1

Electrophysiological Principles

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1.1 Learning Objectives

- Generation of action potentials in pacemaker and non-pacemaker cells.
- Anatomical overview of the electrical conduction system.
- Principles that underpin normal ECG morphology.
- Common ECG abnormalities in the context of diseased states.

Cardiology at its Core, First Edition. Peysh A. Patel.

1.2 Cardiac Action Potential

Every single cell in the heart has the ability to generate action potentials (AP). However, in normal electrophysiology, cardiac AP originate from the sinoatrial node (SAN), which has no true resting potential but instead generates spontaneous AP during diastole. The rate of this **automaticity** determines intrinsic heart rate (HR) and is mediated by cell permeability through hyperpolarisation-activated cyclic nucleotide-gated (HCN) channels via the inward mixed sodium–potassium funny current (I_f). Automaticity is an inherent feature of pacemaker cells located in the SAN, internodal conduction tracts, atrioventricular node (AVN), bundle of His, bundle branches and Purkinje network. The SAN is the dominant pacemaker as its rate of automaticity is highest, at 60–100 beats min^{-1} (bpm). Each time these cells generate an electrical current, the distal slower-firing subsidiary cells are depolarised before they can do so automatically ('overdrive suppression of automaticity'). However, if there is SAN dysfunction or disease of the conduction system, the subsidiary cells can assume pacemaker function in a phenomenon termed **escape pacing**, albeit typically at slower rates (AVN 40–60 bpm, bundle branches 30–40 bpm, Purkinje system 30–40 bpm).

A schematic representation of AP originating in the SAN is provided in Figure 1.1. In the resting state, the high concentration of extracellular sodium and intracellular potassium ions results in an overall negative electrical potential of around −70 mV. When I_f activation reduces potential to a critical membrane threshold of −35 mV (phase 4), there is activation of 'all-or-nothing' long-lasting, dihydropyridine-sensitive calcium channels ('L type'). Opening results in a slow, sustained influx (phase 0). Once the cells have fully depolarised, repolarisation occurs via efflux of potassium ions with a return to resting state (phase 3). Cells do not need to return to resting potential before they can depolarise again, assuming that the membrane threshold is reached. Depolarisation of one cell acts as an electrical impulse on adjacent cardiac cells and enables propagation of current in the direction of depolarisation. Cells in the AVN also have intrinsic pacemaker activity and mechanism of propagation is comparable. Notably, AP are directly susceptible to neural influence. For instance, adrenaline can increase I_f current (i.e. rate of phase 4) with effects on the rate of spontaneous firing. Parasympathetic mediators have contrasting effects.

In comparison, non-pacemaker myocytes demonstrate maintenance at the resting potential without spontaneous depolarisation. Indeed, atrial and ventricular extrasystoles (ectopy) most typically occur because excitability is triggered by adjacent Purkinje cells. Additionally, there are crucial

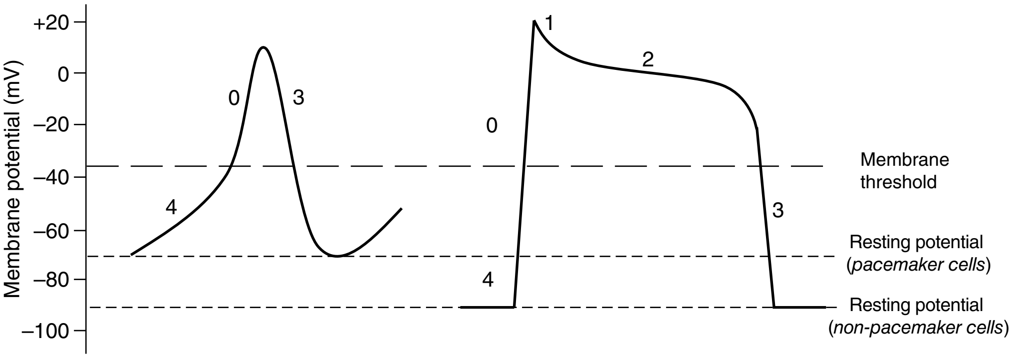


Figure 1.1 Schematic representation of action potential in pacemaker (left) and non-pacemaker (right) cardiac cells. AVN, atrioventricular node; CS, coronary sinus; CT, crista terminalis; CTI, cavo-tricuspid isthmus; EV, Eustachian valve; IAS, inter-atrial septum; IVC, inferior vena cava; RAA, right atrial appendage; SVC, superior vena cava; ToT, tendon of todaro; TV, tricuspid valve.

differences in morphology of AP which are depicted in Figure 1.1. The resting potential is more negative, in the region of −90 mV. Influx in phase 0 is determined by fast sodium channels as opposed to L type calcium channels resulting in a higher rate of depolarisation. The overshoot of AP is more pronounced. There also exists a distinct plateau (phase 2) mediated by prolonged slow repolarisation secondary to influx of calcium (and sodium) and efflux of potassium ions. Indeed, it is this inward calcium current that results in ion availability to initiate the process of excitation–contraction coupling (discussed in Chapter 6). Lastly, phase 4 in non-pacemaker cells involves the activation of sodium-potassium adenosine triphosphate (ATP)ase enzyme, which transports excess sodium out of cells and potassium back in. These pumps are not essential for inherent features of automaticity in pacemaker cells, although they may play a role in modifying depolarisation rate.

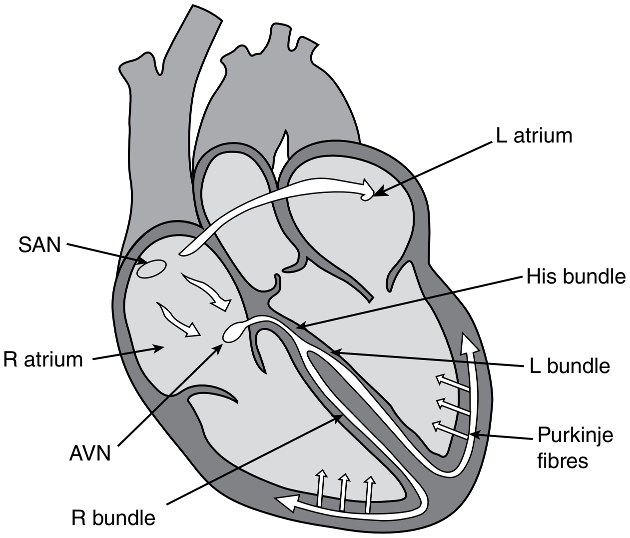
1.3 Electrical Conduction System

From a functional perspective, two categories of cardiac cells can be considered: myocardial and electrical. The myocardial cells contain numerous myofibrils consisting of contractile protein filaments, namely actin and myosin. This enables contractile properties of the myocardium, referring to its ability to shorten and return to its original length upon electrical stimulation. The underlying processes are explored in Chapter 6. By contrast, the specialised cells of the electrical conduction system do not have myofibrils and hence lack the ability to contract. Instead, they demonstrate an abundance of **gap junctions** between cells that permit rapid propagation of impulses in a fashion comparable to that seen in nerve fibres. An overview of the electrical conduction system is depicted in Figure 1.2 and discussed further in this subsection.

1.3.1 Sinoatrial Node

As highlighted, impulses originate from the SAN in normal electrophysiology. This region is a crescent-shaped structure, 2–3 mm wide, which is located laterally in the right atrium (RA) at the **sulcus terminalis**, a fat-filled groove demarcating the junction between RA appendage and

Figure 1.2 Overview of electrical conduction system in the heart.



superior vena cava (SVC) and corresponding internally to the crista terminalis. Blood supply originates from right coronary artery (RCA) territory in approximately 60% of cases, and approaches the node in a counterclockwise direction. The SAN is also densely innervated with postganglionic adrenergic and cholinergic nerve terminals, allowing neurotransmitters to modulate electrical discharge rate via stimulation of β_1- and β_2-adrenergic and muscarinic receptors, respectively.

1.3.2 Internodal Tracts

There is anatomical evidence of three intra-atrial pathways – anterior, middle and posterior. The anterior internodal pathway curves anteriorly around the SVC to enter the **Bachmann bundle** (anterior interatrial band). This extends beyond the right upper pulmonary vein to the left atrium (LA) and provides a branch to the AVN. The middle internodal tract (**Wenckebach bundle**) travels behind the SVC to the crest of the interatrial septum and descends towards the superior margin of the AVN. Lastly, the posterior pathway (**tract of Thorel**) travels posteriorly around the SVC and along the crista terminalis to the Eustachian ridge. It proceeds into the interatrial septum above the coronary sinus where it joins the posterior portion of the AVN. Notably, these pathways do not demonstrate discrete histological features and may therefore be better referred to as internodal atrial myocardium.

1.3.3 Atrioventricular Node

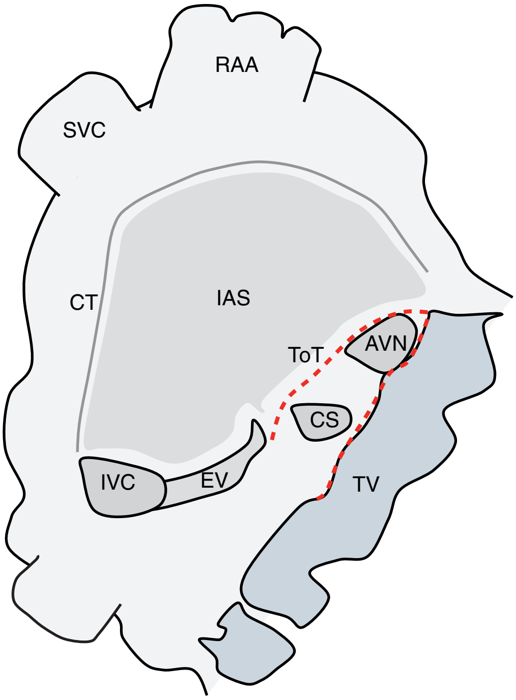
The compact portion of the node is a superficial structure at the base of the atrial septum (i.e. it is an atrial structure). It is formed from merging of fibres of the right and left postero-inferior extensions, which run from the coronary sinus. The compact AVN is directly anterior to the ostium of the coronary sinus and above the insertion of the septal leaflet of the tricuspid valve (TV). It is at the apex of **Koch's triangle** (see Figure 1.3), which is bordered by the septal leaflet of the tricuspid valve anteriorly, the tendon of Todaro posteriorly and the coronary sinus inferiorly. The tendon of Todaro is absent in two-thirds of patients but, when present, originates in the AVN and passes through towards the Eustachian ridge and the rudimentary Eustachian valve. The compact AVN is surrounded by transitional cells and provides a connection between the node and surrounding atrial myocardium.

In 85% of patients, arterial supply originates from the RCA at the crux. In the remaining 15%, it is supplied by the circumflex (Cx) artery. The main function of the AVN is to modulate impulse propagation from atria to the ventricles as a means of coordinating chamber contraction and protecting the ventricle from rapid atrial rates. It achieves this via the phenomenon of **decremental conduction** whereby the more frequently the AVN is stimulated, the slower it conducts. Autonomic innervation to the nodes is not symmetrical as there is a higher abundance of right-sided efferent fibres to the SAN and left-sided fibres to the AVN. This provides some explanation to clarify why left-sided carotid sinus massage for management of narrow complex tachycardias (NCT) (see Chapter 3) is generally more effective in termination of dysrhythmias. Nonetheless, there is added complexity due to the presence of significant overlapping innervation.

1.3.4 His–Purkinje System

The penetrating region of the atrioventricular bundle originates distally from the compact AVN as the His bundle and continues through the annulus fibrosis as it penetrates the membranous

Figure 1.3 Oblique projection of RA to outline structures that define Koch's triangle.



septum. The exact region that differentiates the AVN from the His bundle has not been delineated either anatomically or electrically. There is dual arterial supply from left anterior descending artery (LAD) and posterior descending artery (PDA) territories which enables greater protection from ischaemia. The bundle branches originate from the His bundle. The left bundle cascades downwards beneath the non-coronary aortic cusp and provides an anterior and posterior fascicle. The right bundle extends intramyocardially down the right side of the interventricular septum to the right ventricular apex. The terminal Purkinje fibres connect to distal bundle branches to form interweaving networks on the endocardial surface of both ventricles. This enables simultaneous and coordinated transmission of impulses to the entire left and right endocardium. The fibres terminate at synapses with myocardial cells.

1.4 ECG Morphology

1.4.1 General Principles

Electrical activity of the heart is determined routinely through a 12-lead electrocardiogram (ECG) derived from 10 electrodes. Use of specific leads with distinct anatomical distribution provides the ability to distinguish between normal and abnormal electrophysiology. Conventional lead placement occurs in two planes: transverse and coronal (see Figure 1.4). In the transverse plane there are six chest leads (V1–V6) which correspond roughly to anteroseptal (V1–V2), anteroapical (V3–V4) and anterolateral (V5–V6) territories. Leads in the coronal plane are I/aVL (left lateral surface), II/III/aVF (inferior) and aVR (right atrium). Each lead therefore provides a different perspective of electrical activity and corresponds to a differing ECG pattern. If overall activity is in the direction of the lead, a predominantly positive deflection occurs. Conversely, if it is predominantly directed

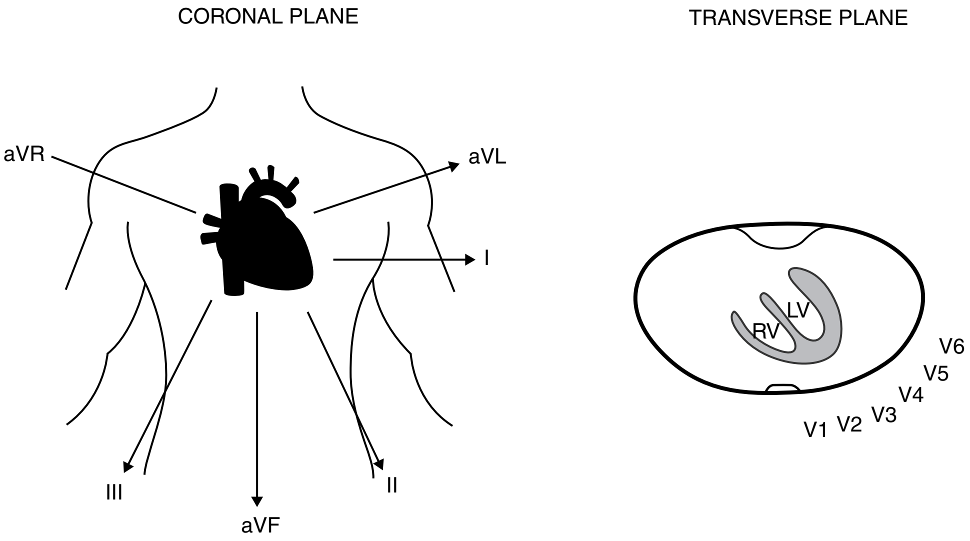


Figure 1.4 Coronal and transverse planes for ECG interpretation.

away, a negative deflection occurs. The **cardiac axis** refers to the average direction of spread of depolarisation waves through the ventricles. A normal axis in the coronal plane is from −30° to +90°.

On a 12-lead ECG, electrical activity in corresponding anatomical segments can be differentiated (see Figure 1.5). The initial positive deflection (P wave) relates to atrial depolarisation. The subsequent deflection (QRS complex) results from ventricular depolarisation and, finally, the T wave due to ventricular repolarisation when ventricles are refractory to excitability. As inferred, the PR interval constitutes duration between atrial and ventricular depolarisation and is normally in the region of 120–200 ms. It is mediated by the AVN. The QT interval refers to the duration

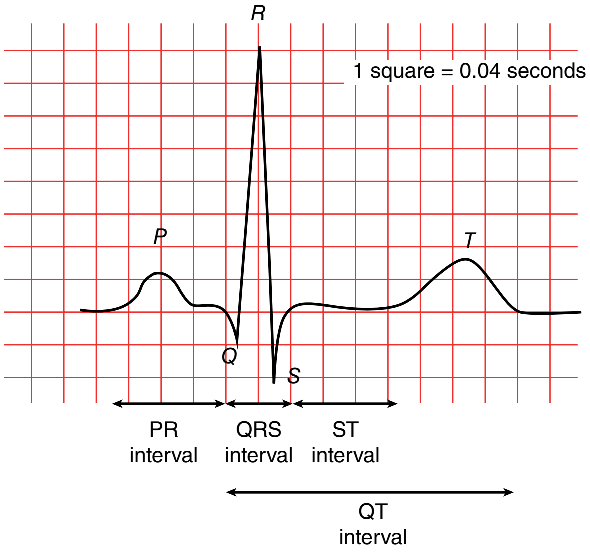


Figure 1.5 Morphology of normal ECG complex.

between the onset of the QRS complex and the end of the T wave. It is adjusted for the resting HR and is presented more meaningfully as a corrected QT interval (QTc), equal to the QT interval divided by √RR interval. QTc is roughly <440 ms for men and <460 ms for women.

1.4.2 P Wave

Propagation of impulses from the SAN through the atria results in atrial depolarisation and a corresponding P wave. This activation begins superolaterally in the RA and proceeds simultaneously towards the LA, via the Bachmann bundle, and inferomedially towards the AVN. Hence, the P wave is usually upright in inferior leads (i.e. II/III/aVF) and inverted in aVR. If these characteristics are absent, the sinus node is unlikely to have initiated the impulse or the leads have been misplaced. Atrial activity is often best seen in leads V1 and II. Overall, RA precedes LA activation, which continues even once RA activation is complete. Normal P wave duration is <120 ms with an amplitude <0.25 mV. The electrical potentials generated by atrial repolarisation are rarely observed due to a combination of low amplitude and superimposition on the QRS complex.

1.4.3 QRS Complex

The earliest sites of ventricular activation are the centre of the left side of the septum and at the anterior and posterior paraseptal walls of the left ventricle (LV). This generally corresponds to the sites of insertion of the left bundle branch. Septal activation hence commences on the left and spreads to the right, and from apex to base. Subsequent wavefronts spread to activate the anterior and lateral walls of the LV, with the posterobasal segment the last to be activated. Excitation of the right ventricle (RV) begins similarly at the insertion point of the right bundle branch, in close proximity to the base of the anterior papillary muscle with spreading to the lateral wall. The final regions to be activated are posterobasal and the pulmonary infundibulum. Hence, in both ventricles, excitation begins in the septal region and is directed down to the apex before migrating to the free wall and posterobasal regions in an apex to base direction. Wavefronts are propagated from endocardium to epicardium via direct conduction between individual myocytes.

The initial negative deflection in the QRS complex is the Q wave, followed by a positive deflection as the R wave and a subsequent negative S wave. A second upright wave following the S wave is termed prime (depicted as R′). This pattern of ventricular activation can be deciphered by simplifying the process into septal and subsequent free wall activation. Initial conduction in the interventricular septum corresponds to directionality from left to right (coronal plane) and posteriorly to anteriorly (transverse plane). Hence, there is an initial positive deflection (R wave) in right-sided leads, with an initial negative deflection (Q wave) in left-sided leads. Subsequent components of the QRS complex reflect LV and RV free wall activation. However, RV mass is significantly lower than that of LV and its negligible contribution mandates consideration only of septal and LV activation. In a right-sided lead, there is subsequent downward deflection (S wave) as the bulk of the LV is depolarised. Conversely, in a left-sided lead, there is an upward deflection (R wave). Thus, QRS complexes in the chest leads demonstrate gradual progression from being predominantly negative (in V1) to positive (in V6). The normal duration of a QRS complex is <120 ms. It is also worth mentioning that Q waves should be distinguished as physiological or pathological. In the context of the latter, they will generally be >0.04 s and exceed 25% of the amplitude of the subsequent R wave.

1.4.4 T Wave

As highlighted, this region of the ECG complex is generated during ventricular repolarisation. It is generally positive in all leads except aVR, V1 and III. It can also be negative in V2 in younger patients and V3 in Afro-Caribbeans. Occasionally, a small U wave of 0.5 mm in amplitude may be observed following the T wave with the same overall polarity. It is best seen in leads V2–V3. Notably, prominent U waves (> 1–2 mm or >25% of T wave amplitude) may be associated with pathological states such as hypokalaemia, severe bradycardia and digoxin toxicity.

1.5 ECG Abnormalities

1.5.1 Peaked and Bifid P Waves

RA depolarisation usually precedes that of the LA. The combined wave, denoted by the P wave, is < 120 ms wide and < 2.5 mm in amplitude. If the RA is dilated, such as in the context of pulmonary hypertension or tricuspid regurgitation, RA depolarisation is longer in duration and its waveform extends to the end of LA depolarisation. This results in a P wave that is of greater amplitude but of normal duration (P-pulmonale or 'peaked' P wave – see Figure 1.6). In LA enlargement, secondary to left ventricular diastolic dysfunction or mitral regurgitation, for instance LA depolarisation lasts longer. Hence, the P wave amplitude is unaffected but is of prolonged duration and may be associated with a notch near its peak (P-mitrale or 'bifid' P wave).

1.5.2 P Wave Inversion

The presence of P wave inversion in the inferior leads (II/III/aVF) is indicative of retrograde conduction and a non-sinus origin for atrial depolarisation. If the PR interval is < 120 ms or there are P waves after the QRS complex, the source of electrical activity lies within the AVN and is often defined as a 'junctional rhythm'. If the PR interval is > 120 ms, the origin is within the atria and associated with premature activity (ectopy).

1.5.3 Left Ventricular Hypertrophy

Left ventricular hypertrophy (LVH) is associated with conditions such as systemic hypertension, aortic stenosis and some cardiomyopathies. In general, the QRS amplitude is increased and is directed more posteriorly. Hence, negative QRS complexes predominate in the right-sided leads. Various diagnostic criteria exist with good specificity and reasonable sensitivity, such as the **Cornell voltage criteria**. Broadly speaking, the most characteristic feature is the presence of tall R waves laterally (V5–V6) and deep S waves anteriorly (V1–V2).

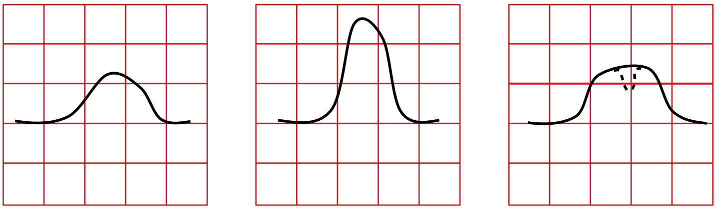


Figure 1.6 Morphology of P waves in right atrial (middle) and left atrial enlargement (right).

1.5.4 Axis Deviation

From the coronal view, as shown in Figure 1.7, the depolarisation wave normally spreads through the ventricles from 11 to 5 o'clock and is defined by a usual axis between −30° and +90°. This results in overall negative deflections in lead aVR and positive in lead II. The average direction of propagation defines the axis and normality can be defined simply by assessing for predominantly positive deflections in leads I, II, and III. If there is right axis deviation (RAD), lead I will be predominantly negative and corresponds coronally with a shift in axis ranging between +90° and +180°. Causes include right ventricular hypertrophy or strain. If there is left axis deviation (LAD), leads II and III will become negative and correlate with a coronal axis situated between −30° and −90°. Causes include LVH, right ventricular pacing and left bundle branch block (LBBB).

1.5.5 Bundle Branch Block

To appreciate the mechanisms underpinning bundle branch block (BBB), it is important to first remember that the septum is normally depolarised from left to right. Second, the left ventricle exerts more influence on the ECG than the right due to its substantial muscle mass. In BBB, there is a conduction delay resulting in QRS complex > 120 ms (see Figure 1.8).

1.5.5.1 Right Bundle Branch Block

In right bundle branch block (RBBB), the septum is depolarised from the left side as per usual, resulting in a small r wave in V1 and a small q wave in V6. Excitation subsequently spreads to the left ventricle and causes a S wave in V1 and R wave in V6. There is delayed excitation of the right ventricle resulting in a second wave (R′) in V1 and a deep s wave in V6. Some find it helpful to recall this pattern of excitation as 'M' in V1 and 'W' in V6. Of note, this pattern may exist in the context of a normal QRS duration, i.e. < 120 ms. This is defined as 'partial RBBB' and not deemed to be of pathological significance.

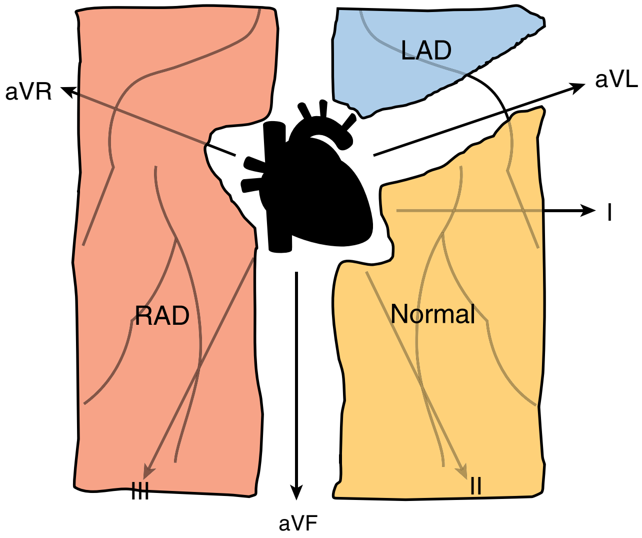


Figure 1.7 ECG axis interpretation.

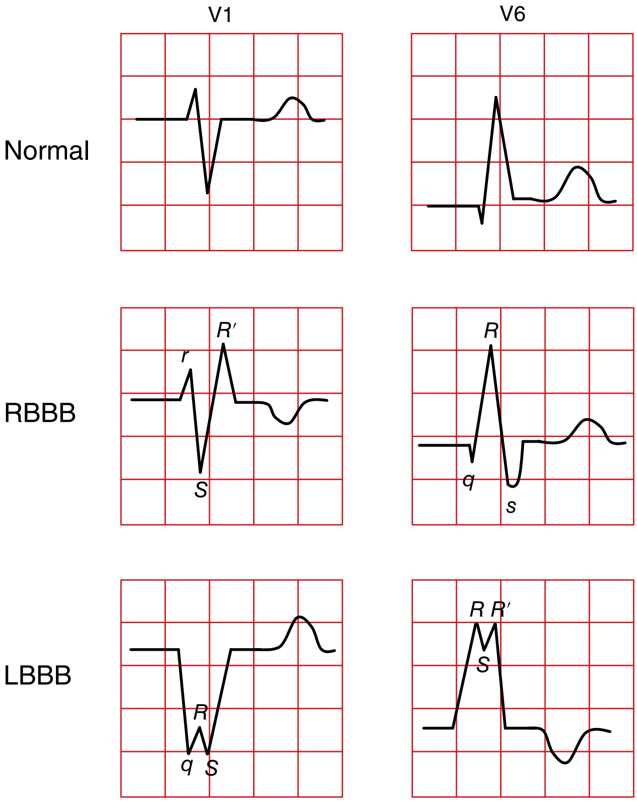


Figure 1.8 Morphology of QRS complexes in the RBBB and LBBB.

1.5.5.2 Left Bundle Branch Block

By contrast, the existence of LBBB irrespective of duration should always be considered abnormal. If there is a conduction defect in the left bundle, the septum depolarises from right to left. This results in a q wave in V1 and R wave in V6. Accordingly, the right ventricle is depolarised before the left which results in a R wave in V1 and an S wave in V6 (often appearing only as a notch). There is subsequent late depolarisation of the left ventricle and it is this that causes a S wave in V1 and an R′ in V6. The classical pattern of LBBB may helpfully be recalled as ‘W’ in V1 and ‘M’ in V6. It can also be associated with lateral T wave inversion.

1.5.6 T Wave Inversion

As indicated, it is normal for T waves to be inverted in aVR, V1, III, V2 (young patients) and V3 (Afro-Caribbeans). Causes of pathological T wave inversion include ischaemia/infarction, ventricular hypertrophy, BBB and digoxin toxicity. LBBB produces T wave inversion in lateral leads and RBBB in right precordial leads. Acute right ventricular strain secondary to saddle pulmonary embolus (PE) produces a similar pattern to right ventricular hypertrophy and may manifest as the classical SI QIII TIII pattern, i.e. S wave in lead I, Q wave in lead III and T wave inversion in lead III. The phenomenon of **biphasic T waves** can occur in the context of significant ischaemia, such as Wellens syndrome with localised changes in V2–V3 that are strongly indicative of proximal, critical LAD artery stenosis. In such contexts, a positive deflection precedes the negative deflection. The opposite biphasic appearance, i.e. negative before positive, is suggestive of severe hypokalaemia. Indeed, there may be coexistence of a second positive deflection after the T wave (i.e. U wave).

1.5.7 Miscellaneous

There are a multitude of distinct ECG abnormalities that have not been explored in this section. Abnormalities include sinus node dysfunction (SND), AVN conduction disease, fascicular block and ST segment changes. These will be explored individually in other chapter subsections and discussed in the context of specific disease states.

Hot Points

- The SAN has the highest rate of inherent automaticity and enables dominant pacemaker characteristics.
- A key difference between action potentials in non-pacemaker cells and pacemaker cells is the presence of a plateau phase (phase 2), that allows excitation–contraction coupling.
- Interpretation of 12-lead ECG involves consideration of lead placements in two planes: transverse (chest leads) and coronal (limb leads).
- A normal ventricular axis exists between −30° and +90°, with deviations manifesting as LAD (−30° to −90°) or RAD (+90° to +180°).
- The concept of BBB is based upon the premise that a) the ventricular septum is depolarised from left to right, and b) the LV exerts more influence than RV.

1.6 Self-assessment Questions

1 In relation to cardiac action potentials, which is the correct statement?

A In the resting state of the SAN, high concentration of extracellular potassium and intracellular sodium ions results in overall negative electrical potential of around −70 mV.

B The term 'overdrive suppression of automaticity' describes the means by which the AVN acts as a dominant pacemaker within the heart.

C Following generation of an action potential, pacemaker cells need to return to resting potential prior to further depolarisation.

D Activation of the sympathetic nervous system enhances I_f current, allowing membrane threshold to be reached more rapidly in phase 4 of the AP, thus increasing HR.

E In contrast to pacemaker cells, non-pacemaker myocytes have no true resting potential; instead, they generate spontaneous AP during diastole.

2 Regarding the electrical conduction system, select the correct statement.

A The SAN is a crescent-shaped structure located laterally in RA at the Eustachian ridge, a fat-filled groove which corresponds internally to the crista terminalis.

B Anatomically, three pathways connecting SAN to AVN are recognised (anterior, middle, and posterior intermodal tracts). However, due to lack of discrete histological features, these may be better referred to as internodal atrial myocardium.

C The AVN is situated at apex of Koch's triangle and is bordered by anterior leaflet of the tricuspid valve anteriorly, tendon of Todaro posteriorly and coronary sinus inferiorly.

D In 65% of patients, arterial supply for the AVN originates from RCA, whilst in the remaining 35%, it is supplied by Cx artery.

E The His–Purkinje system receives dual arterial supply from Cx artery and PDA, enabling protection from ischaemia.

3 Regarding ECG morphology, which of the following is the correct statement?

A The cardiac axis refers to average direction of spread of depolarisation waves through the ventricles, and a normal axis in the coronal plane is between −30° and −90°.

B QTc represents the QT interval adjusted for resting heart rate and is calculated by dividing the QT interval by the RR interval.

C An upright P wave in the inferior leads is indicative of retrograde conduction and non-sinus origin for atrial depolarisation.

D Ventricular activation spreads from epicardium to endocardium via direct conduction between individual myocytes.

E T wave inversion in V3 can be non-pathological in Afro-Caribbean patients.

4 Regarding ECG abnormalities, select the correct statement.

A P-pulmonale generally results from LA enlargement and is associated with pulmonary hypertension.

B Tall R waves in lateral leads and deep S waves in anterior leads are characteristic ECG findings in patients with LVH.

C Causes of LAD include LVH, left ventricular pacing and LBBB.

D An RSR′ pattern in the context of normal QRS duration is termed 'partial RBBB' and is thought to predict development of right ventricular dysfunction.

E Wellens syndrome is characterised by T wave inversion in leads V2–V3 and suggestive of critical left main stem stenosis.

5 Please select the correct statement.

A Phase 4 of the action potential in non-pacemaker cells involves activation of sodium–potassium guanosine triphosphate (GTP)ase enzyme, which transports excess sodium out of cells and potassium into cells.

B Right-sided carotid sinus massage is generally more effective in dysrhythmia termination due to higher abundance of right-sided efferent fibres to the AVN.

C The phenomenon of decremental conduction is a means of protecting the ventricles from rapid atrial rates.

D In the transverse plane, leads V1–V2 roughly correspond with the anterolateral segment of the left ventricle.

E The PR interval describes duration between atrial and ventricular depolarisation and is mediated by the His–Purkinje system.

Further Reading

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