Veterinary Bioscience: Cardiovascular System

WEEK 1 – THE HEART IN THE THORAX

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INTENDED LEARNING OUTCOMES

At the end of this lecture, you should be able to:

- Explain how the electrical and mechanical activity of the heart are linked to achieve effective pumping.
- In particular, at the end of this lecture you should be able to:
- Describe the cellular and subcellular structures responsible for cardiac muscle cell contraction
- Identify salient features of cardiac muscle tissue and conducting tissue in prepared histological specimens
- Define and describe the excitation-contraction process.

KEYWORDS

Actin, Cardiac myocyte, endocardium, epicardium, myocardium, Purkinje fibre, sarcolemma, sarcoplasmic reticulum, T tubule, myosin, troponin, isometric contraction, isotonic contraction.

LECTURE 4 – STRUCTURE FUNCTION RELATIONSHIPS IN THE HEART 2: EXCITATION CONTRACTION COUPLING

HISTOLOGY OF THE HEART

The heart is composed of three layers. From outermost to inner most these are the epicardium, the myocardium and the endocardium. The endocardium has an endothelial layer in contact with the lumen of the heart chamber and two subendothelial connective tissue layers. The myocardium is comprised of cardiac

myocytes, conducting and pacemaker tissue, and the cardiac skeleton. The epicardium covers the exterior of the myocardium and has an outer flattened epithelium of mesothelial cells, supported by an underlying connective tissue layer with elastic fibres and adipose tissue.

STRUCTURE OF MYOCARDIAL CELLS

The structure of cardiac myocytes is fundamentally similar to skeletal muscle cells , but they are smaller than skeletal myocytes, are branched, and are very rich in mitochondria. Cardiac myocytes are connected structurally by desmosomes, and electrically by gap junctions (with pores made up of proteins called connexons). Hence cardiac myocytes form a *functional syncytium.* As in skeletal muscle, the contractile elements of cardiac myocytes are actin and myosin filaments arranged in sarcomeres. Another distinctive feature of the cardiac myocyte is the sarcolemma (cell membrane) that is invaginated to form transverse (T) tubular system. This ensure rapid conduction of the action potential across the entire myocyte. Internally, the sarcoplasmic reticulum (SR) forms terminal cisternae close to, but separated by a narrow gap from T tubules. A very extensive capillary system ensures that metabolism in cardiac myocytes is aerobic.

Contractility is defined as the ability of cardiac muscle to generate force for any given fibre length. **This is primarily dependent on the way that the cell handles calcium.**

INITIATION OF CONTRACTION: EXCITATION/CONTRACTION COUPLING

Cardiac muscle contracts when intracellular Ca^{++} increases above 100nM, in response to an action potential. i.e the **rise in Ca that occurs during the action potential couples the action potential to the contraction**.

- During plateau phase of action potential, Ca enters cell through **L-type voltage gated calcium channels** in the cell membrane (sarcolemma). (The amount of calcium entering the cell is less than 20% of total rise in intracellular Ca.)
- This slight rise in intra-cellular Ca concentration activates **Ca-sensitive release channels** (ryanodine receptor channels) in the sarcoplasmic reticulum, through which stored Ca floods the cytoplasm.
- The rapid increase in Ca concentration leads to contraction. The process is called **calcium-induced calcium release.**
- The amount of Ca^{++} release (and hence force of contraction) depends on how much Ca^{++} is stored in the sarcoplasmic reticulum and the number of release channels activated, hence how much Ca^{++} enters the cell.

GENERATION OF TENSION

This depends on a cross bridging mechanism as for skeletal muscle. In cardiac muscle, intracellular Ca concentration controls cross-bridge formation via the regulatory proteins troponin and tropomyosin

When intracellular Ca concentration rises, Ca binds to troponin, leading to shifting of tropomyosin out of the actin cleft, and exposing myosin binding sites on actin filaments. When binding sites are uncovered, myosin crossbridges form, and tension develops. Tension is related to number of crossbridges formed and will increase until all troponin C is bound to Ca.

RELAXATION MECHANISMS

When $[Ca^{++}]_i$ rises above resting level, Ca pumps in the sarcoplasmic reticulum (**Ca-ATPase pumps**) are activated, and start to pump Ca back from the cytosol into the SR. As the membrane repolarises and voltage gated Ca channels close, the calcium transporter reduces cytosolic Ca towards resting levels. However, a mechanism is needed to extrude Ca from cell, otherwise with each action potential more Ca would enter cell. Excess Ca is transported out of the cell by a Na^+/Ca^{++} exchanger in the cell membrane.

CARDIAC MUSCLE CELL MECHANICS

Cardiac muscle contracts isometrically or isotonically at different phases of the cardiac cycle. When cross-bridges develop in an activated muscle, the muscle can either develop force at a fixed length (an **isometric contraction**) or shorten (an **isotonic contraction**). Which of these happen depends on the external constraints placed on the muscle.

Isometric contraction: The force developed in an isometric contraction is a measure of its maximum ability to produce tension.

Isotonic (fixed tension) contraction: activating an unrestrained muscle causes it to shorten without force development, as it has nothing to develop force against. Under these conditions a muscle shortens with maximal velocity. Adding load to the muscle decreases the velocity and extent of its shortening. **Fractional shortening** is a measure of the capacity of cardiac muscle to contract against a force, and hence a useful measure of cardiac myocyte function.

THE CONCEPTS OF PRELOAD AND AFTERLOAD:

Preload is the degree of tension on a muscle when it begins to contract. For cardiac contraction, preload is generally considered to be the volume of blood in the ventricle at the end of diastole, (i.e. end diastolic volume). Afterload is the load against which the muscle exerts its contractile force. (i.e. arterial blood pressure)

The importance of these concepts lies in the fact that the nature of contraction of cardiac muscle depends on pre and after load, and that pre and after load can vary both in physiological and pathological states.

FURTHER READING

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