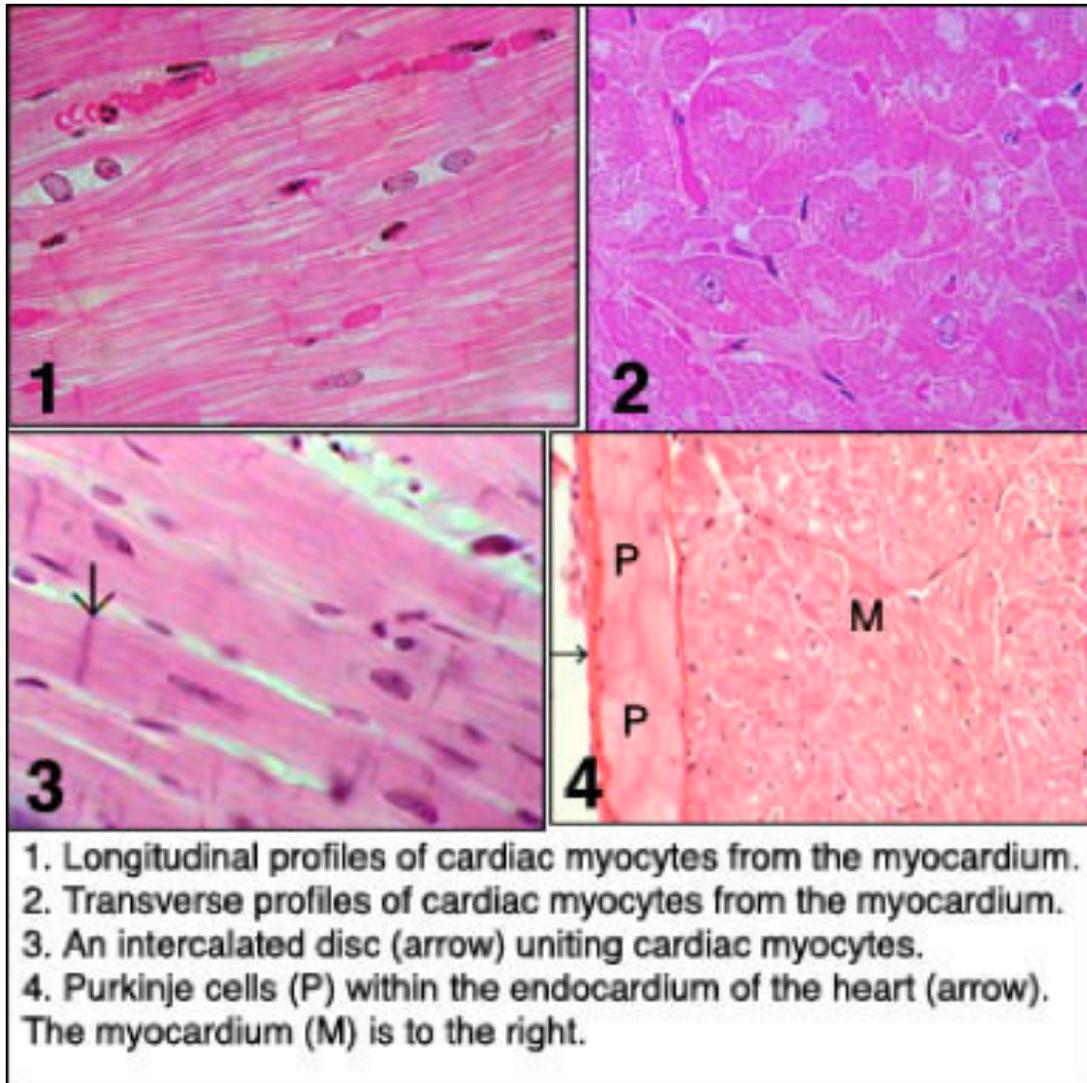


Heart



The heart is a modified blood vessel that serves as a double pump and consists of four chambers. On the right side, the atrium receives blood from the body and the ventricle propels it to the lungs. The left atrium receives blood from the lungs and passes it to the left ventricle, from which it is distributed throughout the body. The wall of the heart consists of an inner lining layer, a middle muscular layer, and an external layer of connective tissue.

Endocardium

The endocardium forms the inner lining of the atria and ventricles and is continuous with and comparable to the inner lining of blood vessels. It consists of a single layer of polygonal squamous (endothelial) cells with oval or rounded nuclei. Tight (occluding) junctions unite the closely apposed cells, and gap junctions permit the cells to communicate with one another. Electron micrographs show a few short microvilli, a thin proteoglycan layer over the luminal surface, and the usual organelles in the cytoplasm. The endothelial cells rest on a continuous layer of fine collagen fibers, separated from it by a basement membrane. The fibrous layer is called the subendothelial layer. Deep to it is a thick layer of denser connective tissue that forms

the bulk of the endocardium and contains elastic fibers and some smooth muscle cells. Loose connective tissue constituting the subendocardial layer binds the endocardium to the underlying heart muscle and contains collagen fibers, elastic fibers, and blood vessels. In the ventricles it also contains the specialized cardiac muscle fibers of the conducting system.

Myocardium

The myocardium is the middle layer of the heart and consists primarily of cardiac muscle. The myocardium is a very vascular tissue with a capillary density estimated to be about 2800 capillaries per mm² as compared to skeletal muscle, which has a capillary density of about 350 per mm². The capillaries completely surround individual cardiac myocytes and are held in close apposition to them by the enveloping delicate connective tissue that occurs between individual muscle cells. The myocardial capillaries are normally all open to perfusion unlike those of other tissues in which a certain percentage are closed to perfusion. In these other tissues as activity increases so does the number of capillaries open to perfusion. The myocardium is thinnest in the atria and thickest in the left ventricle. The myocardium is arranged in layers that form complex spirals about the atria and ventricles. In the atria, bundles of cardiac muscle form a latticework and locally are prominent as the pectinate muscles, while in the ventricles, isolated bundles of cardiac muscle form the trabeculae carnea. In the atria, the cardiac muscle cells are smaller and contain a number of dense granules not seen elsewhere in the heart. These myocytes have properties associated with endocrine cells. They are most numerous in the right atrium and release the secretory granules when stretched.

The granules contain atrial natriuretic factor (ANF), released in response to increased blood volume or increased venous pressure within the atria. Atrial natriuretic factor acts on the kidneys causing vasoconstriction of the afferent arteriole, which increases both glomerular filtration pressure and filtration rate. ANF also acts on the distal and collecting tubules of the kidneys to decrease sodium and chloride resorption and inhibits the secretion of antidiuretic hormone (ADH), aldosterone, and renin. These actions result in increased sodium chloride excretion (natriuresis) in a large volume of dilute urine. Elastic fibers are scarce in the ventricular myocardium but are plentiful in the atria, where they form an interlacing network between muscle fibers. The elastic fibers of the myocardium become continuous with those of the endocardium and the outer layer of the heart (epicardium).

Cardiac muscle cells contract spontaneously (self-excitation) in response to intrinsically generated action potentials, which are then passed to neighboring cardiac myocytes via gap (communicating) junctions located within the intercalated discs. The action potentials are generated by ion fluxes mediated by ion channels in the plasmalemma and T-tubule system of the cardiac muscle cell. The prolonged plateau of the action potential observed during the contraction of cardiac myocytes lasts up to 15 times longer than that observed in skeletal muscle cells. The action potential, as in skeletal muscle, is caused in part by the sudden opening of large numbers of fast sodium ion channels that allow sodium ions to enter the cardiac myocytes. These ion channels remain open only for a few 10,000th of a second and then close. In skeletal muscle, repolarization then occurs and the action potential is over within 10,000th of a second. In cardiac muscle, the opening of two types of ion channels causes the action potential: (1) the fast sodium ion channels as in skeletal muscle and (2) slow calcium channels (calcium-sodium channels). The latter are slower to open and remain open for a much longer period of time. When open both calcium and sodium ions enter the cardiac myocyte and maintain the prolonged period of depolarization resulting in the elongated plateau of the action potential. The permeability of the plasmalemma to potassium ions also decreases

during this period as a result of the calcium influx and prevents an early return of the action potential to a resting level as occurs in skeletal muscle.

A considerable quantity of calcium ion enters the myocyte sarcoplasm from the extracellular fluid by passing through the surrounding plasmalemma and that of T-tubules at the time the action potential is generated. The large diameter of the T-tubules allows the same extracellular fluid containing calcium ion surrounding cardiac myocytes to enter the T-tubule system and be available in the cell interior. The influx of calcium ion that occurs during the development of the action potential is not sufficient to cause contraction of the cardiac myocyte. The entering calcium ion binds to channel proteins of the sarcoplasmic reticulum an event that triggers the release of stored calcium, which in turn initiates cardiac myocyte contraction. For this reason the calcium ion entering at the time the action potential is generated is referred to as trigger calcium. The mechanism of contraction of the cardiac myocyte is similar to that of skeletal muscle.

Epicardium

The epicardium is the visceral layer of the pericardium, the fibrous sac that encloses the heart. The free surface of the epicardium is covered by a single layer of flat to cuboidal mesothelial cells, beneath which is a layer of connective tissue that contains numerous elastic fibers. Where it lies on the cardiac muscle, the epicardium contains blood vessels, nerves, and a variable amount of fat. This portion is called the subepicardial layer. The parietal layer of the epicardium consists of connective tissue lined by mesothelial cells that face those covering the visceral epicardium. The two epithelial lined layers are separated only by a thin film of fluid, produced by the mesothelial cells, that allows the layers to slide over each other during contraction and relaxation of the heart.

Conducting System

The conducting system of the heart consists of specialized cardiac muscle fibers (cells) and is responsible for initiating and maintaining cardiac rhythm and for ensuring coordination of the atrial and ventricular contractions. The system consists of a sinoatrial node, an atrioventricular node and atrioventricular bundle, and Purkinje fibers. Cardiac myocytes, including those of the conducting system, have an initial resting membrane potential of about -90 millivolts that is established by the movement of potassium ions from within the sarcoplasm of the myocyte to the surrounding interstitial fluid. Each cardiac cycle is initiated by the spontaneous generation of an action potential by cardiac muscle cells forming the sinoatrial node. The sinoatrial node is located in the epicardium at the junction of the superior vena cava and right atrium and forms an ellipsoid strip about 13 mm long and 3 mm wide. Nodal cells are smaller than ordinary cardiac muscle cells and contain fewer and more poorly organized myofibrils. Intercalated discs are lacking between cells of the sinoatrial nodes. Because of the high sodium ion concentration in the surrounding extracellular fluid, these ions normally tend to leak into the sinus muscle fibers. It is the inherent leakiness of the plasmalemma of sinus nodal fibers to sodium ions through special sodium ion channels (If channels) that is related to the self-excitation phenomenon. As a result of this leakage, the resting membrane potential of the sinus nodal fibers is lower (-55 to -60 millivolts) in comparison with normal cardiac myocytes of the ventricles (-85 to -90 millivolts). As a result of the less negativity of the resting potential, the fast sodium channels are generally inactive and only the slow calcium-sodium channels open resulting in the development of an action potential. The ends of the cardiac muscle fibers

constituting the sinoatrial node are linked directly to the adjacent ordinary atrial cardiac muscle cells. The spontaneously generated action potential initiated in the node cells then spreads throughout the entire atrial muscle mass to the atrioventricular node located in the posterior wall of the right atrium behind the tricuspid valve and adjacent to the opening of the coronary sinus. Here the action potential is delayed allowing enough time for the atria to empty completely their contained blood into the ventricles before ventricular contraction begins. The sinoatrial node controls the heart beat because its rate of rhythmical discharge is greater than any other region of the heart. Because of the faster discharge rate, nodal cell activity overrides all other potential pacemaker activity by other cells (cells of the atrioventricular node, Purkinje cells) in the heart. Thus, the sinoatrial node functions as the “pacemaker” of the heart.

It is the cardiac muscle tissue of the atrioventricular node that delays the transmission of the cardiac impulse and functions as “gate keeper” for the continued conduction of the impulse into the ventricles. The cardiac myocytes of the atrioventricular node are the slowest conducting fibers in the heart. From here, impulses travel rapidly along the atrioventricular bundle in the membranous part of the interventricular septum. The bundle divides into two trunks that pass into the ventricles, where they break up into numerous twigs that connect with the ordinary cardiac muscle fibers. Thus, the impulse is carried to all parts of the ventricular myocardium. The specialized fibers of these trunks and branches are called Purkinje fibers (cells) and differ from ordinary cardiac muscle in several respects. Purkinje fibers are larger and contain more sarcoplasm, but myofibrils are less numerous and usually have a peripheral location. The fibers are rich in glycogen and mitochondria and often have two (or more) nuclei. Intercalated discs are uncommon, but numerous desmosomes are scattered along the cell boundaries. Purkinje fibers are the fastest conducting fibers in the heart. It is the action potential of the cardiac myocytes throughout the heart that is traced in a normal electrocardiogram (ECG). In a normal ECG the P wave represents atrial depolarization, the QRS wave complex represents ventricle depolarization and the T wave represents repolarization of the ventricle.

The autonomic nervous system influences (modulates) heartbeat. Axons of postganglionic parasympathetic neurons terminate in the tissue of sinoatrial and atrioventricular nodes. Acetylcholine released by these nerve terminals binds to muscarinic acetylcholine receptors (G-protein-linked receptors that inhibit adenylate cyclase and decrease adenosine monophosphate (c-AMP) levels) and decreases heart rate. In contrast, axons of postganglionic sympathetic neurons distributed in the myocardium release norepinephrine which binds to α -adrenergic receptors (G-protein-linked receptors that stimulate adenylate cyclase and increase c-AMP levels) and increase heart rate.

Cardiac Skeleton

The ventricles of the heart are not emptied as other hollow organs, but blood is wrung from their cavities much like water from a soaked towel. The heart has a fibrous skeleton organized in a complicated three-dimensional continuum of dense connective tissue to which its musculature anchors. The main portion of the cardiac skeleton is formed by the annuli fibrosi, rings of dense connective tissue that surround the openings of the aorta, pulmonary artery, and the atrioventricular orifices. Of these, the aortic ring is the strongest. Also contributing to the cardiac skeleton are triangular thickenings of fibrous connective tissue, the trigona fibrosi (left and right) that link the aortic root to the atrioventricular annuli and the septum membranaceum, which is the upper fibrous part of the interventricular septum. The trigona fibrosa in some instances may contain cartilage-like material and in old age may undergo calcification. In addition to providing attachment for the cardiac musculature and components of the valves,

the annuli fibrosi provide support for and maintain the integrity of all four orifices. Without these rings of support the orifices would stretch and the valves would be unable to function properly. The position of the annuli fibrosi around the atrioventricular orifices also provides a physical barrier separating the myocardium of the atria and ventricles. In doing so, the only electrophysiological link between them is the specialized conducting tissue of the atrioventricular bundles, thus ensuring the orderly sequence of events associated with the cardiac cycle.

Valves

Valves are present between the atria and ventricles and at the openings to the aorta and pulmonary vessels. Regardless of their location, the valves are similar in histologic structure. The atrioventricular valves are attached to the annuli fibrosi, the connective tissue of which extends into each valve to form its core. The valves are covered on both sides by endocardium that is thicker on the ventricular side. Scattered smooth muscle cells are present on the atrial side of the valves, while on the ventricular side elastic fibers are prominent. Thin tendinous cords called chordae tendineae attach the ventricular sides of the valves to projections of cardiac muscle called papillary muscles. Semilunar valves of the pulmonary arteries and aorta are thinner but show the same general histologic structure as the atrioventricular valves.

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