

Understanding cardiac arrhythmias

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This review highlights the applied science intrinsic to the interpretation of the electrocardiogram and cardiac arrhythmias in children.

In 1887, Augustus Waller published the first human electrocardiogram (ECG).¹ The early studies were carried out using Waller's dog, Jimmy, who would stand for hours with paws immersed in saline filled jars! Since then the electrocardiogram has become an essential clinical tool that has revolutionised our assessment of cardiac electrophysiology and disorders of cardiac rhythm. An understanding of the scientific basis of the ECG enables a logical interpretation of the ECG findings and an appreciation of abnormalities that may occur. The aim of this review is to highlight the applied science intrinsic to the interpretation of the electrocardiogram and arrhythmias in infants and children.

BASIC CARDIAC ELECTROPHYSIOLOGY

Like all living cells, the inside of the cardiac myocyte has a negative charge. This results in a voltage difference across the cell membrane called the transmembrane potential. Unlike most other cells, cardiac myocytes are excitable. When appropriately stimulated, channels in the cell membrane open, allowing ions to flow across the cell membrane. This results in the cardiac action potential (fig 1). There are three main components to the action potential: depolarisation, repolarisation, and a resting phase. During depolarisation, sodium channels in the cell membrane open and positively charged sodium ions enter the cell, causing a rapid change in the transmembrane potential. This depolarisation spreads to adjacent cells. During repolarisation, the cardiac membrane potential returns to normal by complex interactions involving sodium, potassium, and calcium. During this phase, the myocytes cannot contract (refractory period). The resting phase is the period between action potentials. During the resting phase most myocytes have no net movement of ions across the cell membrane. In some cells, however, the resting phase is associated with a gradual increase in transmembrane potential (phase 4 activity). When this potential is high enough, the appropriate channels open and spontaneous depolarisation begins. The property of cells to increase transmembrane potential during the resting phase is called *automaticity*. This is the mechanism whereby the normal cardiac impulse is generated. Cells in the sinus node usually have the fastest phase 4 and initiate the cardiac

impulse. When the sinus node is diseased, secondary pacemaker cells initiate the heart-beat—usually at the atrioventricular junction.

The autonomic nervous system also plays a role in the myocyte action potential. When cholinergic vagal fibres to nodal tissue are stimulated, acetylcholine is liberated. This results in an increase in the permeability of nodal tissues to K^+ (via muscarinic receptors) and reduces conductance in the Ca^{2+} channel. The effect is to reduce and occasionally transiently abolish spontaneous discharge. This effect is seen in vasovagal syncope. Conversely, stimulation of the cardiac sympathetic system makes the membrane potential fall more rapidly. Noradrenaline increases the rate at which K^+ declines between action potentials and increases conductance in the Ca^{2+} channel. The overall effect is to increase the amplitude of the action potential, the rate of spontaneous discharge, and the strength of each cardiac contraction. Similarly, increased temperature increases the rate of discharge of conduction tissues.

The action potential of the myocyte has a far longer duration than nerve or skeletal muscle. This long action potential, mediated by slow calcium channels, is essential to allow regular independent beats to occur. It also allows modulation of the strength of contraction and is one reason why tetany cannot occur in the cardiac muscle. Abnormalities of the various ion channels give rise to serious cardiac arrhythmias^{2–5} (table 1).

Each myocyte is connected to its neighbour by an intercalated disc at the end of the cell. These discs include gap junctions that contain areas of high conductance called nexi. Each nexus is formed by two half channels, known as connexons, which protrude into adjacent cell cytoplasm and link to a mirror image connexon in the neighbouring cell. Connexons are composed of six protein subunits arranged around a high conductance fluid filled pore. This allows the heart to behave electrically as if it were a single cell. Thus, an electrical impulse can spread through the heart muscle in a similar way to conduction through a nerve cell. Gap junction permeability is increased by ATP and cyclic AMP dependant kinases. This quality enables the gap junction to close if ATP levels fall, thus limiting cell death when one area of the myocardium is damaged. Similarly, conduction increases in response to adrenergic stimulation. Abnormalities of gap junctions are associated with a variety of serious cardiac diseases including arrhythmias.⁶

Spontaneously depolarising pacemaker cells within the sinus node lead to propagation of depolarisation throughout atrial myocardium

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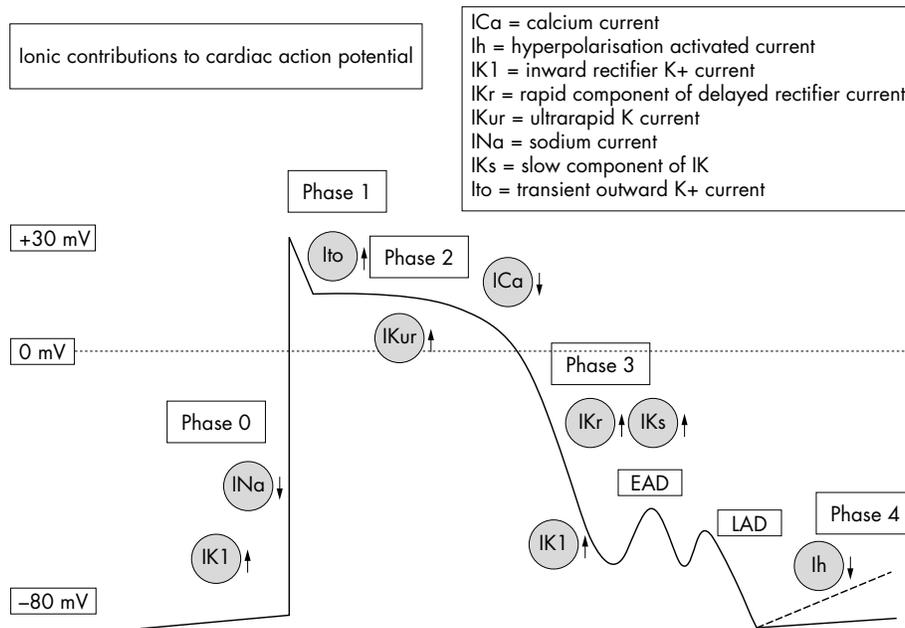


Figure 1 Summary of ionic currents involved in the production of the cardiac action potential. Phase 0, rapid depolarisation; phase 1, initial repolarisation; phase 2, plateau; phase 3, repolarisation; phase 4, slow spontaneous depolarisation (only in pacemaker cells).

and atrial systole. The action potential is then conducted throughout the heart. This conduction is facilitated by specific conduction pathways. These cells are, in general, muscle cells which have become specialised for rapid conduction rather than contraction. In the normal heart, the only electrical connection between atria and ventricles is via the atrioventricular (AV) node. After traversing the AV node, the action potential is propagated rapidly through the bundle of His and into the Purkinje fibres located on the endocardium of the left and right ventricles. Rapid conduction through the atrium causes synchronous contraction of most of the atrial muscle (within 60–90 ms). Similarly, rapid conduction throughout the ventricle leads to synchronous contraction of the bulk of the ventricular myocardium (within 60 ms). This synchrony may be lost in pathological states (for example, left bundle branch block), leading to inefficient myocardial contraction and reduced cardiac output. A recent development in heart failure treatment is the restoration of synchrony using multisite pacing.⁷ Delay in the propagation of the action potential through the AV node (120–140 ms) leads to sequential contraction of the atrium followed by the ventricle. This facilitates atrial filling of the ventricle. Slow conduction in the AV node is associated with a smaller number of gap junctions between cells leading to slowly rising action potentials. The AV node has a unique electrophysiological property known as *decrementation*. This

means that the more rapid the atrial contraction, the longer the conduction time through the AV node. This is an important safety feature, which prevents very rapid atrial tachycardia or fibrillation leading to rapid ventricular rates. At rapid atrial rates the AV node conduction time will increase, leading to prolonging of the PR interval and eventually non-conducted P waves. This is known as the Wenkebach phenomenon.

THE ELECTROCARDIOGRAM

The electrocardiogram (ECG) is based on the property of the body to act as a volume conductor. Fluctuations in electrical potential recorded on the body surface represent the algebraic sum of myocardial action potentials. The ECG may be recorded using an active electrode connected to an indifferent electrode at zero potential (unipolar recording) or between two active electrodes (bipolar recording). In a volume conductor with a current source at the centre, the sum of potentials at the points of an equilateral triangle is zero. A triangle with the heart at the centre can be created by placing electrodes on both arms and the left leg (Einthoven’s triangle). If these electrodes are connected to a common terminal, an indifferent electrode at zero potential is created. Cardiac depolarisation moving towards the active electrode will produce a positive deflection and depolarisation moving away will create a negative deflection.

Ion channel	Syndrome	Gene defect	Arrhythmia
Na ⁺	Brugada	SCN5a	Ventricular fibrillation Sudden death
Na ⁺	Long QT 3	SCN5a	Torsade de Pointes Sudden death
K ⁺	Short QT syndrome	KCNH2	Atrial arrhythmias
	Long QT 1	KCNE1	Torsades de Pointes
	Long QT 2	HERG	
Ca ⁺⁺	Catecholaminergic ventricular tachycardia (Coumel’s)	hRyR2 CASQZ	Bidirectional ventricular tachycardia

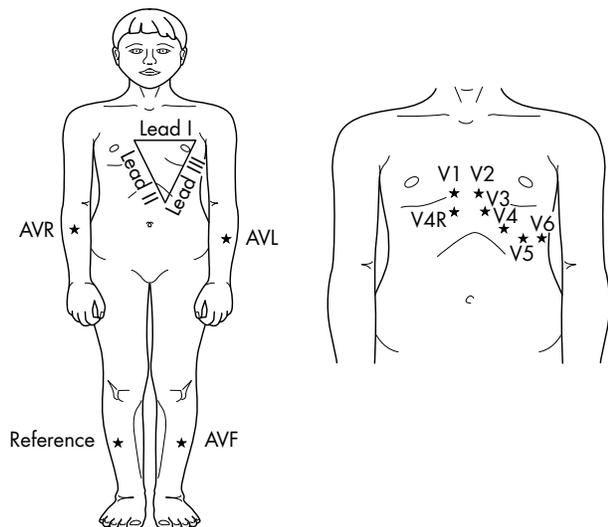


Figure 2 V1, 4th right ICS; V2, 4th left ICS; V3, between V2 and V4; V4, left 5th ICS, midclavicular line; V5, 5th ICS, anterior axillary line; V6, 5th ICS mid-axillary line. Lewis lead: place the negative electrode over the 2nd right ICS and the positive electrode directly below (4th right ICS). ICS, intercostal space.

In the conventional ECG, nine unipolar leads are used (fig 2): six precordial leads (V1–6) and three limb leads on the right arm (VR), left arm (VL), and left leg (VF). It is usual practice to augment the limb leads (aVR, aVL, aVF) by recording between one limb and the other two limbs. This has the effect of increasing the size of potentials by 50% without changing the configuration. Occasionally, in small children an extra lead (V4R) can be used to provide additional information on the right atrium or ventricle. P wave identification can sometimes be facilitated by using the Lewis lead.⁸ Similarly, a transoesophageal lead can be used to identify P waves in difficult cases. The ECG is usually recorded on a time scale of 25 mm/s on the horizontal axis and a voltage sensitivity of 0.1 mV/mm on the vertical axis. Hence, on standard ECG recording paper, one small square represents 0.04 seconds and one large square 0.2 seconds. In

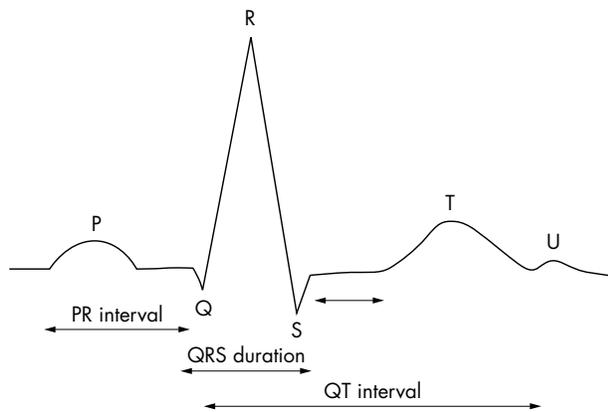


Figure 3 Analysis of surface ECG. P–R interval: taken from the start of the P wave to the start of the QRS complex. It is the time taken for depolarisation to pass from the SA node via the atria, AV node, and His–Purkinje system to the ventricles. QRS complex: time taken for depolarisation to pass through the His–Purkinje system and the ventricular muscles. Q–T interval: taken from the start of the QRS complex to the end of the T wave. Represents the time taken to depolarise and repolarise the ventricles.

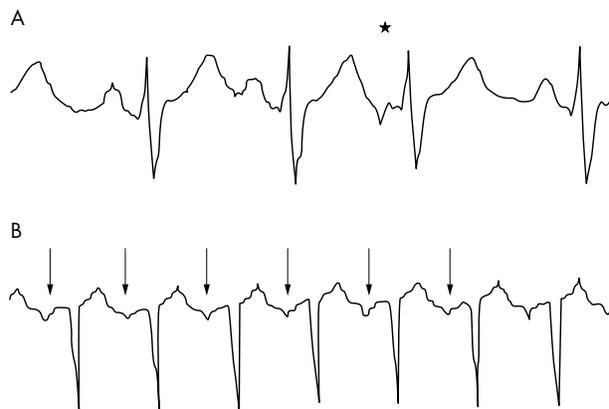


Figure 4 (A) Premature and escape beats. Supraventricular ectopic beat. The third beat (*) is narrow complex, preceded by an abnormal P wave and occurs earlier than a sinus beat. (B) Supraventricular tachycardia. The arrows depict the P waves following each QRS complex in this atrioventricular re-entry tachycardia 150/minute.

the normal ECG waveform the P wave represents atrial depolarisation, the QRS complex ventricular depolarisation, and the T wave ventricular repolarisation (fig 3).

CARDIAC ARRHYTHMIAS

Although serious cardiac arrhythmias are rare in children, a recent prevalence study recorded an arrhythmia or conduction abnormalities in 1.25% of elementary school students and 2.32% of junior high school students.⁹ In the majority these were ectopic beats or bundle-branch block, which are rarely of clinical significance. Cardiac arrhythmias arise as a result of abnormal impulse initiation or conduction. When a stimulus of appropriate strength and duration depolarises the cell to the level of threshold potential, there is an increase in sodium permeability that depolarises the cell membrane and produces a regenerative action potential. The transmembrane potential, which is negative in the resting state, reverses as the cell’s interior changes from –90 mV to about +30 mV. The cell then repolarises and the transmembrane potential

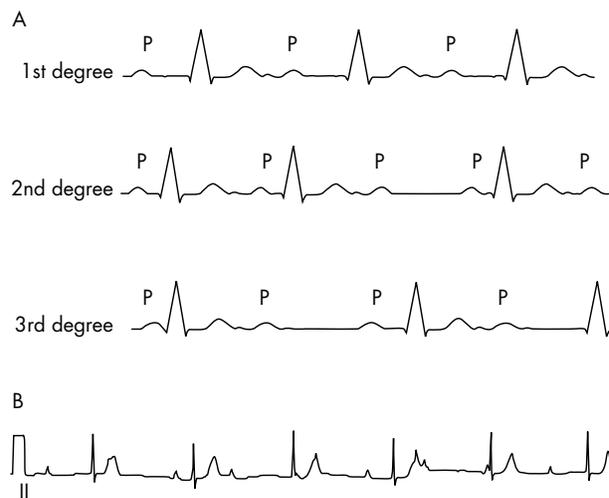


Figure 5 (A) In 1st degree block all impulses conduct to the ventricles but the PR interval is prolonged. In 2nd degree block, every P wave does not induce a QRS complex. In 3rd degree block, none of the P waves are conducted to the ventricles. (B) Alternative picture of complete heart block.

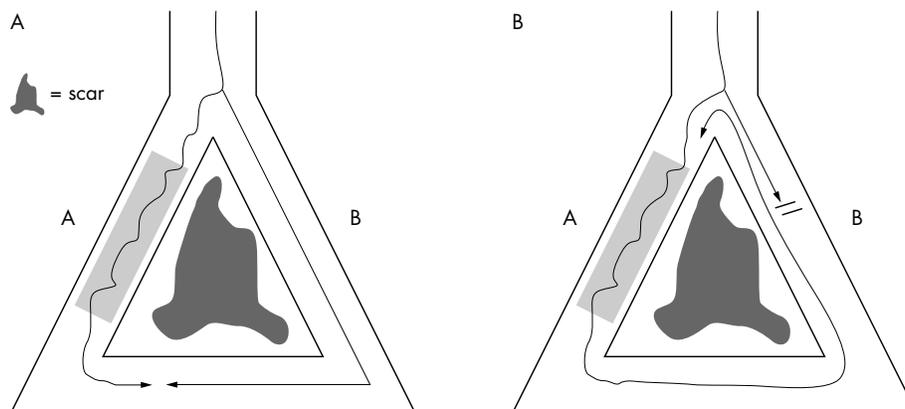


Figure 6 (A) Substrate for re-entry circuit. Two pathways (A and B) form an electrical circuit around a surgical scar. Pathway A has a slower conduction time but shorter refractory (recovery) period than pathway B. (B) Initiation of re-entry circuit. A re-entry tachycardia is initiated when a premature stimulus enters one pathway (pathway A) while the other (pathway B) is refractory. After crossing the pathway, it is conducted retrograde into the other pathway that is no longer refractory. The stimulus then re-enters the initial pathway. This creates a continuous reciprocating tachycardia within the circuit.

returns to -90 mV again. Cardiac arrhythmias can be classified according to the site of origin (atria, atrioventricular junction, or ventricles) and whether the response is abnormally fast and early (tachycardia or premature beats), or abnormally slow and delayed (bradycardia or escape beats). Examples of supraventricular premature beats and tachycardia are shown in fig 4. Arrhythmias are usually classified according to rate: bradyarrhythmias (too slow) and tachyarrhythmias (too fast).

Bradyarrhythmias

Bradycardias may be due to either a failure of impulse generation or a failure of impulse propagation.

Failure of impulse generation

This is a disorder of automaticity. If the sinus node fails to produce a fast enough heart rate to meet the body's metabolic demands, symptoms develop. This symptomatic bradycardia is called sick sinus syndrome. This may occur de novo or may be a consequence of cardiac surgery (for example, the atrial switch procedure for transposition of the great arteries). When the rate is very slow, subsidiary pacemakers take over the function of the sinus node. This will be associated with an abnormal or absent P wave depending on the site of origin of the subsidiary pacemaker.

Failure of impulse propagation

This is a disorder of propagation of the action potential from atria to ventricles. This is known as heart block and is due to disease of the AV node or His–Purkinje system. When present at birth, this is usually caused by damage to the conduction tissue from maternal autoantibodies reacting with ribonucleoproteins in the fetal conduction tissue.² Heart block may also occur as a consequence of other insults such as infection or cardiac surgery. Varying degrees of heart block exist (fig 5).

Tachyarrhythmias

There are two main electrophysiological mechanisms which cause tachyarrhythmia: re-entry and enhanced automaticity. These can act as the substrate for arrhythmias of atrial, AV junctional, and ventricular origin.

Re-entry

Re-entry (fig 6) is the most common mechanism of arrhythmia formation. For re-entry to occur, two conducting pathways must be linked around an area of non-conducting tissue. This can be pathological (for example, surgical scar) or

a natural electrical barrier (for example, the fibrous skeleton of the heart or a caval vein). This is the mechanism responsible for most supraventricular and many ventricular tachycardias. The most common mechanism of supraventricular tachycardia in children is orthodromic AV re-entry tachycardia. In this arrhythmia, an atrial ectopic beat conducts down the AV node, re-enters the atrium via an accessory pathway straddling the fibrous AV ring, and passes back down the AV node again, causing a narrow complex tachycardia.

Enhanced automaticity

Automatic arrhythmias are relatively uncommon in children but can be difficult to treat and, when incessant, may lead to cardiomyopathy.^{10–11} Automatic arrhythmias often have a metabolic cause (electrolyte imbalance, hypoxia, cardiac ischaemia, pyrexia) and are frequently seen in acutely ill children. They may be exacerbated by intravenous sympathomimetics and lung disease. These arrhythmias behave in similar ways to sinus rhythm. They will speed up and slow down according to metabolic requirements and are refractory to DC cardioversion. A third mechanism of arrhythmogenesis exists (triggered activity) which has features of both automaticity and re-entry. This is similar to enhanced automaticity with positive ions entering the cell at the end of the action potential (phase 3 or 4). If this ion flux is large enough, the fast Na channel opens and an action potential is induced. These after-potentials are a feature of many drug induced arrhythmias. Similarly, triggered activity may be associated with the induction of ventricular dysrhythmias in long QT syndrome.¹² An understanding of the molecular pathophysiology can lead to potential diagnostic tools and treatment modalities. For example, flecainide (a sodium channel blocker) shortens the QT interval in patients with long QT 3 syndrome and has been suggested as a potential treatment.¹³

CONCLUSION

In conclusion, a good understanding of the electrophysiological basis of the ECG and cardiac arrhythmias enables the clinician to have a more logical approach to diagnosis and treatment of arrhythmias in childhood. Moreover, current advances in electrophysiological research at a molecular level offer the promise of more effective treatments for cardiac arrhythmias in the future.

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ARCHIVIST**Neonatal encephalopathy and cerebral palsy**

Most children with neonatal encephalopathy do not develop cerebral palsy and most children with cerebral palsy have not had neonatal encephalopathy. A study in Western Australia (Nadia Badawi and colleagues. *Developmental Medicine and Child Neurology* 2005;**47**:293–8, see also Commentary, *ibid*: 292) has provided more information about cerebral palsy following or not following neonatal encephalopathy.

The case control study included 840 term infants born between June 1993 and December 1996; 276 with moderate or severe neonatal encephalopathy and 564 control infants. Neonatal encephalopathy was defined as either seizures or at least two of four other criteria (abnormalities of consciousness, tone, feeding, or respiration, each of presumed central origin and lasting for at least 24 hours) in the first week of life. Twenty-five infants with neonatal encephalopathy died in the neonatal period. Survivors were followed up for 6 years and 32 (13%) developed cerebral palsy (15/178 (8%) of those with moderate neonatal encephalopathy and 17/73 (23%) of those with severe neonatal encephalopathy). Data from the Western Australian Cerebral Palsy Register showed that over the period of the study there were 82 995 live term births and 131 children were identified as having cerebral palsy by the age of 5 years. Of these 131 children 99 did not have a history of neonatal encephalopathy.

Children with cerebral palsy after neonatal encephalopathy were more likely to be severely affected. They were twice as likely (47% vs 25%) to have severe cerebral palsy when compared with children with cerebral palsy not preceded by neonatal encephalopathy, and more likely to have spastic quadriplegia or dyskinetic cerebral palsy. They were more likely to have epilepsy or cognitive impairment and their cognitive impairment was more likely to be severe. They were also more likely to be non-verbal, to have a severe composite disability score, and to die within a few years of the diagnosis of cerebral palsy.

About one in eight of the survivors of moderate or severe neonatal encephalopathy at term developed cerebral palsy. About three quarters of term-born children with cerebral palsy had not had neonatal encephalopathy. Cerebral palsy is likely to be more severe in the survivors of neonatal encephalopathy.