Preferential conduction pathways - 2017

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Many authors use the non-compromising term of "preferential conduction pathways" (not bundle branchs).
It is clear in the territory of the mentioned preferred routes there are Purkinje cells and gap junctions.
After initial SAN excitation, depolarization spreads throughout the atria. The exact mechanisms involved in the spread of impulses (excitation) from the SAN across the atria are still today, somewhat controversial (1,2).
However, it is generally accepted that: The spread of depolarizations from nodal cells can go directly to adjacent myocardial cells; and Preferentially ordered myofibril pathways allow this excitation to rapidly transverse the right atrium to both the left atrium and the atrioventricular node.
It is believed by many that there are three preferential conduction pathways from the SAN to the AVN (1,18). In general, these can be considered as the shortest electrical routes between the nodes. Note that there are microscopically identifiable structures, appearing to be preferentially oriented fibers, that provide a direct node-to-node pathway. In some hearts, pale staining Purkinje-like fibers have also been reported in these regions.
More specifically, the anterior preferential conduction pathways is described as extending from the anterior part of the SAN, bifurcating into the so-called Bachmann's pathway which importantly delivers impulses to the left atrium and with a second preferential conduction pathways that descends along the interatrial septum that connects to the anterior part of the AVN.
The middle (or Wenckebach's pathway) extends from the superior part of the SAN, runs posteriorly to the superior vena cava, then descends within the atrial septum, and may join the anterior preferential conduction pathways as it enters the AVN.
The third preferential conduction pathways is described as being posterior (Thorel's) which, in general, is considered to extend from the inferior part of the SAN, passing through the crista terminalis and the Eustachian valve past the coronary sinus to enter the posterior portion of the atrioventricular node.
In addition to excitation along these preferential conduction pathways, general excitation spreads from cell to cell throughout the entire atrial myocardium via the specialized connections between cells, the gap junctions,

that typically exist between all myocardial cell types In contrast to tight and adherens junctions, gap junctions do not seal membranes together, nor do they restrict the passage of material between membranes.
Rather, gap junctions are composed of arrays of small channels that permit small molecules to shuttle from one cell to another and thus directly link the interior of adjacent cells.
Importantly, gap junctions allow electrical and metabolic coupling among cells because signals inititated in one cell can readily propagate to neighboring cells. In general, the upper limit for passage through gap junctions is roughly 1000 daltons (Da).
Aside from ions, important examples of molecules that readily pass include cyclic AMP (329 Da), glucose-6-phosphate (259 Da) and nucleotides (250-300 Da).
Gap junctions are seen with an electron microscope as patches of varying size where the plasma membranes of neighboring cells are separated by a beautifully uniform gap, roughly 2-3 nm in width.
The gap reflects areas of the two membranes that are connected by hexagonal tubes called connexons which form aqueous pores roughly 2 nm in diameter between the two cells. The major protein in purified preparations of gap junctions is connexin, which, when expressed in cells that normally do not have gap junctions, allows them to form. Different species of connexin are seen in different organisms and among different tissues within an organism.
However, all connexins share a common structure of having four membrane-spanning domains.
A connexon is formed from six connexin molecules which extend a uniform distance outside the cells. Alignment of connexons from each cell across the gap results in the formation of the pores which functionally define the gap junction.
Gap junctions are dynamic structures because connexons can open and close. Elevated intracellular calcium and low intracellular pH are established stimuli for rapid closing of connexons.
This may of importance when one cell within a group becomes damaged - the idea is that closing the gap junctions in the damaged cell would effectively isolate that cell and prevent spreading of the injury. Gap junctions are seen in virtually all cells that contact other cells in tissues, which of course includes pretty much all cells in the body. Some representative examples of their importance in physiology include:

· - Electrical coupling: Gap junctions are abundant in cardiac and smooth muscle.

- Depolarization of one group of muscle cells rapidly spreads to adjacent cells, leading to well-coordinated contractions of those muscles.

- Metabolic coupling: Many hormones act by elevating intracellular concentrations of cyclic AMP, which initiates a signalling pathway inside the cell. Cyclic AMP readily passes through gap junctions and thus, hormonal stimulation of one cell can lead to signal propagation to a cluster of cells.

Gap junctions are specialized membrane regions which directly connect the cytoplasmic compartments of two adjacent cells and enable intercellular communication.
Cardiac gap junction channels constitute the basis for the electrical syncytial properties of the heart and propagation of the action potential. The gap junction channel is formed by two connexons which are located on adjacent myocytes and consist of six proteins (connexins). Two major isoforms of connexins with a molecular weight of 40 and 43 kDa are specific for the cardiac tissue, with connexin 40 predominantly expressed in the atrial myocardium and the conduction system.
In addition, connexin 45 is found in conduction tissue. Increased dephosphorylation of connexins secondary to inhibition of protein kinases, activation of phosphatases, or a loss of ATP increases the turnover of connexins and causes functional changes of connexin proteins.
Remodelling of gap junctions associated with a decrease in the expression and/or redistribution of connexins leads to impaired intercellular communication and reduced conductance between cardiomyocytes.
There is evidence that links connexin 40 polymorphism (specifically, lack of connexin 40) to enhanced atrial vulnerability and increased risk of AF. Local angiotensin II can modify gap junction properties and losartan has been shown to prevent worsening of cell communication in cardiomyopathy.
This effect is mediated by an increase in gap junctional conductance and by the reduction of interstitial fibrosis. Among traditional anti-arrhythmic drugs, only tedisamil has been reported to enhance gap junctional conductance at early stages of cardiomyopathy in hamsters, by activating adenylcyclase and consequent phosphorylation of connexins. This prompted interest in agents

that specifically increase gap junction conductance via activation of protein kinase C and enhanced phosphorylation of connexins.

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