Diagnosis, evaluation and treatment of cardiac arrhythmias

Edmund J Ladusans

Abstract

Paediatric cardiac arrhythmias commonly occur in the absence of structural heart disease, and are classified according to their cardiac site of origin. Although a detailed history and examination are invaluable, a correct diagnosis cannot be made unless the ECG is analysed, taking into account features specific to this age group. A 24-hour ECG recording may also be helpful. As many of these conditions have a genetic basis, a careful family history should be taken. For patients presenting acutely with haemodynamic collapse, paediatric life support measures should be instigated. For others, there is more time to undertake investigations prior to treatment. A relatively small number of agents, described here, are used in therapy, and in older children, radiofrequency ablation or fitting of a pacemaker offers a more permanent treatment. Advances in genetics suggest the chance of improved screening and treatment for those conditions which are inherited.

Keywords adenosine; amiodarone; atrioventricular node; beta-blockers; cardiac arrhythmia; digoxin; ECG; flecaainide; genetics; radiofrequency ablation; tachycardia

Introduction

The term ‘arrhythmia’ refers to the absence of normal sinus rhythm. Cardiac arrhythmias can occur at any time in the paediatric population. At all ages we can classify arrhythmias according to the presence or absence of structural heart disease, and according to whether the heart rate is too fast or too slow. This review is concerned predominantly with tachycardias occurring in the structurally normal heart.

Arrhythmias are further classified according to site of origin above, at, or below the atrioventricular (AV) junction. The term ‘supraventricular tachycardia’ (SVT) is usually applied to tachyarrhythmias that have a narrow QRS complex width and a regular rapid rate. Nomenclature is flawed in that these tachycardias are most commonly caused by AV re-entry with an accessory pathway. They, therefore, require atrium, AV node, His bundle and ventricle to be maintained. The only arrhythmias that are considered to be narrow complex in the adult can be broad until late childhood and normal QRS duration at all paediatric ages should be less than 0.09 seconds. Thus, what is considered to be narrow complex in the adult can be broad complex in the child.

An important principle in the management of arrhythmias is not to commence treatment without electrocardiogram (ECG) documentation. It is impossible to make a rhythm diagnosis on history and physical examination alone and incorrect drug treatment can have grave consequences.

Clinical features

A detailed history is invaluable in the assessment of possible arrhythmia. Symptoms in children will vary with age and in the very young, accounts from parents and carers are essential. In infants, parents may report poor feeding, breathlessness and irritability but often diagnosis is delayed until heart failure and collapse occurs. In the toddler, vivid descriptions may be forthcoming but only in the older child can palpitations, heart racing, breathlessness, chest pains and dizziness be elicited. Observers may note pallor and alteration of consciousness and syncope. Life-threatening arrhythmia may present as seizures.

It is important to note the onset and termination of symptoms. Most arrhythmias start and stop suddenly. Children may discover simple vagal tricks such as handstands, which can terminate an attack. Occurrence of very rapid heart rates at rest is suggestive, whilst it may be difficult to differentiate normal sinus tachycardia in those that only occur on exercise. Documentation of the timing of events is helpful in differentiating secondary sinus tachycardias from primary arrhythmias.

Many arrhythmias have a genetic basis and a family history of arrhythmia, fits, syncope or premature sudden death should not be forgotten.

Physical examination, whilst important, is usually normal in between attacks. Attention should be directed to the cardiovascular system to exclude structural heart disease but also to general examination to detect systemic disorders, such as anaemia and thyrotoxicosis.

Investigations

All children suspected of arrhythmia should have an echocardiogram to exclude structural heart disease, including Ebstein’s anomaly and mitral prolapse. Attention is paid to chamber size and ventricular function and the exclusion of dilated and hypertrophic cardiomyopathy. Almost invariably cardiac structure is normal.

The ECG and demonstration of the relation of atrial to ventricular activity during tachycardia is the key to diagnosis. Measurements on the 12-lead ECG are age-dependent and tables of age ranges for intervals and wave axes are available.1 Remem-ber that heart rates of over 200 bpm can be seen in sinus tachycardia in the neonate. The mean frontal QRS axis should be inferior until late childhood and normal QRS duration at all paediatric ages should be less than 0.09 seconds. Thus, what is considered to be narrow complex in the adult can be broad complex in the child.

The ECG is often normal in between symptoms. A 24-hour ECG recording is useful in documenting the frequency of ectopy and heart rate variations. Unless symptoms are very frequent it seldom captures an attack.

External event recorders can either be applied to the chest during symptoms or worn with electrodes on a belt. When fixed with electrodes they have the advantage that a period of ECG before the attack is recorded and the onset of tachycardia can

Edmund J Ladusans BSc FRCPE FRCPC is a Consultant Paediatric Cardiologist at the Royal Liverpool Children’s Hospital, Alder Hey, Liverpool, UK.
be demonstrated. They allow transtelephonic transmission of the ECG and printout remotely.

For infrequent symptoms that are of a potentially sinister significance or if there is syncope so manual activation is impossible, there are implantable devices that allow automatic recording of events. The loop recorder is usually placed in a pre-pectoral pocket. It can be activated manually and auto-activated to detect heart rates above and below programmed limits. Battery life is up to 14 months and will store a period of ECG before and after the activation.

Exercise testing is useful in the assessment of premature ventricular extrasystoles. In children with normal hearts, suppression of extrasystoles on exercise indicates a benign outlook. This is not necessarily the case in those with structural disease. Exercise testing has also been used to assess changes in the QT interval that normally shorten as exercise increases. Occasionally it precipitates arrhythmia where exercise provocation is a feature.

**General treatment principles**

In the acute presentation with haemodynamic collapse, treatment is guided by the principles of advanced paediatric life support. Electrical cardioversion starting at 2 J/kg should not be delayed.

In situations where the arrhythmia is tolerated and the child is stable there is time to assess the situation and obtain an ECG diagnosis. A full 12-lead ECG is essential, as is a paper recording of the ECG during all treatment interventions. This is invaluable as how a tachycardia starts and terminates can reveal the arrhythmic substrate to the expert.

Urea and electrolytes should be checked and correction given to ensure normal levels of potassium, calcium and magnesium. Magnesium intravenously is a very effective anti-arrhythmic agent in its own right.

Adenosine is the first-line drug for acute termination of supraventricular tachycardias. It is an endogenous purine nucleoside, which pharmacologically acts on the sinus and AV nodes. The principal effect is to slow AV conduction and produce AV block. It has a very short half-life, which limits its toxicity of hypotension, bradycardia, asystole, flushing and bronchospasm, but also limits efficacy in maintaining sinus rhythm. Adenosine is given by rapid injection into a central vein where possible, starting with 100 μg/kg in children and 200 μg/kg in infants to a maximum of 300–500 μg/kg.2

Adenosine is an important diagnostic tool. It will have no effect on the rate of ventricular tachycardia (VT) but may by slowing the atrial rate reveal AV dissociation and confirm the diagnosis. It does not produce any haemodynamic deterioration in VT.

Adenosine can differentiate the mechanism of SVT. It may unmask pre-excitation by blocking the AV node and increasing conduction down an accessory connection where previously not apparent. Alternatively it may show changes in PR interval indicative of dual AV nodal pathways. In atrial tachycardias and atrial flutter with rapid ventricular response where the diagnosis is not obvious, the increased AV block and slowed ventricular rate after adenosine will reveal the underlying atrial rhythm.

Where tachycardias have responded to adenosine it is logical to start a nodally active drug when recurrence requires treatment. Digoxin still has a role but requires monitoring and it has a narrow therapeutic range. It is contraindicated where there is overt pre-excitation on the ECG in sinus rhythm since it may increase the speed of conduction of an accessory pathway. Beta-blocking drugs are safe and there is no contraindication in Wolff-Parkinson-White syndrome (WPW). Long-acting preparations, such as nadolol, are particularly important in the treatment of life-threatening arrhythmia. Verapamil although very effective in adults and older children, is absolutely contraindicated in infancy where ventricular function is very calcium-dependent and deaths have been reported.

For arrhythmias where membrane stabilising activity is important or refractory arrhythmias, flecainide has been the mainstay in many institutions. It should not be used where there is structural heart disease or impaired ventricular function. It does require monitoring and drug levels have to be measured early after starting treatment to exclude values in the toxic range. As with many drugs, therapeutic efficacy may be achieved with low drug concentrations. Flecainide is useful in combination with digoxin in AV nodal tachycardias in older children.3

Amiodarone is a very powerful drug with class III action and a degree of beta-blocking action. It acts on atrial myocardium, the AV node and ventricular myocardium and is minimally negatively inotropic. The drawback is a potential for serious long-term adverse effects including hepatotoxicity, thyroid dysfunction and photosensitivity. It also causes corneal microdeposits, which are, however, reversible. Pulmonary toxicity, seen in adults, has not been a problem in children.4 It is effective intravenously with a very long half-life and builds up in the myocardium. It can be used in combination with digoxin for added AV nodal effect and as with flecainide, amiodarone increases the level of digoxin and maintenance doses need to be reduced.

Radiofrequency ablation has been more widely applied in children since the 1990s. Although possible in infancy, it is reserved for refractory and life-threatening arrhythmia in the very young. There is still concern in the small heart as to long-term complications of the lesions produced. In the older child, it offers the prospect of cure of the arrhythmia and avoidance of drug associated side effects. Success rates for ablation of accessory pathways are as high 95%.5 Caution has to be employed where pathways are close to the AV node and when considering ablation for AV nodal re-entry tachycardia. Ablation is applicable to some VTs and has a special role in the treatment of arrhythmias after surgery for congenital heart disease.

**Specific arrhythmias**

**Tachycardias confined to the atrium**

Atrial tachycardias are common in the foetus and neonate and then diminish in frequency until adult life. They are important arrhythmias in children and adults with corrected congenital heart disease where there has been atrial dilatation or surgical suture lines in the atrium.

**Atrial flutter**

This is not uncommon in the foetus and neonate. The rapid AV conduction at this age can result in very high ventricular rates, causing hydrops and heart failure in the newborn. Flutter waves are usually apparent or made obvious after adenosine. The ventricular rate can be reduced by drugs that increase AV block. Flutter can be termi-
nated pharmacologically with amiodarone or flecainide in association with digoxin to prevent paradoxical increase in ventricular rate as the flutter rate is reduced. Cardioversion is effective and once sinus rhythm is attained the arrhythmia very rarely recurs.

Atrial ectopic tachycardia
Atrial ectopic tachycardia is caused by an aberrant focus of excitation. ECG shows an abnormal P wave axis, the morphology of which depends on the site in the atrium the focus arises. The ventricular rate can vary with accelerations and deceleration. In infancy, spontaneous resolution is common; in older children they often are incessant and cause secondary impairment of ventricular function and clinical heart failure. The impaired ventricular function resolves when the tachycardia is abolished, and this may require radiofrequency ablation.6

Atrial fibrillation
In contrast to adult practice, this arrhythmia is rarely seen in childhood and usually associated with congenital heart disease leading to atrial dilatation and previous cardiac surgery. The surface ECG shows the typical fine irregular baseline between irregular ventricular complexes. An important association is with WPW. Theoretically patients with accessory pathways are at increased risk of atrial fibrillation as the atrium may be excited prematurely in a vulnerable phase that induces fibrillation. This is thought to be the mechanism of rare sudden death in WPW where rapid anterograde conduction down the accessory pathway leads to rapid irregular broad complex tachycardia (Figure 1) and ventricular fibrillation.7

Tachycardias involving the AV junction
There are two common types of tachycardia arising at the AV junction: AV re-entry tachycardia involving an accessory pathway and AV nodal re-entry tachycardia.

Re-entry tachycardia secondary to accessory pathway
This is the most common type of SVT overall in childhood and has a peak incidence in infancy then diminishing to rise again in adolescence.8

An accessory pathway is a microscopic bridge of muscle between atrium and ventricle that bypasses the normal electrical insulation of the AV ring. Accessory pathways can occur anywhere in the AV junction and can be close to the AV node or more commonly lie in a left lateral position. In sinus rhythm, if the accessory connection can conduct from atrium to ventricle, pre-excitation will be manifest on the ECG as a slur on the QRS upstroke (δ-wave) and a short PR interval. When pre-excitation

Figure 1 Atrial fibrillation in Wolff-Parkinson White syndrome. Irregularly irregular broad complex tachycardia is seen with ventricular rate in excess of 300 b.p.m.
is associated with episodes of SVT it is termed Wolf-Parkinson White syndrome. The degree of pre-excitation will depend on the degree of conduction down the AV node and down the accessory connection. Accessory pathways may be ‘concealed’ and only able to conduct retrogradely from the ventricle to atrium. They will not then be visible on the ECG during sinus rhythm.

In the usual form of SVT, impulses pass down the AV node to the ventricles and then re-enter the atrium via the accessory pathway cycling again down the AV node. This ‘orthodromic’ tachycardia is narrow complex as ventricular activation is via the normal conduction tissue. An inverted P wave will be seen usually mid-way between the QRS complexes in a lateral pathway reflecting the delay in impulses reaching the site of the connection (Figure 2). The P wave will be closer to the QRS complexes when the site of atrial insertion is near the AV node. Less commonly in ‘antidromic’ tachycardia conduction is down the accessory connection and back up the AV node. This produces a broad complex tachycardia, which has to be differentiated from ventricular tachycardia.

Recurrent SVT can be controlled usually by beta-blockers, flecainide, amiodarone or a combination in refractory cases. The tendency to SVT will resolve in most infants. In older children and in those where the accessory pathway can conduct very rapidly, RF ablation is curative.5,9

**AV nodal re-entry tachycardia**

AV nodal re-entry is the predominant mechanism of SVT in older children. This is caused by dual pathways in the AV node. One pathway has a fast conduction time and a short refractory period whilst the other is slow but with a long refractory period. Typically during re-entry tachycardia, conduction proceeds down the slow pathway and returns up the fast pathway to reactivate the atrium and AV node. These pathways are now known to be anatomically distinct, the slow pathway activating the ventricle near the mouth of the coronary sinus and the fast pathway entering in the region of the normal AV node insertion.

In sinus rhythm, the ECG is normal without pre-excitation. In re-entry tachycardia the atrial activation occurs simultaneously with the ventricles and the P wave is buried in the QRS complexes and not visible on the surface ECG.

Medical treatment with nodal drugs such as beta-blocking agents or digoxin may be effective but usually the combination of flecainide and digoxin is required. Ablation, whilst often curative, in our practice is deferred if possible for older children and teenagers where they can give fully informed consent to the procedure. This is because of the rare risk of the order of 1% of heart block leading to permanent pacemaker insertion.5,10

**Incessant junctional reciprocating tachycardia**

In this condition the heart rate is relatively slow and children do not present because of the acute increase in heart rate but from symptoms of congestive cardiac failure resulting in a rhythm-related cardiomyopathy. Some come to light on routine examinations when a tachycardia is noted.

The underlying basis is a concealed accessory pathway, which has much slower conduction than usual. This allows both AV node and the accessory pathway to recover excitability in between depolarisations and leads to the incessant nature. On
ECG, the retrograde P wave is close to the following QRS complex giving a long RP interval. Medical treatment is difficult but ablation is usually possible.\textsuperscript{11}

\textbf{Junctional ectopic tachycardia}

The anatomic basis of this arrhythmia is thought to be a small focus of abnormal automaticity in the AV node or bundle of His. It accounts for 8\% of all SVTs seen in children. ECG shows narrow complex morphology because of the site of origin. There is usually no retrograde activation of the atrium and typically there is complete AV dissociation with the atrium activated by the normal sinus impulses at a much slower rate.

Most commonly, junctional ectopic tachycardia (JET) occurs after cardiopulmonary bypass especially with suturing near the AV junction. Postoperative JET develops within hours of discontinuing bypass and the high ventricular rate with AV dissociation lead to haemodynamic decompensation. JET also occurs as a congenital arrhythmia first described by Coumel as His bundle tachycardia. It usually presents in the neonatal period or infancy with incessant tachycardia.

In the postoperative situation, surface cooling is effective in reducing the ventricular rate and improving haemodynamics. Electrolyte imbalance has to be corrected and use of inotropes minimised. Atrial pacing at a faster rate may lead to capture and restoration of AV synchrony. Amiodarone is the drug usually chosen to minimise negative inotropic side effects. Postoperative JET usually resolves after these supportive measures.

In congenital JET, treatment is directed to improving the ventricular rate and various drugs have been used alone or in combination, such as sotalol, flecainide and propafenone. Amiodarone is probably the most effective.\textsuperscript{12} Radiofrequency ablation is associated with a high degree of complete heart block and lifelong pacemaker requirement.

\textbf{Ventricular arrhythmias}

Ventricular arrhythmias are defined as originating distal to the bundle of His. VT comprises less than 5\% of tachycardias in children and symptoms depend on the ventricular rate. Ventricular arrhythmias and sudden death are well-documented to occur after cardiac surgery for complex congenital heart disease and this has been extensively studied in long-term follow-up after repair of tetralogy of Fallot. VT may also arise secondary to metabolic disturbance, drug toxicity (tricyclic antidepressants, solvent abuse), myocarditis or cardiomyopathy.

ECG shows a wide complex tachycardia. QRS duration for a neonate greater than 0.075 seconds and greater than 0.09 seconds in older children is prolonged. The presence of AV dissociation is diagnostic and may be unmasked after the administration of adenosine. VT can occur, however, with 1:1 retrograde conduction to the atrium and it then has to be differentiated from antidromic AV re-entry tachycardia in WPW or SVT with aberrant conduction, which is usually of right branch bundle morphology. Other suggestive features on ECG are a superior QRS axis in tachycardia, capture beats where an atrial impulse passes through the AV node and manages to excite the ventricle producing an interpolated narrow complex. Fusion beats are where partial activation occurs from the sinus node and an intermediate complex is produced.

Idiopathic monomorphic VT in infancy and childhood carries a good prognosis in general if intra-cardiac structure is normal.\textsuperscript{13} If the ventricular rate is slow, treatment may not be required. An incessant form of VT can be seen in infancy, which arises from the left ventricle and has right bundle branch block with superior QRS axis. This condition is thought to be due to small ventricular harmatomas. Suppression can be achieved with flecainide or amiodarone if necessary combined with a beta-blocker. Spontaneous resolution is usual.

A similar morphology, monomorphic VT occurs in older children and teenagers in the absence of structural cardiac abnormality. This left posterior fascicular tachycardia can be responsive to verapamil. Ablation has been successful and curative in refractory cases. Idiopathic right ventricular outflow tachycardia is also described.

\textbf{Genetic conditions associated with ventricular arrhythmia and risk of sudden death}

These conditions have an importance which outweighs their incidence since they can result in the tragic sudden death in otherwise fit and normal children. They are increasingly recognised and the molecular genetic basis defined. This will give the opportunity of mutation specific therapy and automated mutation analysis will in the future simplify screening.

\textbf{Long QT syndrome}

Congenital prolonged QT syndrome is a disorder of ventricular repolarisation characterised by prolongation of the QT interval on the ECG. The autosomal dominant Romano-Ward syndrome is the most common form. The Jervell-Lange-Neilsen syndrome is associated with congenital deafness and inherited as an autosomal recessive condition with a poor prognosis.

The mutations cause defects in various ion channels that affect myocardial repolarisation. This causes predisposition to ventricular arrhythmia – the hallmark of which is a polymorphic VT known as ‘torsades de pointes’. This arrhythmia is often self-limiting but can deteriorate to ventricular fibrillation and lead to sudden death. Typically, patients present with syncopal episodes precipitated by exercise, intense emotion or loud noises and startle. Hypotension can cause secondary hypoxic seizures and diagnosis is not uncommonly delayed and initially mistaken for epilepsy. Most patients present between 9 and 15 years of age but cases have been described in infancy and even presenting in the foetus.

Eleven mutations have now been detected. For the most common phenotype-genotype correlations have been described and some have therapeutic implications.\textsuperscript{14} LQT1 and LQT2 are associated with mutations of genes KCNQ1 and KCNH2 (HERG), respectively. These genes code for subunits of potassium channels. LQT3 is associated with mutations affecting the SCN5A gene, which codes for a cardiac sodium ion channel. LQT1 generally is associated with a broad T wave, LQT2 with low amplitude and often double peaked T waves and LQT3 with a very delayed symmetrical T wave. Syncopal episodes and torsades typically are triggered on exercise and especially swimming with LQT1. LQT2 patients typically are provoked by auditory stimuli and attacks in LQT3 often occur at sleep or resting situations.

Therapy of choice is beta-blockade and a long-acting agent such as nadolol is preferred. Studies have shown that mortality is reduced considerably in treated patients.\textsuperscript{15} Theoretically, sodium...
channel blockers such as mexilitine may be effective in LQT3. Syncope despite beta-blockade is an indication for an automated implantable cardiac defibrillator (ICD). Small units are now available that can allow implantation in young children, although the effects of growth on the electrodes and requirement for repeated revisions is a problem. Trials are underway of a ‘leadless’ ICD that should eventually improve this concern. Treatment with beta-blocking drugs is still required and inappropriate defibrillator activation can occur and cause psychological disturbances.

**Catecholaminergic polymorphic ventricular tachycardia**

Coumel described this familial condition in a series of children who developed syncope secondary to exercise, stress, or startle. There is a typical pattern of a bidirectional ventricular tachycardia (Figure 3) – it can deteriorate to polymorphic VT and sudden death. An autosomal dominant form is related to mutations in the cardiac ryanodine receptor gene and a less common autosomal recessive variety associated with mutations in the calsequestrin 2 gene. Both genes are involved in intra-cardiac calcium transport. Treatment with beta-blocking drugs is effective but poor compliance and syncope despite treatment are indications for consideration of implantation of an ICD.

**Arrhythmogenic right ventricular dysplasia**

The clinical features of arrhythmogenic right ventricular dysplasia are an abnormal resting ECG with T wave inversion in the right praecordial leads and ventricular tachycardia with typical left bundle branch block morphology. The condition is associated with fibro-fatty replacement of myocardium in the right ventricle. It is one of the major genetic causes of juvenile sudden death and inherited as an autosomal dominant condition with variable penetrance. Several different loci have been demonstrated in this condition including a ryanodine-receptor mutation.

**Brugada syndrome**

In this condition syncope occurs due to idiopathic ventricular fibrillation. It is associated with typical ECG changes consisting of right bundle branch block pattern and variable ST segment elevation in the right praecordial leads. It is considered mainly a disease of young adults but was first described in children and events are commonly associated with febrile illnesses in the young and often occur at night. The ST elevation has a coved or ‘saddle type’ appearance and may be revealed after the administration of sodium channel blocking drugs such as mexilitine or flecainide, which can be used as a diagnostic test. Spontaneous presence of the typical pattern is a risk factor for sudden death. There is autosomal dominant inheritance and mutations have been found in the SCN5A gene in 20–30% of patients.

**Summary**

The spectrum of arrhythmias in children is now well-defined. Correct diagnosis and management depends on the capture and analysis of an ECG during symptoms. Most arrhythmias can be controlled successfully with a relatively small range of drugs. Treatment is given until either there is spontaneous resolution or the age is reached where ablation and pacemaker therapies have the least risk. Refractory arrhythmias require multidisciplinary collaboration from paediatric cardiologists, cardiac surgeons, electrophysiologists, and geneticists. Genetic advances offer the

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**Figure 3** Holter recording showing simultaneous ECG channels demonstrating an episode of bidirectional VT in a patient with history of syncope. Alternating different morphologies of ventricular complex are seen during tachycardia. This is diagnostic of Catecholaminergic polymorphic VT.
prospect of improved screening and specific treatment for life-threatening inherited conditions.

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Practice points

- Cardiac arrhythmias can be classified as supraventricular, nodal or ventricular, and in terms of whether or not they are occurring secondary to structural damage
- The correct diagnosis and management of a cardiac arrhythmia depends on the analysis of an ECG during symptoms, as well as on a detailed history and examination
- Most arrhythmias can be controlled successfully with a relatively small range of drugs
- Treatment is given until either there is spontaneous resolution or the child is old enough to undergo radiofrequency ablation or pacemaker therapies with least risk
- Refractory arrhythmias require multi-disciplinary collaboration from paediatric cardiologists, cardiac surgeons, electrophysiologists, and geneticists
- Genetic advances offer the prospect of improved screening and specific treatment for life threatening inherited conditions