Introduction

The sinoatrial node (SA node) is a natural pacemaker. It starts the electrical signal that travels across the upper 2 chambers or atria of the heart to the atrioventricular node (AV node).

The AV node transfers the electrical signal from the upper part of the heart to the lower 2 pumping chambers or ventricles. The bundle branches are specialized tissues that help send electrical impulses through the ventricles. This makes a normal heart beat, called normal sinus rhythm ***(Rubart and Zipes, 2012)***.

There are two major types of arrhythmias, tachyarrhythmia (the heart rate is too fast more than 100 beats per minute), and bradyarrthymia (the heart rate is too slow less than 60 beats per minute).

Tachyarrhythmia are classified according to the site of impulse generation in relation to the atrioventricular (AV) conduction system. Supraventricular tachycardias (SVT) originate above AV node and have normal QRS duration (=0.12 seconds). While ventricular tachycardias originate below AV node and have prolonged QRS duration. Each type of tachycardia can then be subdivided according to regularity of the rhythm ***(Zimetbaum, 2012)***.

Bradyarrythmias are classified to sinus bradycardia, sinus arrest and atrioventicular block which further subdivided into first, second and third degree heart block ***(Wellens, 2007).***

Artificial pacemakers are electronic devices that stimulate the heart with electrical impulses to maintain or restore a normal rhythm in people with slow heart rhythms. A variety of types of pacemakers have been developed to restore or sustain a regular heartbeat in different ways.

Temporary pacemakers are intended for short-term use during hospitalization. While Permanent pacemakers are those intended for long-term use. Pacemakers may be single, dual, or triple chambered ***(Gillis et al., 2012).***

Emergency indications of temporary pacemakers are acute myocardial infarction with asystole, symptomatic bradycardia, bilateral bundle branch block (BBB) or Mobitz type II second-degree AV block. Further indications are terminating ventricular tachyarrhythmia secondary to bradycardia and suppression of drug-resistant ventricular tachyarrhythmia or supraventricular tachycardia. Cardiac surgeries such as Aortic surgery, Tricuspid surgery and ventricular septal defect closure are also indication to use pacemaker ***(McCann, 2007)***.

Pacemakers may cause undesirable complications during and after implantation. Complications associated with the implantation procedure are uncommon, but include bleeding,

infection, or collapsed lung. Pacemaker complications can be divided into acute (immediate) or chronic according to implantation time (or date). Lead or pocket complications according to the site of complication and implantation or system failure ***(Gul and Kyrak, 2011).***

Aim of the Work

The purpose of this study is to discuss electrophysiology of heart. Mechanisms and classifications of arrhythmia. Types, modes, indications, complications and problems of artificial pacemaker.

Chapter (I):
Electrophysiology of the Heart

The heart wall, which encases the heart, is made up of three layers: epicardium, myocardium, and endocardium. The epicardium, the outermost layer, consists of squamous epithelial cells overlying connective tissue. The myocardium, the middle and thickest layer, makes up the largest portion of the heart's wall. This layer of muscle tissue contracts with each heartbeat. The endocardium, the heart wall's innermost layer, consists of a thin layer of endothelial tissue that lines the heart valves and chambers ***(Follin and Moundin, 2006).***

The heart is composed of three major types of cardiac muscle: atrial muscle, ventricular muscle, and specialized excitatory and conductive muscle fibers. The atrial and ventricular types of muscle contract in much the same way as skeletal muscle, except that the duration of contraction is much longer. Conversely, the specialized excitatory and conductive fibers contract only feebly because they contain few contractile fibrils; instead, they exhibit either automatic rhythmical electrical discharge in the form of action potentials or conduction of the action potentials through the heart, providing an excitatory system that controls the rhythmical beating of the heart ***(Guyton and Hall, 2010)***.

I-Cardiac cells

There are five functionally and anatomically separate types:

1. Sinoatrial node.
2. Atrioventricular node.
3. His-purkinje system.
4. Atrial muscle.
5. Ventricular muscle

(1) Cardiac muscle:

- Automaticity (chronotropy): the ability to initiate cardiac impulse.
- Conductivity (dromotropy): the ability to conduct an electrical impulse.
- Contractility (inotropy): the ability to contract.
- Lusitropy: the ability to fill and contract.

(Banerjee, 2005).

The heart has two primary functions:

(1) To collect oxygen poor blood and pump it to the lung for release of carbon dioxide in exchange with oxygen.

(2) To collect oxygen rich blood from the lungs to all tissues in the body to provide oxygen in exchange with carbon dioxide ***(Weinhaus and Rubarts, 2009).***

(2) The conducting system:

The heart's electrical impulse originates in the sinoatrial (SA) node, high in the right atrium near the superior vena cava. From the SA node, the impulse spreads radially across both atria. When it reaches the atrioventricular (AV) groove, the impulse encounters the fibrous "skeleton" of the heart, which separates the atria from the ventricles. The fibrous skeleton is electrically inert, and therefore stops the electrical impulse (**Fig-1**) ***(Fogoros, 2007)***.

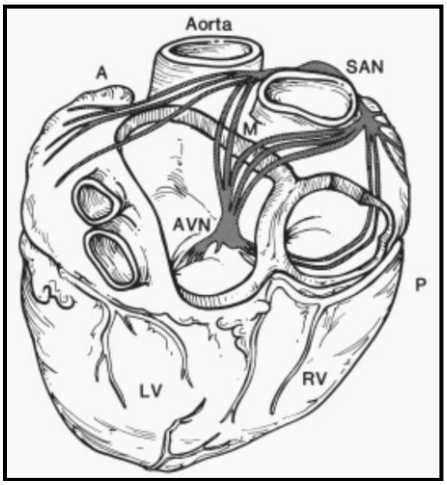

Figure (1): Posterior schematic of the heart with internodal pathways connecting the sinoatrial node and atrioventricular node. A, M, P: are the anterior, middle, and posterior internodal tracts respectively ***(Packer, 2007).***

The only way for the impulse to cross over to the ventricular side is by means of the specialized AV conducting tissues-the AV node and the His-Purkinje system.The AV node conducts electricity slowly; when the electrical impulse enters the AV node, its passage is delayed ***(Tomaselli, 2008)***.

After the impulse leaves the AV node it travels into the specialized infranodal conducting system, that is, through the His bundle, right and left bundle branches, and into the Purkinje network. The Purkinje network extends or fans out throughout the ventricular endocardium. The excellent insulation of the His-Purkinje system facilitates rapid conduction with near-simultaneous activation of the ventricles. Once out of the Purkinje network, the impulse proceeds relatively slowly through cell-to-cell contact through gap junctions from the endocardial to epicardial ventricular surface ***(Zimetbaum and Josphson, 2009).***

II-Cardiac cycle.

The cardiac cycle is a term referring to all or any of the events related to the flow or blood pressure that occurs from the beginning of one heart beat to the beginning of the next (**Fig**.**2**). The frequency of the cardiac cycle is described by the heart rate. Each beat of the heart involves five major stages. The first two stages, often considered together as the "ventricular filling" stage, involve the movement of blood from atria into ventricles. The next three stages involve the movement of blood from the ventricles to the pulmonary artery (in the case of the right ventricle) and the aorta (in the case of the left ventricle).There is a similar cycle on both sides of the heart, but the pressures in the right ventricle and pulmonary arteries are less than those in the left ventricle and aorta. Systole refers to contraction, while diastole refers to relaxation. Both contraction and relaxation can be isometric, when changes in intraventricular pressure occur without a change in length of the muscle fibres ***(Guyton and Hall, 2010)***.

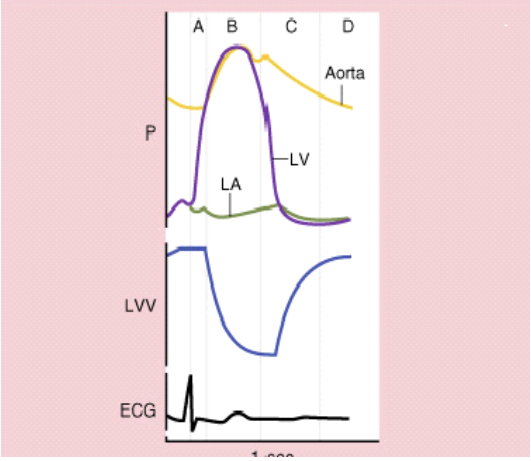

Figure (2): Time sequence of events during a single cardiac cycle. Pressures (P) in the aorta, left ventricle (LV), and left atrium (LA) are shown. The four phases of the cardiac cycle are also illustrated: isovolumic contraction (*A*), ejection (*B*), isovolumic relaxation (*C*), and filling (*D*) ***(Burkhoff and Weisfeldt, 2004***).

At end-diastole, ventricular pressure is at its resting level **(*end-diastolic pressure*)** and ventricular volume is at its maximal value ***(end-diastolic volume).*** Aortic pressure declines gradually during this period as the blood ejected into the aorta during the prior ventricular contraction discharges to the peripheral circulation. Just before the onset of ventricular systole, atrial contraction provides a final boost to ventricular volume. As ventricular contraction begins about 120 milliseconds later, pressure increases inside the ventricular chamber and exceeds the pressure in the atrium; this pressure differential causes the mitral valve to close. Ventricular pressure is still less than that of the aorta, so the aortic valve remains closed. Because both valves are closed, no blood enters or leaves the ventricle during this time; this first phase of the cardiac cycle is called *isovolumic contraction* ***(Markes, 2012)***.

As systole progresses, ventricular pressure eventually exceeds that of the aorta, so the aortic valve opens. As muscular contraction continues, blood is ejected from the ventricle into the aorta, and ventricular volume decreases during the *ejection phase* of the cycle. As contraction of the cardiac muscle reaches its maximal effort (end of systole), ejection ends as ventricular volume reaches its lowest point *(end-systolic volume)* ***(Grant and Durrani, 2009)***.

As the muscles relax, ventricular pressure falls below that in the aorta, and the aortic valve closes. Muscular relaxation proceeds and pressure continues to decrease. Ventricular volume is constant during this phase of *isovolumic relaxation* because both the mitral and aortic valves are closed. Eventually, ventricular pressure falls below the pressure in the left atrium; the mitral valve opens and blood can flow from the atrium into the ventricle during the *filling phase* ***(Packer, 2007)***.

III-Properities of Cardiac ion channels.

Ion channels are large membrane spanning proteins. They provide relatively low resistance pathways for the passive movement of ions across the lipid bilayer ***(Atlee, 2000)***.

Ion channels show ion selectivity, in that they usually allow only one type of ion to pass ***(Garratt, 2001)***.

A change in membrane potential that decreases the electronegativity inside a resting myocyte is called depolarization.

The return of membrane potential toward its resting level in a depolarized myocyte is repolarization, whereas an increase in the resting potential of an unexcited cell is hyperpolarization. Action potentials must include at least two phases (***Fig. 3***): one of depolarization; the other of repolarization. Action potential amplitude, which is usually expressed in millivolts (mV), defines the extent to which cellular electronegativity changes from its resting level, including any reversal to electropositivity ***(Katz, 2011).***

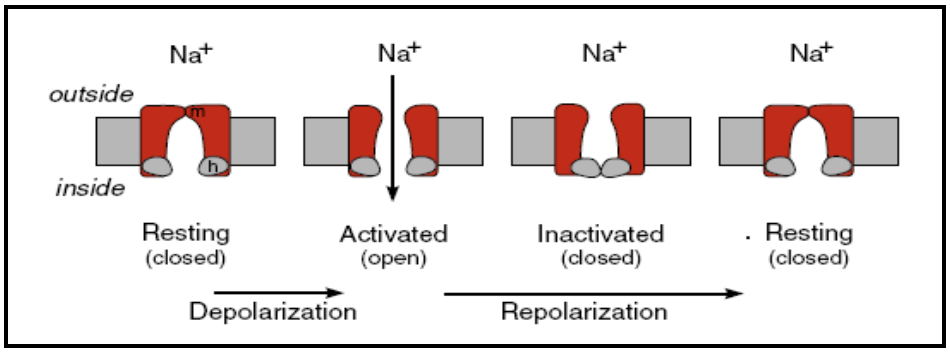

Figure (3): Open and close (activation gates) are closed, although the h-gates (inactivation gates) are open. Rapid depolarization to thresholded states of fast sodium channels in cardiac myocytes. In the resting (closed) state, the m gates opens the m-gates (voltage activated), thereby opening the channel and enabling sodium to enter the cell. Shortly thereafter, as the cell begins to repolarize, the h-gates close and the channel becomes inactivated. Toward the end of repolarization, the m-gates again close and the h-gates open. This brings the channel back to its resting state ***(Klaubande, 2011)***.

An inward current, according to electrophysiological convention, is the flux of charge that would occur if a positive ion moved across the plasma membrane into the cell. Because the interior of the resting cell is negatively charged, inward currents cause depolarization. Most inward currents in the heart are generated when positively charged sodium and calcium ions

enter the cell; however, the outward movement of a negative ion has the same effect on membrane potential as the inward movement of a positive ion, so that the efflux of an anion like chloride also generates an inward current. An outward current can be generated when a positively charged ion leaves the cell interior, or when a negatively charged ion enters the cell. Both increase electronegativity within the cell. In resting cells, outward currents cause hyperpolarization, while outward currents that follow depolarization, and so return membrane potential toward the resting negativity,cause repolarization **(TableI-1)** ***(Klaubande, 2011)***.

Table (I-1): Ions as Charge Carriers across Cell Membranes

Ion	Charge	Direction of passive flux	Current generated	Effect on membrane potential
Calcium	Positive	Inward	Inward	Depolarizaion
Sodium	Positive	Inward	Inward	Depolarization
Potassium	Positive	Outward	Outward	Repolarization
Chloride	Negative	Inward	Outward	Repolarization

(Katz, 2011).

Types of ion channels:

1-Sodium channels:

Voltage-gated sodium channels (VGSC) cause the rapid depolarization that marks the rising phase of action potentials in the majority of excitable cells**.**In the myocardium VGSCs are required for initiation of the fast action potential upstroke that is required for cardiac excitation and conduction. Recent data

suggest variable localization of ion channel isoforms within the myocardium, and even within the same ventricular myocyte ***(Song et al., 2009)***.

In the sinoatrial node (SAN), a unique collection of ligand and voltage gated channels are required for automaticity, an implicit cellular property that initiates cardiac excitation ***(Jalife et al., 2009)***.

2-Potasium channels:

There are many potassium channels whose names, along with those of the currents that they carry, can describe the order of their discovery (e.g., i_{K1}), the duration of their open state (e.g., i_{to1}), the timing of their opening (i_{Kr} and i_{Ks}), and substances that open (e.g., $i_{K.Ca}$, $i_{K.\ Ach}$) or close (e.g., $i_{K.\ ATP}$) the channel. Many of the potassium channel α-subunits are regulated by β-subunits and other small membrane proteins, all of which can be substrates for regulatory protein kinase-catalyzed phosphorylations ***(Gutman et al., 2005)***.

Potassium channels that open in depolarized cells are called outward rectifiers. An outward current called i_{to1}, which causes a transient repolarization immediately after cells are depolarized, is caused by the opening of a channel that carries the slower $i_{to,\ slow}$, and two channels that carry a more rapid $i_{to,\ fast}$. The subsequent opening of several outward rectifier channels generates the delayed rectifier currents i_{Kr}, i_{Ks}, and i_{Kur} that return membrane potential to its resting level ***(Ordog et al.,2006)***.

3-Calcium channels:

Most important calcium channels in the heart are L- and T-type calcium channel whose names reflect the slower inactivation of L-type calcium channels than the T-type calcium channels, so that L=long lasting, T=transient lasting. L-type calcium channels also have a lower threshold for activation than T-type channels. So that "L" also stands for "Low threshold", and because T-type channels carry a smaller depolarizing current, "T"can also stand for "tiny" ***(Clusin, 2008)***.

4- Chloride channels:

Chloride channels function as homodimers in which each subunit forms a pore. When open, Chloride ion channels can carry either an inward or outward current, depending on the membrane potential; because they are regulated by cell deformation, they also serve as stretch sensors. Calcium-activated repolarizing currents, called $i_{Cl,\ Ca}$, have been attributed to three different classes of chloride channel; these include CLCA1 (Calcium activated chloride channels) that also carry a transient repolarizing current, called i_{to2}, which occurs immediately after the initial depolarization of atrial, ventricular, and His-Purkinje cells. Another type of chloride channel found in the heart, the CFTR (cystic fibrosis transmembrane conductance regulator) channels, contain five subunits: two transmembrane α-helices, two nucleotide-binding domains, and a regulatory subunit ***(Duan, 2009)***.

The cardiac ions have intracellular and extracellular ion concentrations in cardiac muscle **(Table I-2)** ***(Rubart and Zipes, 2012)***.

Table (I-2): Intracellular and extracellular ion concentrations in cardiac muscle.

Intra and extracellular ion concentrations (mmol/L)				
Element	**Ion**	**Extracellular**	**Intracellular**	**Ratio**
Sodium	Na^+	135 - 145	10	14:1
Potassium	K^+	3.5 - 5.0	155	1:16
Chloride	Cl^-	95 - 110	20 - 30	4:1
Calcium	Ca^+	2	10^{-4}	2×10^4

(Rubart and zips, 2012).

IV-Action potential (AP).

The AP differs in fundamental ways between tissues responsible for slow impulse conduction (nodal tissue) and those responsible for rapid impulse propagation (His-Purkinje system [HPS], ventricular myocardium). Furthermore, important differences exist between the AP of ventricular tissues which appear to be dependent on the layer of cells that are examined (endo-, mid-, and epicardial tissue layers ***(Zimetbaum and Josphson, 2009).***