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Review

The diagnosis and management of fetal cardiac arrhythmias

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Key content

- Fetal cardiac arrhythmias are relatively common and account for up to 20% of referrals to fetal cardiologists.
- Arrhythmias may occur because of structural abnormalities of the fetal heart, or because of abnormal functioning of the cardiac conduction system in an otherwise structurally normal heart.
- Arrhythmias may be diagnosed using ultrasound and M-mode and Doppler echocardiography.
- Transplacental therapy for tachyarrhythmias has been one of the success stories of fetal cardiology, and good outcomes can be expected in the absence of hydrops.
- Congenital heart block is most commonly caused by the transplacental passage of anti-Ro and anti-La antibodies and transplacental therapy is less successful in managing this.

Learning objectives

- To enable clinicians to provide better counselling for patients about the prognosis of fetal arrhythmias.
- To learn how to diagnose fetal arrhythmias and know when to refer to a specialist centre if the diagnosis is suspected.
- To understand the treatment options available and the evidence-based antenatal care schedule.

Keywords: antenatal diagnosis / arrhythmias / cardiology / fetal medicine

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Introduction

A fetal cardiac arrhythmia is defined as a heart rate that is either too fast (usually >200 beats per minute [bpm]) or too slow (usually <100 bpm), or has an irregular rhythm. Fetal cardiac arrhythmias occur as a result of abnormal activation or beating of the myocardium. They are usually noted during a routine mid-trimester anomaly scan and are reported in up to 3% of pregnancies.[1] The commonest form of fetal cardia arrhythmia, atrial extrasystoles, have been reported in 14% of healthy babies.[2] Fetal cardiac arrhythmias account for up to 20% of referrals to fetal cardiologists.[3]

It is important to understand the difference between changes in the heart rate that are outside the normal range but are a normal physiological response to extracardiac factors, and those arising because of disturbance of the cardiac conduction system or the myocardium itself. An understanding of arrhythmias has important implications for antenatal and peripartum care. Therefore, general obstetricians, as well as fetal medicine specialists, should be familiar with the different types of arrhythmia and their management. Fetal arrhythmias are different from almost all other fetal cardiac abnormalities because of the use of transplacental treatment and, in particular, antiarrhythmic agents administered for management of fetal tachyarrhythmias.

Fetal cardiac rhythm abnormalities are relatively frequently referred for specialist fetal cardiac or fetal medicine review. Despite this, arrhythmias relatively rarely cause significant fetal compromise. In a series of more than 4000 fetuses referred to a tertiary centre with a suspected cardiac abnormality,[4] 12.7% had an arrhythmia but only 1.7% of these showed evidence of haemodynamic compromise.

Obstetric and fetal medicine centres have different approaches to the management of fetal arrhythmias. There is a clear need to elaborate on, and implement, standardised, evidence-based protocols.

Pathophysiology

The fetal cardiac conduction system (Figure 1) is functionally developed at 16 weeks of gestation.[5] The normal cardiac impulse starts at the sinoatrial node, in the upper part of the

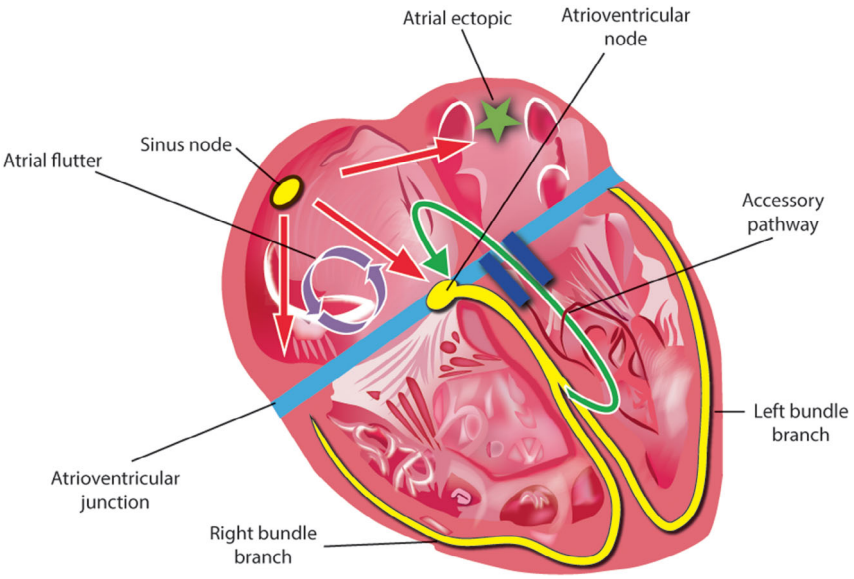

Figure 1. Basic diagram of cardiac conduction system. Figure shows the sinus node in the right atrium, the atrioventricular node on the right of the atrioventricular junction and the right and left bundles. An impulse is generated in the sinus node causing atrial contraction, propogated to the atrioventricular node and from there to the bundles causing systole. The atrioventricular junction acts as an electrical barrier between the atria and ventricles. An ectopic beat can arise from anywhere in the atria or ventricles causing an irregular rhythm. Re-entry tachycardia occurs when there is an abnormal electrical connection or pathway across the atrioventricular junction. Alternatively, a persistently irritable atrial focus may result in atrial flutter. Heart block may occur in association with structural heart disease or as a consequence of antibody-mediated inflammation of the cardiac conduction system.

right atrial wall. The impulse is conducted across the atria, causing atrial contraction, then progresses to the atrioventricular node, on the right side of the atrioventricular junction. The impulse then progresses through the His bundles to the right and left ventricles, causing ventricular systole. The atrioventricular junction acts as electrical insulation, preventing direct conduction between the atria and ventricles and vice versa.

Ectopics (extra beats) can occur anywhere within the myocardium – they more often originate in the atria than the ventricles, but in both cases can cause an irregular rhythm. They may occur as isolated extra beats, but also as multiple or coupled beats, which can make interpretation of the underlying fetal heart rhythm difficult.

Most fetal tachycardias occur either when there is an abnormal irritable focus of atrial tissue causing persistent rapid impulse propagation (atrial flutter), or because of an abnormality of the atrioventricular junction, which allows the ventricular impulse to re-enter the atria, producing a re-entry circuit (atrioventricular re-entry tachycardia).

Heart block may occur in some forms of structural congenital heart disease, either because the cardiac conduction system develops abnormally (for example, left atrial isomerism), or because it takes an abnormal course through the myocardium (for example, congenitally corrected transposition). A more common reason for heart block is inflammation of the cardiac conduction system caused by transplacental antibody transfer in mothers with anti-Ro and anti-La antibodies. Rarely, it can occur as a primary disease of the myocardium.

Fetal cardiac rhythm assessment

Arrhythmias may be noted on auscultation at a routine antenatal appointment or during routine ultrasound. Several different modalities have been used to assess the fetal heart rhythm, including fetal electrocardiography (fECG) and fetal magnetocardiography (fEMG). While these techniques may have benefits in a research setting (see Table 1), the mainstay of diagnosis in current clinical practice remains fetal echocardiography using two-dimensional (2D) imaging, M-mode echocardiography and Doppler studies.

Two-dimensional imaging provides real-time assessment of the fetal heart rate, rhythm regularity and whether there is synchrony between the atrial and ventricular contraction. Cross-sectional examination should also evaluate cardiac structures, heart size and function. Careful assessment with cross-sectional imaging during a routine scan is usually sufficient to decide whether any given arrhythmia is benign or requires more detailed study to diagnose the heart rhythm abnormality using M-mode and Doppler in addition to 2D imaging.

Table 1. Imaging modalities used in the assessment of fetal cardiac arrhythmias

Modality	Application
2D cardiac imaging and Doppler studies	Assessment of structural cardiac defects, atrial and ventricular function, chamber sizes, flow velocities at valves
M-mode	Atrial and ventricular contraction, coordination, sequence and interval of AV contraction
Extracardiac ultrasound imaging	Assessing extracardiac abnormalities, amniotic fluid volume, umbilical artery, middle cerebral artery pulsatility indices and systolic velocities
Fetal electrocardiography (fECG)	Invasive fECG methods (also known as ST analysis [STAN]) have been used in intrapartum settings to monitor for fetal academia. Non-invasive fECG methods, which discern fetal heart rhythms from 17 weeks of gestation with electrodes placed on the maternal abdomen, have recently been used to diagnose fetal arrhythmias. These have the advantage of providing additional information over a longer time period than traditional echocardiography, but there remain concerns around this technique's ability to discern fetal atrial activity, and presently this technique is limited to research settings.
Fetal magnetocardiography (fMCG)	Fetal magnetocardiograms are another technology presently limited to research settings. The trace is acquired using biomagnetometers and recordings must be performed in a magnetically shielded room. fMCG has been used as an adjunct to traditional echocardiography in the diagnosis of fetal arrhythmias and structural heart defects.

M-mode echocardiography facilitates detailed evaluation of the heart rate, the time intervals between different events in the cardiac cycle and the relationship between atrial and ventricular contraction. By placing the M-mode cursor across the atrial and ventricular walls, simultaneous recording and comparison of atrial and ventricular activity is achieved (Figure 2).[6]

Doppler studies allow the fetal heart rate to be determined and, with appropriate cursor placement across ventricular inflow and outflow, can be used to confirm sinus rhythm and to measure the time interval between atrial and ventricular contraction (A-V interval), equivalent to the PR interval on a 12-lead ECG (Figure 3a). Interpretation of this becomes more difficult when the rhythm is abnormal, in which case Doppler assessment of a central vein and artery (for example, aorta and superior vena cava[7] or pulmonary artery and vein[8]) is required (Figure 3b).

Tissue Doppler imaging may be useful in evaluating cardiac arrhythmias.[9] It requires specialist software for interpretation and remains of limited use, but has some value in demonstrating improvement in cardiac function after conversion to sinus rhythm in successfully treated fetuses.

In all cases of a documented arrhythmia, a detailed ultrasound assessment of fetal anatomy, which looks for extracardiac anomalies, including evidence of fetal haemodynamic compromise, growth, Dopplers and amniotic fluid volume, should be undertaken.

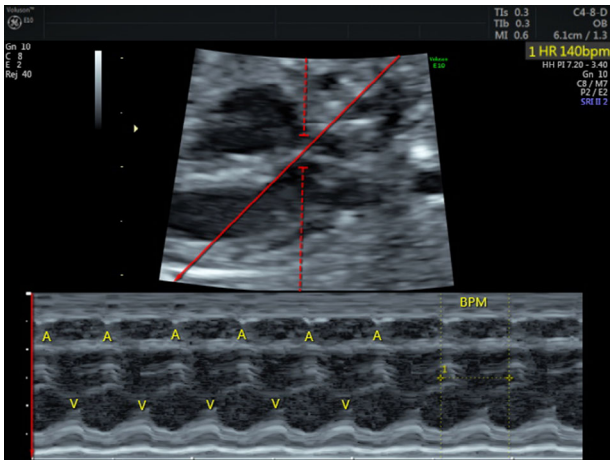

Figure 2. M-mode tracing of atrial and ventricular contraction during sinus rhythm. The M-mode cursor crosses the atrial wall at the top of the image and the ventricular wall below. Note the 1:1 relationship between atrial (A) and ventricular (V) contraction with a fetal heart rate of 140 beats per minute (BPM).

Ectopic beats

Ectopic beats are the commonest detected fetal arrhythmias and are usually noted in the third trimester.[10] Ectopics arise from a locus in the myocardium, separate from the normal pacemaker. The site is most often in the atrium, but they can originate in the ventricles. An ectopic beat may be conducted

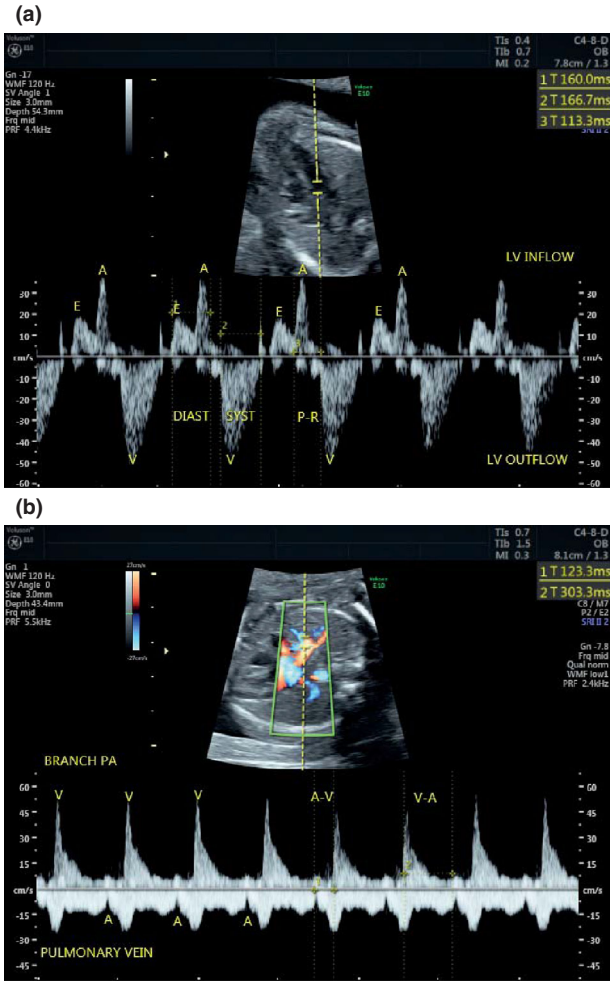

Figure 3. Spectral Doppler tracing in sinus rhythm. (a) Spectral Doppler tracing in sinus rhythm with cursor placed to record inflow and outflow in the left ventricle showing normal diastolic, biphasic E and A wave filling of the left ventricle followed by the V wave of ventricular systole. The A-V interval is measured from the beginning of the A wave to the beginning of the V wave. This interval is equivalent to the PR interval on an electrocardiogram. (b) Spectral Doppler tracing in sinus rhythm with cursor placed to record pulmonary artery (above the baseline) and pulmonary vein flow (below the baseline) simultaneously. In the pulmonary Doppler flow spectral, the A wave is characterised by a sharp reduction (or even reversal) in pulmonary venous inflow as the atrium contracts (A) and increases intra-atrial pressure. The sharp spike above the baseline V wave is the pulmonary artery flow in ventricular systole. Identification of the A wave and V wave in the tracing enables precise measurement of the A-V and V-A intervals. Note in sinus rhythm, the A-V interval is shorter than the V-A interval.

to the ventricles or blocked at the atrioventricular node. A conducted atrial ectopic, or an ectopic from the ventricle, will result in ventricular contraction occurring sooner than the next expected sinus beat. Consequently, the stroke volume of an ectopic beat will be less than a sinus beat (Figure 4). A nonconducted atrial ectopic beat occurs when the impulse arrives at the atrioventricular node when it is in its refractory state, thus preventing ventricular propagation. This resets the sinoatrial node such that the next ventricular beat will occur one cycle length after the blocked ectopic beat, giving the impression of a missed beat or a compensatory pause (Figure 5). With increased filling time, the stroke volume will be greater than a normal sinus beat.

It is challenging to correctly identify ectopic beats when they occur regularly, producing a regular irregular rhythm such as bigeminy. If regular ectopic beats are not conducted from the atrium to the ventricle, this can manifest as a regular bradycardia and can easily be mistaken for heart block (usually 2:1 block). Understandably, this has led to premature emergency delivery in some cases, so careful assessment of the overall fetal condition is essential. In the absence of evidence of haemodynamic compromise in an active fetus, a period of inpatient observation or further cardiac assessment 1 week later, when the ectopics may have resolved, can avoid premature delivery and thereby reduce perinatal morbidity. Ectopic beats almost never cause significant haemodynamic compromise, even when there is an associated bradycardia. In almost all cases, the ectopic beats will settle spontaneously before the end of the pregnancy and the long-term prognosis is excellent. If ectopics persist and are present during labour, fetal monitoring is challenging and the risk of requiring caesarean section is increased. However, a small percentage (2–5%) of fetuses with ectopic beats will develop a sustained supraventricular tachyarrhythmia.[11] This risk may be higher when there is bigeminy or multiple ectopic beats.

Tachyarrhythmias

It is helpful to divide tachyarrhythmias into two categories: supraventricular tachycardia and ventricular tachycardia.

Supraventricular tachycardia

This describes any tachycardia where the origin is atrial rather than ventricular. Supraventricular tachycardia is much commoner than ventricular tachycardia. The origin is most often a re-entry circuit, which crosses between the atria and ventricles, but also may arise from an ectopic focus or a re-entry circuit within the atria. Supraventricular tachycardias may occur with a 1:1 atrioventricular conduction relationship or with some degree of atrioventricular block, as seen in atrial flutter.

Supraventricular tachycardia with 1:1 conduction

Most supraventricular tachycardias with 1:1 conduction have a regular heart rate of 240–260 bpm. These cases account for approximately 66% of fetal tachycardias presenting for fetal cardiac assessment.[3] Rarely, rates as high as 300 bpm are

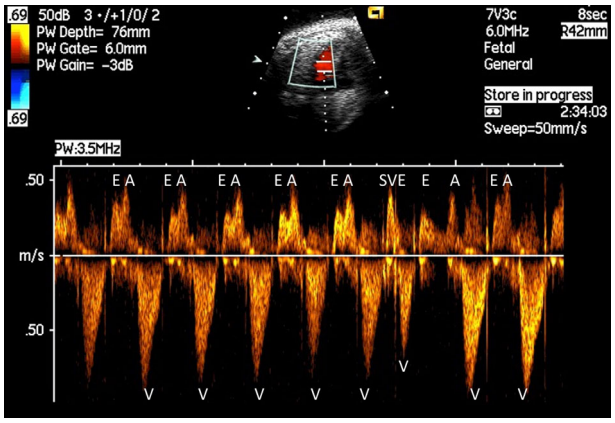

Figure 4. Doppler spectral tracing across LV inflow (E and A waves, above baseline) and LV outflow (V wave, below baseline). Figure shows isolated conducted atrial extrasystole (SVE) occurring prematurely with loss of normal biphasic LV inflow followed by a smaller V wave caused by decreased ventricular filling. The LV inflow pattern after the extrasystole is prolonged before sinus rhythm is restored.

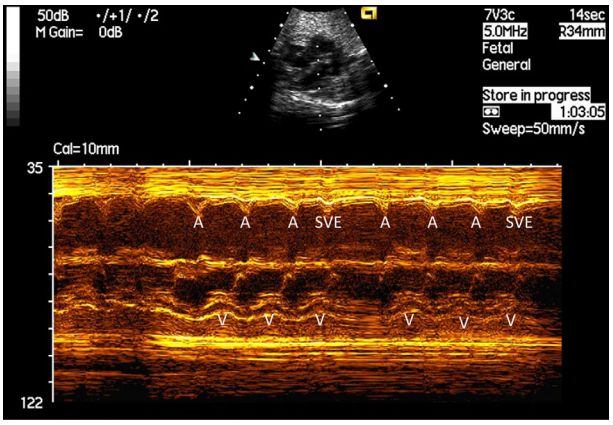

Figure 5. M-mode tracing through atrial (A) and ventricular (V) wall. Figure shows isolated, nonconducted atrial extrasystoles (no ventricular contraction seen after nonconducted SVE) followed by a pause until the next sinus beat occurs with a normal A–V relationship restored.

seen.[12] Atrial and ventricular rates will be the same and this 1:1 relationship is demonstrated on M-mode echocardiography or using Doppler. The basis of most tachycardias of this type is a re-entry circuit associated with an accessory pathway crossing the atrioventricular junction, as described in Wolff–Parkinson–White syndrome. In this arrhythmia, atrioventricular conduction occurs via the atrioventricular node and the impulse returns to the atria by a rapidly conducting retrograde accessory pathway, which conducts faster than the atrioventricular node. The rapidly conducting retrograde accessory pathway causes a

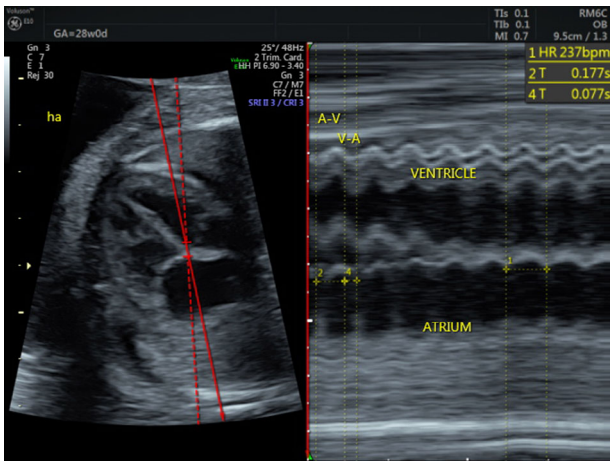

Figure 6. M-mode tracing of fetal tachycardia showing fetal heart rate of 237 bpm. Note the regular 1:1 atrioventricular relationship. A-V and V-A time intervals are measured showing that this is a short VA tachycardia.

characteristic short ventricular–atrial (V-A) conduction interval (short VA tachycardia). A short VA tachycardia is defined as one in which the V-A interval is less than the atrial–ventricular (A-V) interval. In contrast, supraventricular tachycardias with a long ventricular–atrial interval (long VA tachycardias, when the V-A interval is longer than the A-V interval) are less common and are usually caused by atrial ectopic tachycardias.[3] Measurement of V-A intervals is possible using both M-mode and Doppler interrogation (Figure 6). This distinction has clinical relevance because short VA tachycardias are more responsive to transplacental antiarrhythmic therapy, with a greater percentage of fetuses converting to sinus rhythm. When there is a long VA tachycardia, it is usually more difficult to re-establish sinus rhythm prenatally.[6,13] However, fetal heart rate can usually be reduced with transplacental therapy, thereby improving cardiac output. Both short and long VA tachycardia can be intermittent. Therefore, this diagnosis should be considered in fetal hydrops, even if a tachyarrhythmia is not noted at the time of scanning.

Supraventricular tachycardia with atrioventricular block (atrial flutter)

Atrial flutter is caused by a re-entry circuit confined within the atrial tissue. It accounts for up to 25% of all cases of fetal tachyarrhythmias[14] and is usually diagnosed later than supraventricular tachycardia with 1:1 conduction.[6] When occurring during fetal life, the re-entry circuit is usually in the right atrium. The rhythm may or may not be regular. The atrial rhythm is very fast, often 450–500 bpm. However, the atrioventricular junction cannot conduct that fast, so blocks some of the atrial beats. This may be a regular block, such as 2:1, which pertains to around 80% of cases,[14] or a variable

block, in which case the fetal heart rate will be irregular and slower than in 2:1 block. This may be associated with a lower risk of hydrops.

In most cases of flutter, the heart rate is between 200 and 250 bpm. In some cases, 2D imaging is sufficient to make the diagnosis when it is obvious that atrial contraction is considerably faster than ventricular contraction. It is also possible to demonstrate atrial flutter on M-mode, which will show the rapid atrial rate and allows the degree of block to be calculated (Figure 7).

Ventricular tachycardia

Ventricular tachycardias are uncommon in fetal life and account for 1–2% of fetal tachyarrhythmias.[15] The fetal heart rate tends to be slower than in supraventricular tachycardia and correct diagnosis can be difficult. In most cases, M-mode can be used to demonstrate a slower atrial than ventricular rate, but ventricular tachycardia can occur with a 1:1 relationship. It may occur in association with underlying myocardial disease (for example, myocarditis) as well as with abnormalities of the conduction system, such as congenital long QT syndrome, when it can be paroxysmal.[13]

Management of tachycardias

After assessing the nature of the tachycardia, management principles will depend on factors such as gestational age at diagnosis, the fetal heart rate and whether the tachycardia is paroxysmal or incessant. The identification of findings of haemodynamic compromise, such as cardiomegaly, atrioventricular valve regurgitation, impaired ventricular function and/or fetal hydrops, also have an effect.

An expectant approach to treatment may be reasonable when the diagnosis is made near term and there are no signs of compromise. However, regular, continuing assessment is needed to ensure there is no haemodynamic deterioration, which may influence the success of both prenatal and postnatal treatment. Prenatal treatment with transplacental therapy is the preferred option when there is evidence of haemodynamic compromise or at a gestation of fewer than 36 weeks. Delivery of a premature infant with hydrops and tachyarrhythmia presents a formidable neonatal management challenge, but there is a better outcome if the rhythm can be controlled before delivery. Most studies report a high percentage of therapeutic success in treating supraventricular tachycardia (1:1 conduction and atrial flutter) when antiarrhythmic therapy is given to the mother.[16,17] In the absence of hydrops, successful treatment can be achieved in around 90% of cases, dropping to around 60% when there is evidence of fetal hydrops.

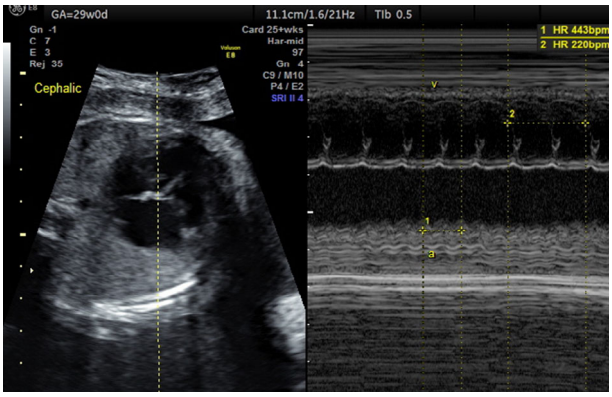

Figure 7. M-mode tracing in atrial flutter. Figure shows atrial and ventricular contraction with atrial rate at the bottom of the screen and ventricular rate at the top. This demonstrates atrial flutter with 2:1 block with an atrial rate of 440 bpm and a ventricular rate of 220 bpm.

There is little consensus as to the most efficacious antiarrhythmic agent. A lack of randomised controlled trials has resulted in differing protocols. The most frequently used antiarrhythmics include digoxin, flecainide, sotalol and – less frequently – amiodarone (for doses, see Table 2). Early treatment protocols used digoxin with some success, but it was soon recognised that transplacental transfer of digoxin in the presence of fetal hydrops was significantly reduced.[18] Consequently, alternative agents such as flecainide were used, but this was associated with a series of fetal deaths in one early series reported by Allan et al.,[19] raising concerns about safety. These deaths were associated with a possible proarrhythmic effect, as seen in adults, but may have been exacerbated by severe fetal haemodynamic compromise and hypoxia. Despite this, flecainide is still widely used and, in most studies, appears efficacious, is well tolerated and confers a minimal risk of in utero demise.[17] Because of continuing concern about flecainide, some units prefer sotalol as an alternative. However, note should be taken of the study by Hill et al.,[16] which suggested that sotalol was marginally less efficacious than flecainide.

The use of a single agent frequently restores sinus rhythm relatively quickly in short VA tachycardia and is recommended in most cases. However, some of the long VA tachycardias, and atrial flutter, may require more than one antiarrhythmic drug for successful treatment.[20] Our preferred treatment algorithm is given in Figure 8.

Transplacental treatment inevitably exposes the mother to potential adverse drug effects. However, side effects prompting dose adjustment are rare: 3.9% with digoxin, 3.8% with flecainide and 2.3% with sotalol. Nausea and dizziness are the commonest reported side effect, but do not usually require dose adjustment.[16] Most units recommend a baseline 12-lead ECG for all mothers starting flecainide or sotalol and serum levels of digoxin, flecainide and (if possible) sotalol are required at the appropriate times (see Table 2) to ensure adequate therapeutic levels and no toxicity.

Table 2. Transplacental therapy for fetal tachyarrhythmias

Drug	Therapeutic maternal dose range	Therapeutic level and effect	Toxicity
Digoxin	Loading dose: 1200–1500 µg/24 h IV, divided every 8 h Maintenance dose: 375 750 µg daily, divided every 8–12 h postoperatively	0.7-2.0 µg/mL Nausea, fatigue, loss of appetite, sinus bradycardia, first degree AV block, rare nocturnal Wenckebach AV block	Nausea/vomiting +++ sinus bradyarrhythmia or AV block +++, proarrhythmia
Flecainide	100 300 mg daily, divided every 8–12 h postoperatively	0.2–1.0 µg/mL Mild P and QRS widening, first degree AV block, QTc <0.48 s, headache	Visual/central nervous system symptoms, BBB, QTc >0.48 s, maternal/fetal proarrhythmia
Sotalol	160–480 mg daily, divided every 8–12 h postoperatively	Levels not monitored Bradycardia, first degree AV block, P and QRS widening QTc <0.48s	Nausea/vomiting, dizziness, QTc >0.48 s, fatigue, BBB, maternal / fetal proarrhythmia

Abbreviations: AV = atrial–ventricular; BBB = blood-brain barrier; IV = intravenous

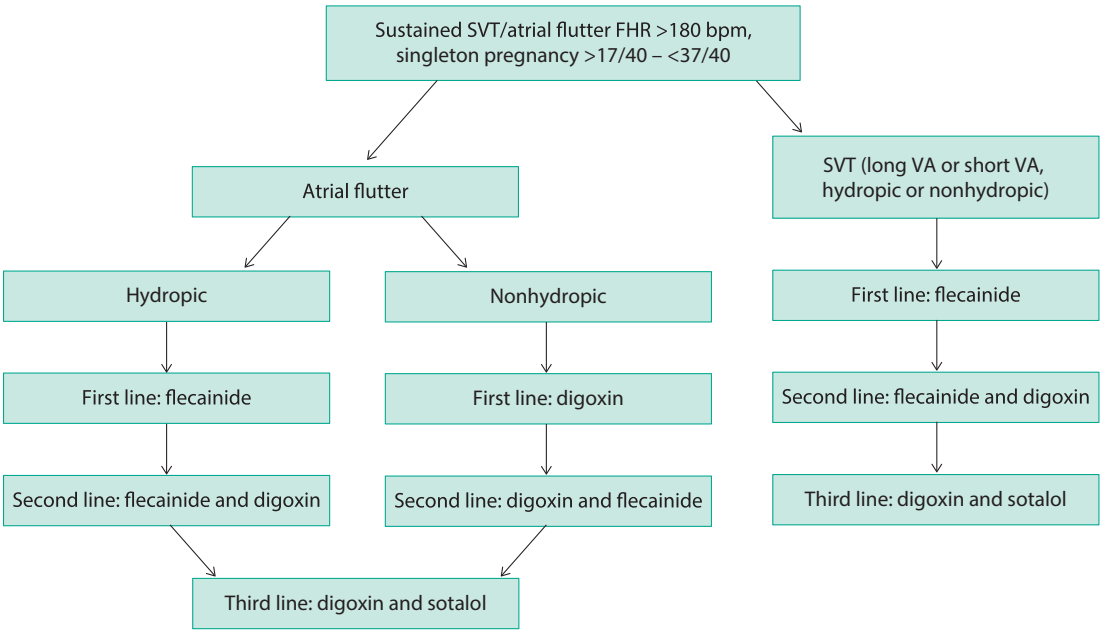

Figure 8. Treatment algorithm for sustained tachycardia. FHR = fetal heart rate; SVT = supraventricular tachycardia.

There are reports of successful amiodarone use,[21,22] but they are mostly anecdotal. Its use is limited by the maternal side effect profile and the length of time it takes to achieve therapeutic levels in the fetus. Amiodarone has also been used for treatment of ventricular tachycardia, as has maternal magnesium infusion.[23] Direct fetal therapy, using an intramuscular or intraperitoneal route, has been reported for digoxin, amiodarone, adenosine and verapamil,[15] but problems associated with this method of administration and concerns over its efficacy limits its clinical use. In a series of 13 fetuses treated with direct antiarrhythmic drug administration into the umbilical vein, all with hydrops and all refractory to transplacental medical treatment, six babies died in utero or in the early neonatal period. Two of these had a cardiac arrest in utero.[24] The route of therapy, cordocentesis, has been associated with an excess risk of fetal demise.[25]

Outcome

The neonatal outcomes following antenatal treatment of tachyarrhythmias are one of the success stories of fetal cardiology. As indicated above, successful treatment is possible in up to 90% of fetuses with an uncomplicated tachyarrhythmia. The need for long-term postnatal antiarrhythmic therapy in these children is usually limited to less than 5% of cases, in our postnatal experience. Even with rate control, rather than restoration of sinus rhythm, the long-term outlook is good. However, a greater proportion of these children will require long-term antiarrhythmic management and sometimes, subsequent electrophysiology study and ablation. In atrial flutter, where sinus rhythm has not been restored, neonatal electrical cardioversion is usually required. Even in these patients, a need for long-term antiarrhythmic treatment is extremely rare. The outcome for ventricular tachycardia is less certain because of the small numbers involved. Given it can be associated with myocardial pathology or long QT syndrome,[23] the outlook is probably less favourable.

Peripartum care

If rate control is established, there are no signs of fetal haemodynamic compromise, and no other obstetric or fetal contraindications, an induction of labour between 38 and 40 weeks can be considered, with continuous fetal monitoring. If rate control is not established, effective monitoring in labour is problematic, so fetal compromise may be less easy to discern and caesarean section should be considered. If there are signs of fetal compromise, including hydrops, then early delivery by caesarean section will probably be required. The timing of delivery in these cases will involve multidisciplinary team (MDT) planning with obstetricians, fetal medicine specialists, neonatologists and fetal cardiologists.

Bradycardias

Fetal bradycardia is defined as a heart rate that is consistently below 100 bpm. This is common in the mid-trimester, particularly during ultrasound when there may be a transient bradycardia, often caused by pressure on the fetus itself. This is self-limiting and not associated with haemodynamic compromise.

Prolonged bradycardia may indicate a serious underlying arrhythmia. However, it is also imperative to look for other signs of fetal distress and decide whether urgent delivery is required. Distinguishing between a bradycardia caused by severe hypoxia and one caused by an underlying cardiac rhythm abnormality may prevent unnecessary and potentially dangerous premature delivery.

Blocked ectopic beats as a cause of fetal bradycardia have been discussed above. Distinction between this rhythm and heart block can be difficult, but blocked ectopics frequently resolve and do not cause fetal haemodynamic compromise.

Fetal bradycardia in association with 1:1 conduction can be seen when there is an abnormality of the sinoatrial node, such as in left atrial isomerism. In this condition, frequently associated with severe congenital cardiac defects, the normal sinoatrial node is small, in an abnormal position, and generates a slower-than-normal rate. In some cases of left isomerism, the sinoatrial node may be completely absent; this is associated with complete heart block. Long QT syndrome can be associated with abnormal delays in cardiac repolarisation, which – in turn – may produce bradycardia with 1:1 conduction. One study[26] suggests this condition may account for up to 17% of cases of fetal bradycardia with a structurally normal heart. In addition to often being the only sign of fetal long QT syndrome, the fetal bradycardia itself may be borderline: up to 35% of cases may have a fetal heart rate of between 110 and 120.[26]

Heart block

This is divided into first, second and third-degree (complete) heart block. It may occur with structural congenital cardiac lesions, such as left atrial isomerism and congenitally corrected transposition, but most frequently occurs with maternal anti-Ro and anti-La antibodies. Rarely, it can be associated with primary myocardial disease or in association with long QT syndrome.

While first-degree heart block does not manifest as a bradycardia, it is worth discussing because it may be the precursor to second and third-degree heart block. In first-degree heart block, the interval between atrial and ventricular contraction is prolonged (Figure 9). Measurement of this

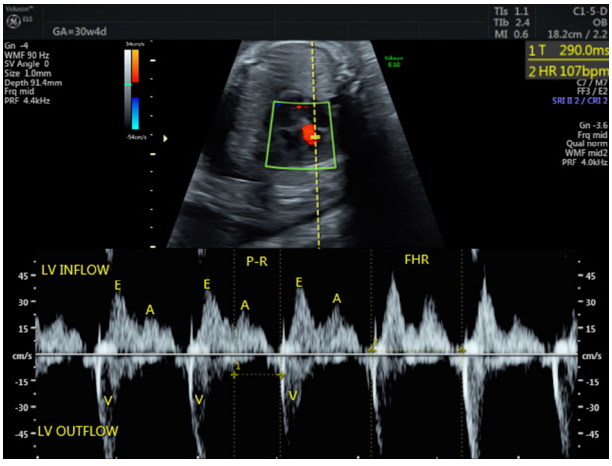

Figure 9. Doppler spectral tracing of LV inflow and LV outflow. Figure demonstrates fetal bradycardia with a prolonged A-V interval (290 ms), confirming first-degree heart block.

interval in women with anti-Ro/anti-La antibodies may provide prognostic information and might suggest the need to start treatment with steroids or intravenous immunoglobulins to try and prevent progression from first-degree to second or third-degree heart block. However, there is a paucity of evidence to suggest treatment benefit at this stage. We have used intravenous immunoglobulin with apparent improvement in one case in this setting.[27]

Second-degree block occurs when there is an intermittent loss of impulse conduction between the atria and the ventricles, resulting in a dropped beat. This may be in a fixed relationship (Mobitz type 2) or, more unusually in fetal life, where there is gradual prolongation of the A-V interval resulting in a dropped beat before the PR interval resets (Mobitz type 1).

In third-degree block, there is absence of conduction between the atria and ventricles and, while the atrial rate may be normal, the ventricular rate, which is regular, depends on the ventricular escape rhythm, usually between 40 and 80 bpm. M-mode echocardiography or Doppler will illustrate complete dissociation between atrial contraction and ventricular contraction (Figure 10) in third-degree block.

When complete heart block occurs in association with structural heart defects, such as left atrial isomerism or with congenitally corrected transposition, the prognosis for the baby is poor.[28] It frequently results in fetal hydrops and intrauterine fetal demise.

In the absence of structural heart disease, our experience indicates that fetal complete heart block is associated with anti-Ro or anti-La antibodies in more than 90% of cases. Cardiac findings in the fetus may be the first manifestation of this condition and only a small minority of mothers will have evidence of active connective tissue disease. Anti-Ro/La antibodies can cross the placenta from approximately 16 weeks of gestation, so it is rare to see heart block attributable to maternal antibodies before this stage.[29] Equally, the risk of developing antibody-mediated heart block in the last trimester is reduced,[29] so the most important period for increased surveillance is between 18 and 28 weeks. Most cases of antibody-mediated heart block in pregnancy present as complete heart block. Fetal echocardiography demonstrates cardiomegaly, usually with preserved ventricular function. In some cases, there may be evidence of atrioventricular valve regurgitation. This does not necessarily confer a poor prognosis. It is assumed that the antibodies initiate an inflammatory process, most frequently in the cardiac conduction system, but sometimes in other areas of the myocardium. In addition to complete heart block, increased myocardial echogenicity and pericardial effusions may be seen with or without accompanying heart block.

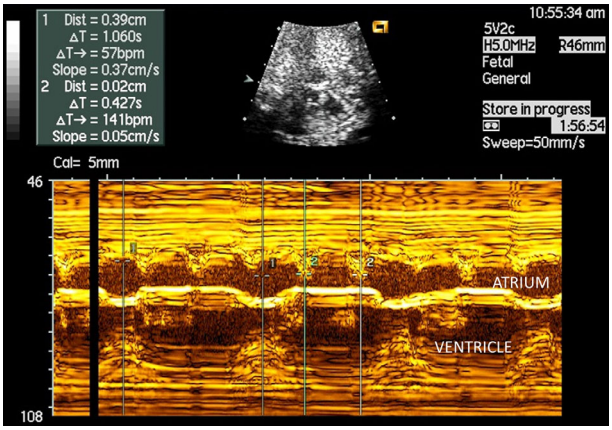

Figure 10. M-mode tracing of antibody-mediated complete heart block. Figure confirms fetal bradycardia (ventricular rate 57 bpm) and dys-synchrony between atrial and ventricular contraction.

Management of complete heart block

The prognosis for complete heart block is influenced by the presence of structural cardiac lesions (see above), gestation at presentation, the ventricular heart rate and whether there is evidence of hydrops. In isolated complete heart block, without hydrops and with a ventricular rate greater than 60 bpm, there is a very good chance of live delivery at or near term. In some cases, neonatal pacemaker implantation is required, but this can often be deferred until sometime in the second decade of life, with minimal symptoms in between.

Modulation of the inflammatory process has been attempted with maternal steroid therapy. Hydroxychloroquine, intravenous immunoglobulin and plasmapheresis, either alone or in combination, have also been trialled. Conclusive data to support such interventions is difficult to interpret from the published studies,[30] but steroid therapy is still practiced in most units.

Beta-sympathomimetics, such as salbutamol and terbutaline, have also been used. While it is possible to increase the fetal heart rate by giving intravenous infusions of these agents to the mother, doses must be high, the effect is short-lived and maternal side effects are poorly tolerated.

When there is worsening hydrops and deteriorating cardiac function, premature delivery may be considered; however, the logistics of pacing a premature small baby must be carefully considered. Fetal haemodynamic deterioration may be a function of antibody-induced myocarditis, rather than the bradycardia alone. This carries a poor prognosis. Almost inevitably, if there is a plan for active postnatal intervention, delivery must be by caesarean section to circumvent the difficulties of effective monitoring during labour.

Both open and minimally invasive cardiac pacing to improve cardiac output have been trialled in complete heart block. Some reports[31,32] have shown it is possible to pace the fetal cardiac ventricle, but attempts to do this have been

complicated by difficulties with lead placement and lead dislodgement. A new micro pacing device, which is wireless, leadless and percutaneously implantable, has been used in animal models and may have human applications in due course.[33]

An algorithm for the management of fetal bradyarrhythmias is presented in Figure 11.

Managing women with anti-Ro/La antibodies

In our centre, women with anti-Ro/La antibodies who have had a previous pregnancy affected by fetal heart block are started on hydroxychloroquine before 10 weeks of gestation. A fetal echocardiogram is offered at 18 weeks of gestation, and the fetal heart rate is monitored with a handheld Doppler at midwifery-led appointments every 2 weeks from 20 weeks. There is evidence that prophylactic treatment with hydroxychloroquine reduces the risk of fetal heart block in women with a previously affected pregnancy, but not in primiparous women or in parous women with a previously unaffected infant.[34] Therefore, this latter cohort are not offered hydroxychloroquine, but are otherwise offered the same protocol of a fetal echocardiogram at 20 weeks and subsequent fetal heart rate monitoring at midwifery-led appointments every 2 weeks from 20 weeks.

Regular echocardiograms are not offered because there is no strong evidence of any prolonged or predictable progression from first-degree to complete heart block in pregnancies complicated by the presence of anti-Ro/La antibodies. Therefore, there does not appear to be an effective 'treatment window' prior to the onset of complete heart block.[35]

Outcome

Outcomes for fetal bradyarrhythmias have been less satisfactory than for fetal tachyarrhythmias. However, with a multidisciplinary approach involving fetal medicine specialists, fetal and paediatric cardiologists and neonatologists, there is now a more optimistic outlook. This probably has less to do with advances in prenatal treatment and more to do with improvements in neonatal intensive care and advances in pacemaker technology.

Peripartum care

Pregnancies complicated by fetal heart block and signs of haemodynamic compromise should be delivered by caesarean section. This is both because of the probably diminished fetal reserve to tolerate labour, and the difficulties in monitoring during labour given the

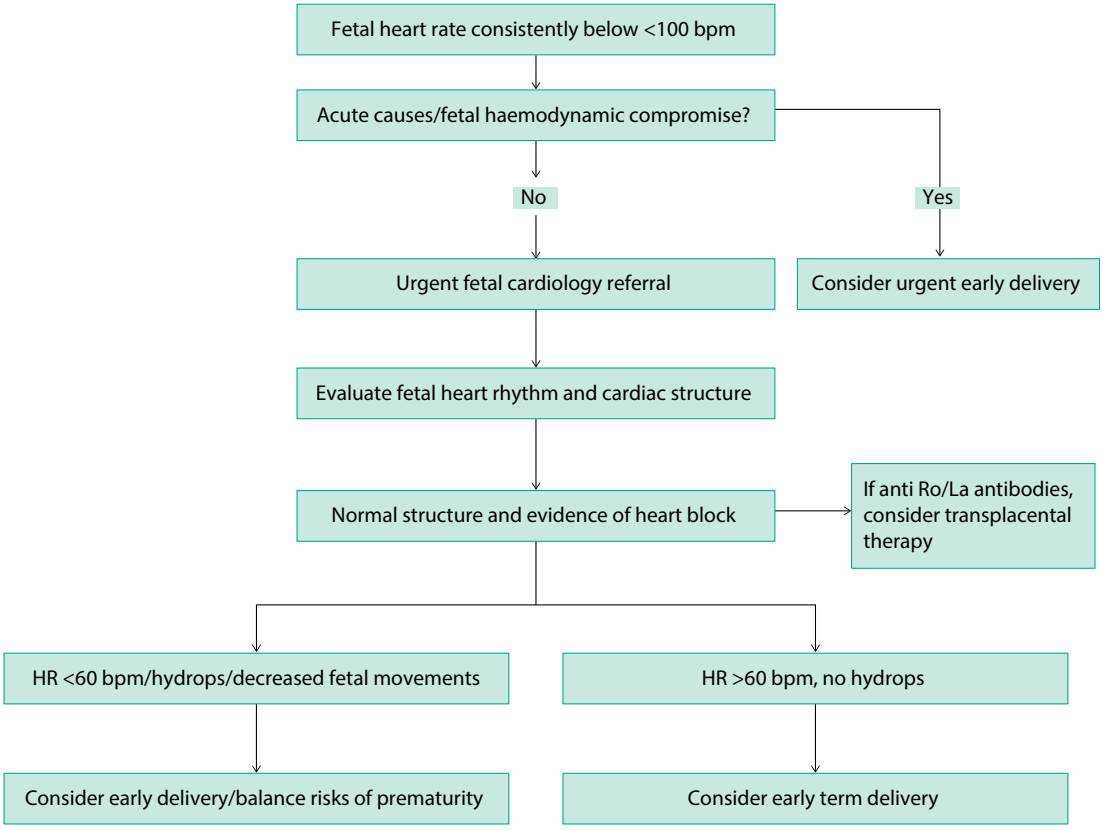

Figure 11. Investigation and management of fetal bradyarrhythmias.

background bradycardia. The timing of delivery should be discussed with MDT involvement, but if there are no signs of fetal compromise and no other obstetric concerns, an early term delivery may be considered.

Conclusion

Fetal arrhythmias are a common source of referral to the fetal medicine unit and have important implications for peripartum planning.

There is good evidence for trialling maternal transplacental therapy under the direction of specialist fetal and neonatal cardiologists in selected cases of supraventricular tachycardia and atrial flutter. In the absence of poor prognostic indicators such as fetal hydrops, a good outcome should be expected in cases when rate control can be achieved.

The evidence base for transplacental treatment in cases of fetal heart block is less well established. However, again, the prognosis for these cases is improved with involvement of specialist fetal echocardiographers and cardiologists and MDT planning for delivery.

Disclosure of interests

There are no conflicts of interest.

Contribution to authorship

DS wrote initial drafts of the manuscript, was involved in planning and editing the manuscript and writing the tables and algorithms. PP, GA and JL were involved in planning, oversight and editing of the manuscript. JW was involved in planning the manuscript and sourcing figures and illustrations. RY was involved in in planning and oversight of the manuscript, compiled the tables and extensively edited the manuscript.

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