic System lectures and lab.

V. Summary Table of the Blood Vessels

TABLE 10-1. Summary of Vascular System

	Large arteries, > 1 cm	Medium-sized arteries, 1 cm-0.5 mm	Small arteries, 0.5 mm-20 µ	Capillaries, 4-12 µ	Small veins, 20 µ-1 mm	Medium veins, 1 mm-1 cm	Large veins, > 1 cm
Intima (longitudinal)......	Thick, endothelium polygonal, collagenous and elastic fibers	Thin, endothelium, collagenous and elastic fibers, Internal elastic membrane	Endothelium, basement membrane, Internal elastic membrane	Endothlium, flat, basement membrane	Endothelium, collagenous fibers	Endothelium, collagenous and elastic fibers	Endothelium, collagenous and elastic fibers
Media (circular)..............	Elastic membranes, collagenous fibers, smooth muscle	Smooth muscle, collagenous and elastic tissue, external elastic membrane	Smooth muscle, collagenous and elastic fibers		Over 45 µ, smooth muscle cells which become continuous layer at 200 µ	Thin, some smooth muscle, collagenous fibers	Poorly developed
Adventitla (longitudinal).............	Relatively thin, collagenous and elastic tissue	> media, collagenous and elastic tissue	Loose collagenous tissue		At 300 µ elastic and collagenous tissue	> media, smooth muscle, collagenous and elastic tissue	Much > media, elastic and collagenous tissue, smooth muscle
Smooth muscle/diameter......... ...	+ +	+ + − + + +	+ + + − + + + +	0	± − +	+	+ − + +
Elastic tissue....................	+ + + +	+ + − +	+ − ±	0	± − +	+	+ +
Vasa vasorum................	+ +	+	0	0	0	+ + − +	+ + +
Lymphatics................	+ +	+	0	0	0	+ +	+ + +
Blood pressure................	100 mm Hg	90-75	75-35	35-15	15-8	8-4	4-0
Velocity of flow.................	300 mm/sec	↓	↓ ↓	↓ ↓ ↓ 5 mm/sec	↑	↑ ↑	↑ ↑ 60 mm/sec
Cross-sectional area....	x	————	————→		————	————→	2x
Permeability..............	±	± − +	+ − + +	+ + + +	+ + +	+ +	+ +