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Fetal dysrhythmias

Olus Api
Doctor

Julene S. Carvalho*
Doctor
Brompton Fetal Cardiology, Royal Brompton Hospital and Fetal Medicine Unit, St George's Hospital, London, United Kingdom

Fetal cardiac dysrhythmias are potentially life-threatening conditions. However, intermittent extrasystoles, which are frequently encountered in clinical practice, do not require treatment. Sustained forms of brady- and tachyarrhythmias might require fetal intervention. Fetal echocardiography is essential not only to establish the diagnosis but also to monitor fetal response to therapy. In the last decade, improvements in ultrasound methodology and new diagnostic tools have contributed to better diagnostic accuracy and to a greater understanding of the electrophysiological mechanisms involved in fetal cardiac dysrhythmias. The most common form of supraventricular tachycardia – that caused by an atrioventricular re-entry circuit – should be differentiated from other forms of tachyarrhythmias, such as atrial flutter and atrial ectopic tachycardia. Ventricular tachycardia is rare in the fetus. Sustained tachycardias, intermittent or not, might be associated with the development of congestive heart failure and hydrops fetalis. Prompt treatment with either anti-arrhythmic drugs or delivery must be considered. Persistent fetal bradycardias associated with complete heart block are also potentially dangerous, whereas bradyarrhythmia due to blocked ectopy is well tolerated in pregnancy. Heart block can be associated with maternal anti-Ro/La autoantibodies or develop in fetuses with left atrial isomerism or with malformations involving the atrioventricular junction. The treatment of fetuses with immune-mediated heart block remains debatable. The use of antenatal steroid therapy is not widely accepted and there is concern over the risks and benefits of its use in the fetus. Direct fetal cardiac pacing has rarely been attempted.

Key words: arrhythmia; bradycardia; diagnosis; Doppler; echocardiography; fetus; tachycardia; treatment.

* Corresponding author. Consultant Fetal and Paediatric Cardiologist, Royal Brompton Hospital, Sydney Street, London SW3 6NP, United Kingdom. Tel.: +44 20 7351 8361; Fax: +44 20 7351 8758.
E-mail address: j.carvalho@rbht.nhs.uk (J.S. Carvalho).

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INTRODUCTION

The development of fetal echocardiography (FE) and other sophisticated techniques has led to a dramatic surge in the prenatal diagnosis of rhythm disturbances. Unlike most forms of structural congenital heart disease (CHD), fetal dysrhythmias might require prenatal treatment – either transplacentally or given directly to the fetus. Although life-threatening dysrhythmias are rare, the fact that they are potentially treatable means that accuracy in diagnosis is essential so that appropriate treatment can be commenced. In most instances, however, rhythm disturbances in the fetus are benign.

Fetal dysrhythmias can present as an irregular rhythm, as an abnormally slow (<100 bpm) or fast (>180 bpm) heart rate, or as a combination of these. They are diagnosed in at least 2% of pregnancies[1], the vast majority being intermittent extrasystoles[2], which have little clinical relevance. Less than 10% of referrals are due to sustained tachy- or bradyarrhythmias.[3] These include supraventricular tachycardia (SVT), atrial flutter and complete atrioventricular (AV) block. The primary objective of this chapter is to provide an update on current aspects of new and established diagnostic techniques, and an overview on treatment of fetal dysrhythmias.

DIAGNOSTIC METHODS

The fetal electrocardiogram (ECG) was initially utilized to define cardiac conduction and rhythm patterns but its use later in pregnancy was limited by the poor signal-to-noise ratio caused by the insulating effect of vernix caseosa.[4] More recently, there have been reports on improved-quality ECG[5,6], as well as on the potential clinical use of fetal magnetocardiography (MCG).[7,8] Over the years, however, FE has become the essential and clinically important tool to diagnose and manage rhythm abnormalities in the fetus. Additionally, it allows exclusion of any underlying CHD that might co-exist with rhythm abnormalities.[9–11]

Analysis of cardiac rhythm (normal or abnormal) is based on the ability to record atrial and ventricular contractions simultaneously. This is essential for accuracy of diagnosis, whatever diagnostic modality is used. Each method has advantages and limitations. These are influenced by image/signal resolution, fetal position, gestational age and complexity of the arrhythmia; they are also dependent on correct interpretation by the operator.

Ultrasound-based techniques

M-mode and pulsed-wave Doppler echocardiography

M-mode imaging (M-mode) and pulsed-wave Doppler (PWD) echocardiography are the most commonly used and useful ultrasound modalities for assessing fetal dysrhythmias.[12–20] With M-mode, the ultrasound beam (cursor line) is usually applied at the level of the four-chamber view, enabling atrial and ventricular wall movements to be recorded simultaneously. However, image resolution and fetal position can pose diagnostic limitations. A relatively new advance in the digital processing of images allows the cursor line to be rotated[21] (Figure 1), which can facilitate the diagnosis.[22]

With PWD, the signal can be obtained from various sites (Figure 1), including the left ventricular inflow–outflow tract area[15,23], the inferior vena cava–descending aorta[18], the superior vena cava (SVC)–ascending aorta[19,24] and the pulmonary artery–pulmonary vein.[20,25] PWD is also dependent on fetal position but the choice of various sampling sites minimizes this limitation.

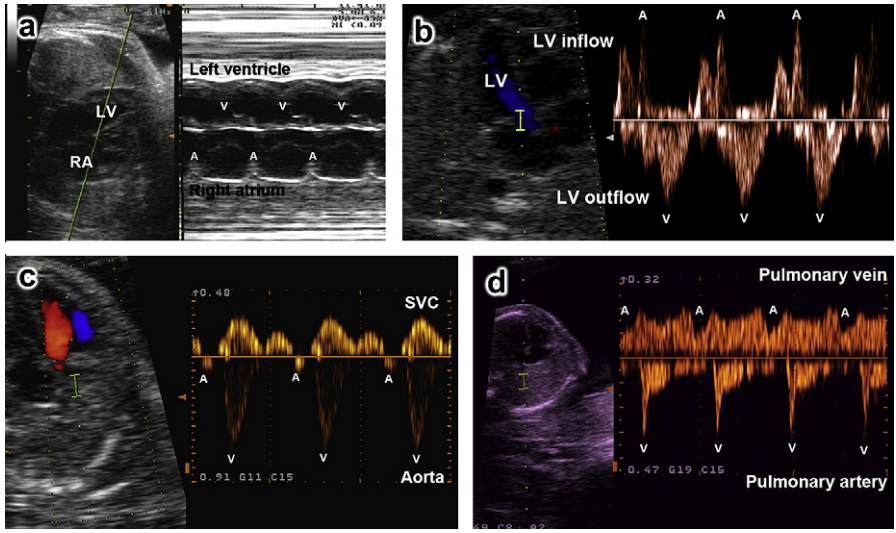

Figure 1. Normal sinus rhythm as shown on (a) M-mode with free-angular cursor line and PWD recordings in (b) left ventricular inflow and outflow tracts, (c) aorta and SVC and (d) pulmonary artery and vein. Atrial and ventricular contractions are identified in (b) by the start of A wave in mitral valve signal and aortic flow, in (c) by retrograde A wave in SVC and ascending aorta flow and in (d) by start of A wave in pulmonary venous waveform and pulmonary arterial flow respectively.

Tissue Doppler

Tissue Doppler velocity imaging is a relatively new ultrasound-based technique for diagnosing and monitoring fetal dysrhythmias and for the accurate measurement of cardiac intervals.[26,27] It relies on obtaining high-frame-rate, four-chamber-view images for sampling atrial and ventricular wall motion. Tissue velocity data are subsequently analysed off-line using commercially available software. This generates velocity curves that can be used to assess the temporal relationship between atrial and ventricular contractions. The limited availability of tissue Doppler and related software in most obstetric equipment precludes its wider use in clinical practice. However, by optimizing PWD settings, such as velocity and gain, tissue wall motion velocity can be obtained with standard equipment.[28] A similar principle can be used to obtain colour M-mode Doppler tissue imaging as an adjunct to most commonly used techniques for differentiation of fetal dysrhythmias.[29]

Electrocardiogram and magnetocardiogram

Transabdominal fetal ECG and MCG have become commercially available and can provide further insight into electrophysiological aspects of the fetal heart. Over the years, acquisition of fetal ECG has suffered from poor signal-to-noise ratio[30] but advances in data processing now allow better separation of fetal–maternal information and high-quality ECGs can be obtained. Yield success rates of 75–91% for serial fetal ECG measurements in normal fetuses have recently been reported.[6] However, satisfactory acquisition of adequate signals is less successful between 27 and 36 weeks[5,6], when fetal tachycardias and extra-systoles usually occur.[5] Fetal ECG is often averaged

over a number of cardiac cycles, which can restrict its use in rhythm disturbances, although it seems of value to measure cardiac time intervals.[5,6,31]

Fetal ECG signals have also been obtained in animal experiments using invasive (fetoscopic) techniques via the transesophageal route.[32] This has allowed recording of atrial and ventricular activity as well as external electrical stimulation and capture of the fetal heart. Whether this proves to have any clinical applicability in human fetuses with refractory tachycardias remains to be seen.

Fetal MCG is a recording of the magnetic field produced by the electrical activity of the fetal heart. It shows the typical electrocardiographic P-QRS complex waveforms.[7] Acquisition of fetal MCG is also accompanied by a maternal signal, which has to be subtracted from the overall data. MCG provides better signal quality than ECG as the transmission properties of magnetic signals are more favourable[8] and might be useful for measurement of cardiac time intervals. The relatively high cost of the equipment and the need for a dedicated area isolated from other magnetic fields have precluded its use which only recently has been reported in unshielded environment.[33]

The atrioventricular and ventriculo-atrial time intervals

On ultrasound, the atrioventricular (AV) interval acts as a surrogate for the PR interval on the ECG. This is useful when assessing patients at risk of fetal heart block. The interval can be measured using ultrasound techniques, as well as by ECG and MCG. Reference ranges vary according to the methodology used.[26,34–37] Analysis of the AV interval during sinus rhythm is the only way to diagnose first-degree AV block in the fetus. During tachycardia, measurement of AV and ventriculo-atrial (VA) intervals, and their temporal relationship, gives insight into the mechanisms of tachycardia[19,20,38]; these might influence drug therapy.

PRESENTATION AND MANAGEMENT OF FETAL DYSRHYTHMIAS

Irregular fetal heart rhythm

Irregularity of fetal cardiac rhythm is common. It is often due to premature contractions and is unlikely to have serious consequences. In Copel's series, ectopics were seen in approximately 43% of all referrals; only 2.4% of these had significant dysrhythmias, the remainder had normal rhythm.[2] Premature contractions are more common in the third trimester of pregnancy, being detected in 1.7% of fetuses between 36 and 41 weeks' gestation.[1] Atrial ectopics are far more common than ventricular ones (Figure 2). They can be conducted to the ventricles or blocked, the latter being a physiological block due to ventricular refractory period. Often referred to as 'missed' or 'skipped' beats', ectopics usually occur at random, although rhythmic patterns are also possible.

Isolated ectopics – conducted or not – of atrial or ventricular origin do not require treatment. Spontaneous resolution is often the rule and most fetuses have an uneventful prenatal and perinatal course.[39] The ectopics are not associated with fetal distress and do not constitute an indication for delivery.[40] However, development of a tachyarrhythmia that might require fetal intervention is a potential risk. This is often due to an ectopic triggering a re-entry circuit via an accessory pathway between atria and ventricles. Such a risk is less than 5%.[14,39] Atrial ectopics, if frequent and blocked, can also result in bradycardia (see below).

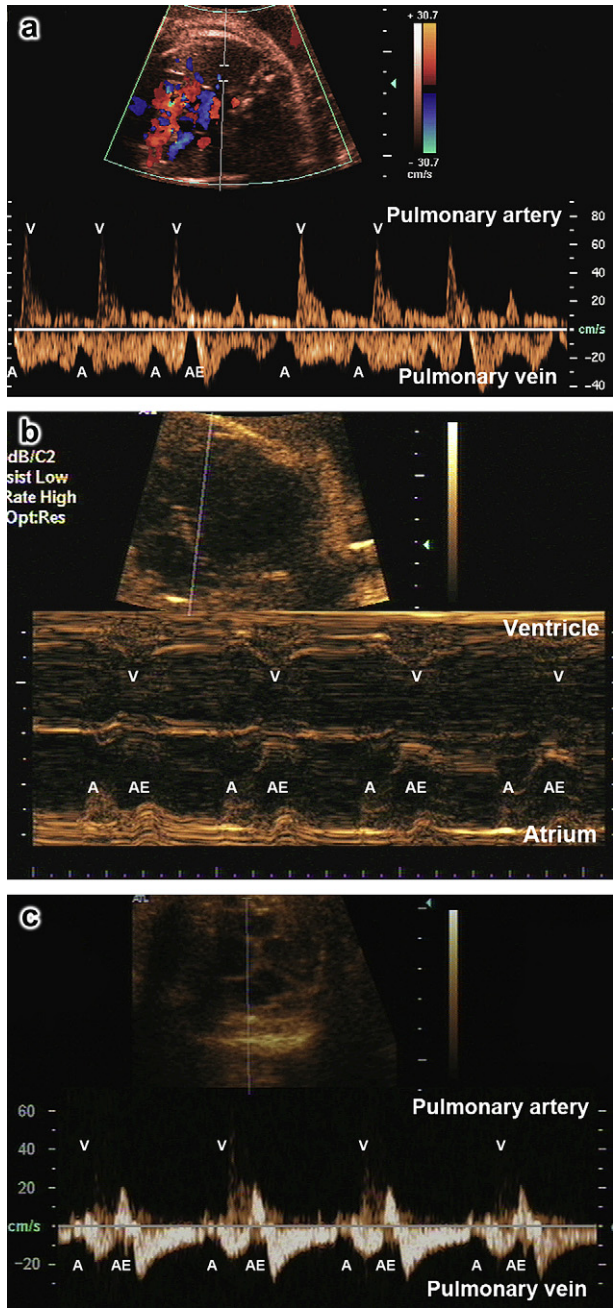

Figure 2. Examples of atrial ectopics. In (a) isolated, blocked atrial ectopic (AE) registered by PWD in pulmonary vessels (a). In (b), (c) blocked atrial bigeminy leading to bradycardia as seen on (b) M-mode and (c) PWD of pulmonary vessels. Note the presence of paired atrial beats (A, sinus beat; AE, ectopic beat) for every ventricular contraction (V).

Management of ectopic beats

Irregular rhythms noticed on routine prenatal care require further assessment because a significant, albeit small, proportion of cases might have important dysrhythmias, such as partial forms of AV block[2,41] and a small number might have structural CHD.[2] Once the diagnosis is established, subsequent follow-up can be done through routine care.[2] We usually recommend that fetal heart rate and rhythm are documented on subsequent routine antenatal visits, every 2–4 weeks. This not only reassures the families but also allows for the rare cases that might develop tachycardia or bradycardia to be referred back for reassessment. If the rhythm is chaotic, or if coupled ectopics or non-sustained tachycardia are seen, we recommend outpatient surveillance on a weekly basis and will schedule the patient for reassessment of fetal haemodynamics. Using this protocol, we have observed the development of tachycardia in only one case presenting initially with very frequent ectopics.[20]

Fetal tachycardias

Sustained fetal tachycardia causes morbidity and mortality. Fast heart rates (>180 bpm) on routine prenatal care usually prompt referral, which might also be made because of polyhydramnios and hydrops. Fetal therapy is often effective, thus establishing the correct diagnosis is important. Structural CHD is reported in 1–5% of cases.[14] Examples include Ebstein's anomaly[14], coarctation of the aorta[20] and cardiac tumours.[42,43]

The most common fetal tachyarrhythmias are SVT and atrial flutter, which account for 66–90% and 10–30% of cases, respectively.[9,10,42,44] Other types include sinus tachycardia, ventricular tachycardia (VT) and atrial fibrillation. The tachycardia rate and heart rate variability can aid differential diagnosis but do not distinguish between them. Echocardiography is the standard way by which the diagnosis has been made over the years. More recently, measurement of AV and VA time intervals have refined the diagnosis further by providing insight into the electrophysiological mechanisms involved; these could influence the choice of pharmacological therapy.[38]

Supraventricular tachycardia and atrial flutter

The most common mechanism of fetal SVT is an atrioventricular re-entry tachycardia (AVRT) caused by the presence of an accessory pathway between atrium and ventricle. This forms a circuit that allows normal (antegrade) conduction through the AV node and faster (retrograde) conduction from ventricle to atrium (VA conduction). The result is the typical SVT with short VA interval (VA/AV ratio < 1), characterized by a 1:1 ratio of atrial to ventricular contractions, a heart rate usually around 220–240 bpm (Figure 3) and loss of variability. This electrophysiological mechanism underlies around 90% of fetal SVT.[45]

Other mechanisms include atrial ectopic tachycardia (AET) and permanent junctional reciprocating tachycardia (PJRT). These are less common, have a long VA interval (VA/AV ratio > 1) and can be more refractory to treatment.[38] AET is often due to enhanced automaticity arising in the atrium, which can occasionally be associated with rhabdomyomas.[43] Fetuses with frequent atrial ectopics can develop AET and also have bradycardia due to blocked atrial bigeminy, as well as periods of sinus rhythm and a heart rate varying from 80, 140 and 200 to 240 bpm. During tachycardia, there might be higher heart rate variability due to a warm-up phenomenon[46] with heart rate acceleration. PJRT is even less common. This long-VA-interval form of tachycardia is associated with a conducting pathway near the coronary sinus orifice that allows slow VA conduction.[47]

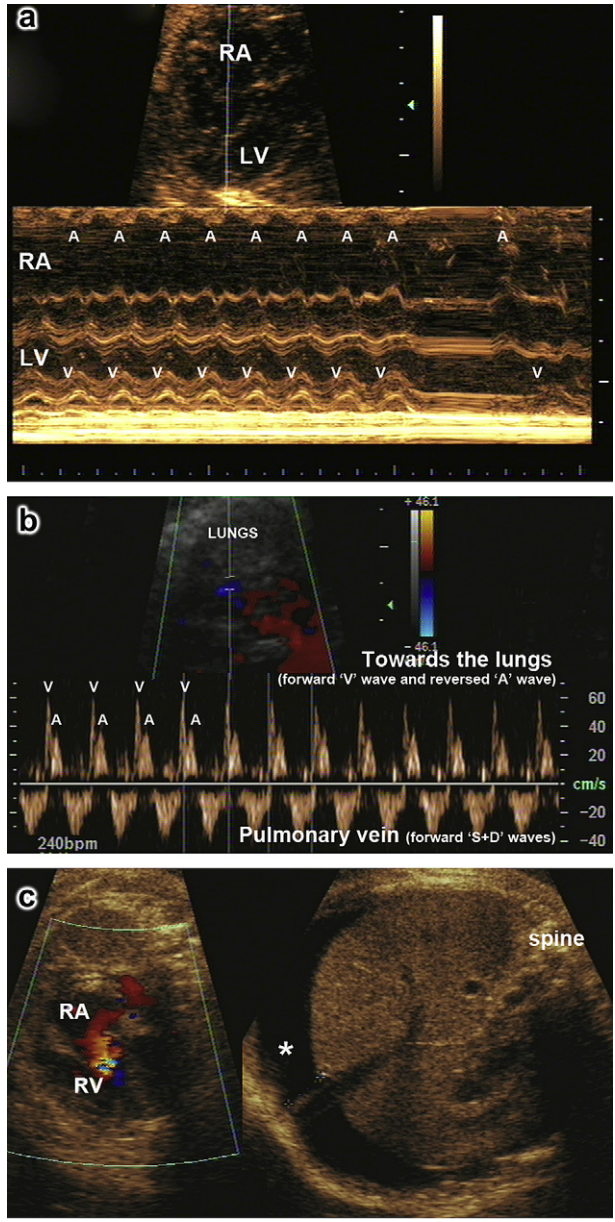

Figure 3. Example of tachycardia. In (a), (b) SVT with 1:1 conduction as seen on (a) M-mode and (b) PWD of pulmonary vessels. In (b), note AV interval shorter than VA interval in typical pattern of AVRT. In (c) fetal cardiomegaly with tricuspid regurgitation (left panel) and fetal ascites (right panel) (*) due to persistent SVT. A, atrial contraction; LV, left atrium; RA, right atrium; V, ventricular contraction.

Atrial flutter most commonly results from a re-entry circuit involving pathways within the atria and occurs later in gestation than SVT.[48,49] Atrial rates vary between 350 and 500 bpm. At the upper end of this, flutter 1:1 conduction is rare. One documented case with ventricular rate of 480 bpm led to fetal demise.[50] The presence of AV block results in better-tolerated ventricular rates of about 220–240 bpm (Figure 4) but haemodynamic compromise still occurs. The degree of AV block is usually 2:1 but higher degrees are possible.

Other forms of tachycardia

Sinus tachycardia has similar characteristics to sinus rhythm but a faster rate, usually 180–200 bpm. It can be caused by fetal and maternal conditions such as fetal distress, anaemia, infections, maternal β-stimulation and fetal thyrotoxicosis.[51] Its appropriate management is prompt treatment of any known underlying cause.

VT is rarely detected *in utero*. Heart rates vary from around 180 to over 300 bpm. The diagnosis is based on AV dissociation, i.e. no temporal relationship between atrial and ventricular contractions, with ventricular rate being faster. Although fetuses with hypertrophic cardiomyopathy and cardiac tumours can present with VT[45], genetic abnormalities of ion channel function (such as prolongation of QT interval) should be

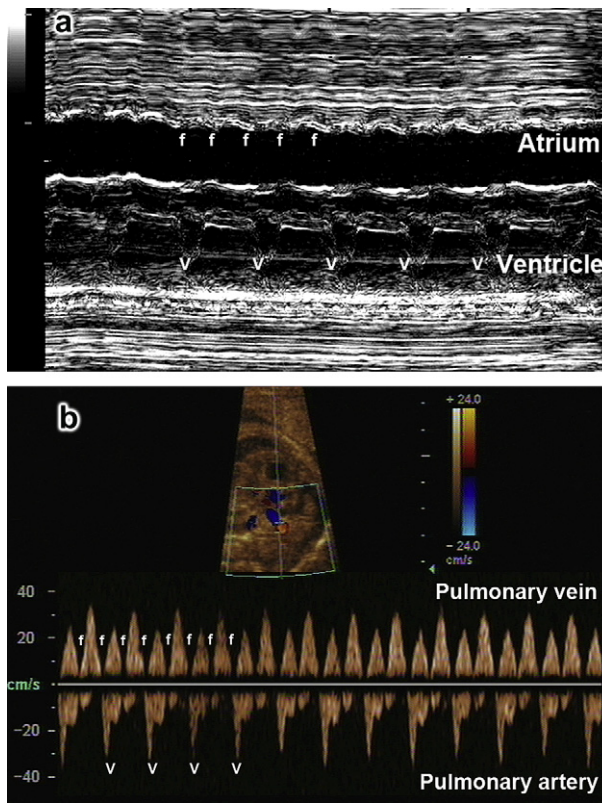

Figure 4. Example of atrial flutter with 2:1 AV conduction as seen on (a) M-mode and (b) PWD of pulmonary vessels. Atrial rate ~480 bpm, ventricular rate ~240 bpm. f, flutter wave; V, ventricular contraction.

suspected. These fetuses can present with a combination of VT, sinus bradycardia and AV block.[52,53]

Atrial fibrillation is also extremely rare in the fetus and results from an extremely rapid and disorganized electrical stimulation of atrial muscle. AV conduction is blocked at the AV node, resulting in variable and irregular ventricular rhythms.[54]

Management options for fetal SVT and atrial flutter

The fetus with tachycardia requires urgent cardiac and obstetric evaluation. There are three approaches to management: (1) no intervention but close monitoring; (2) anti-arrhythmic drug therapy; and (3) delivery. The exact management option and choice of pharmacological therapy varies from centre to centre but takes into account fetal and maternal factors. Not all cases will require the initiation of anti-arrhythmic drugs prenatally and only those with mature lung development will be delivered early.

No intervention (either pharmacological or delivery) can be considered for fetuses with intermittent tachycardia and no signs of haemodynamic impairment, such as AV valve regurgitation and cardiomegaly. Close surveillance is necessary either to commence treatment or to deliver the fetus at the appropriate time.

The choice between immediate delivery or drug therapy should be a balanced assessment of gestational age and lung maturity, the circulatory changes present in the fetus, available neonatal facilities for postnatal management and maternal choice. If there is persistent tachycardia or circulatory compromise, prompt intervention should be instituted to prevent congestive heart failure and fetal death.[55–57] A 'tachycardia-induced cardiomyopathy' might also develop[56,58] but is potentially reversible.[59] Hydrops fetalis has been shown to be the most important factor in determining the outcome of tachyarrhythmias, its presence being associated with a mortality risk of 27% against 0–4% in cases without significant heart failure.[10] In-utero treatment can decrease fetal mortality below 5–10%[9,10,60] and, although neurological morbidity has been linked to hydrops secondary to tachycardia[61], the neurological outcome of hydropic fetuses seems to be reasonably good. In a recent retrospective study, no abnormalities were found in 73% of cases and cognitive function was reported as normal in all surviving fetuses. The prognosis seemed particularly good when treatment was successful and delivery occurred at term. Therefore, treatment for hydropic fetuses should not be withheld or delayed based solely on the assumption of poor neurological outcome.[62]

Prenatal anti-arrhythmic therapy can be transplacental – usually the preferred method – and/or direct to the fetus. To be effective, maternal-administered drugs must reach effective concentrations in the fetus. The direct fetal route is used for acute treatment of incessant, poorly tolerated and refractory tachycardias, especially in the setting of severe hydrops and placental edema. The risk of cordocentesis in hydropic fetuses with tachyarrhythmia is, however, higher than that for other indications.[63] No prospective controlled trials document the superiority of any anti-arrhythmic drug to treat fetal tachycardia. Based on retrospective studies, several agents are considered effective and relatively safe. Among these, digoxin has been widely accepted as first-line treatment for many years. Other commonly used agents include flecainide, sotalol and amiodarone. Direct fetal administration of adenosine, digoxin and amiodarone has also been attempted.

The choice of drug depends on the type (atrial flutter or SVT) and mechanism (short or long VA interval) of the tachycardia, drug availability and experience with its use. Parents should be well informed about potential risks and benefits of treatment – a balance of side-effects of drug therapy against the life-threatening nature of the

arrhythmia. Ideally, anti-arrhythmic therapy should be started in hospital but some centres might opt for outpatient treatment. Baseline maternal ECG should be performed. It is also advisable to check serum electrolyte levels and liver and renal function tests.[64]

Digoxin slows the ventricular rate by partially blocking the AV node. In non-hydropic fetuses, serum levels range from 70 to 100% of maternal values, whereas placental passage is significantly impaired and adequate fetal concentrations cannot be achieved in hydropic ones. Although maternal digoxin monotherapy is ineffective in these cases, it remains a reasonable choice for treating the non-hydropic fetus with atrial flutter or AVRT. A recent meta-analysis found no statistical difference between the success rate of digoxin as first-line treatment for flutter (~45%) or SVT (~52%), although there was a significantly lower conversion rate in hydropic fetuses (~20%) than in non-hydropic (~63%) cases.[48] However, if the mechanism of SVT is taken into account, digoxin is almost certainly ineffective in AET and PJRT.[38]

Although therapeutic levels vary from 0.8 to 2.0 ng/ml[65], some authors recommend a higher target plasma concentration of 2.0–2.5 ng/ml.[66] Relatively high loading and maintenance dosages are required but protocols vary between centres. A loading dose of 0.5–1.0 mg can be given intravenously and followed by 0.25 mg oral maintenance, three times a day.[14] Others use 0.25–0.5 mg intravenous loading dose 8 hourly over 2–3 days.[64] An alternative regime is to start oral digoxin at a dose of 0.25 mg three times a day.[65] In our experience, levels around 1.0 ng/ml are often achieved after three oral doses of 0.5 mg digoxin given 8 hourly. Dosage is adjusted according to the therapeutic range.

Flecainide slows the conduction velocity in most cardiac pathways. It has excellent bioavailability, 95% with oral therapy and 80% in the presence of fetal hydrops.[67] Conversion into sinus rhythm can be expected in 72 hours but can take up to 14 days. An initial fall in heart rate is thought to represent an early therapeutic response.[60] Pro-arrhythmic effects have been reported in adults with myocardial infarction and in children with tachyarrhythmias[68,69] but have not been positively observed in fetuses. However, it is difficult to ascertain if any reported fetal death is related to the tachyarrhythmia, a pro-arrhythmogenic effect of flecainide or other factors such as cordocentesis.[67] Flecainide is usually given orally as 100 mg three times daily[10,67], preferably in a hospital setting. Serum target concentration levels are 200–1000 ng/ml.

Sotalol is a β-blocking agent with additional anti-arrhythmic properties and mild negative inotropic effect. Placental transfer is quick and almost complete, with fetal levels being almost identical to those of maternal plasma. Sotalol is effective in treating digoxin-refractory fetal tachyarrhythmias[70] and has been proposed as first-choice therapy for atrial flutter. Side effects and pro-arrhythmic risk are dose related.[71] Despite initial safety concerns[72], no statistical difference was found in mortality related to its use in SVT when compared with that of other studies.[73] Close maternal monitoring of QT interval on the ECG, and of electrolyte levels, especially during the initiation process, is recommended.[73] Sotalol is usually started orally at 80 or 160 mg twice a day.[70,73] An incremental dosage scheme of 80 mg per three days, starting with 80 mg twice daily to a maximum of 160 mg thee times a day, has been proposed as a means of minimizing complications.[73] Concerns about fetal growth restriction have been raised but no association has been found.[73]

Amiodarone is effective for SVT but has poor transplacental transfer (10–40%), which is further impaired in hydropic fetuses. However, serum levels increase constantly due to a long elimination half-life and accumulation in the fetal compartment. It has been suggested as a second-line therapy for refractory SVT in hydropic

fetuses.[65] The combination with digoxin also appears safe in incessant tachycardia with ventricular dysfunction.[74] An oral or intravenous loading of 1200 mg/day for 4–6 days is followed by a maintenance oral dosage of 600–900 mg/day.[64] Having a long half-life also makes it an ideal drug for direct fetal treatment by reducing the number of cord punctures. Repeated doses of 2.5–5 mg/kg estimated fetal weight are recommended via the umbilical vein, given over 10 min to avoid the danger of bolus injection causing severe bradycardia and cardiac arrest.[9,75] Amiodarone contains 37% iodine and resembles thyroxine, thus potentially affecting maternal and fetal thyroid function. Prolonged fetal exposure can cause transient neonatal hypothyroidism and possible fetal growth restriction[76–79]; thyroid function should be carefully assessed after birth.[76]

Adenosine slows conduction within the AV node and stops a re-entry circuit. It has an immediate but short-lasting effect that is useful in children for the acute but not long-term treatment of AVRT.[80] Direct injection into the umbilical vein is required and has rarely been reported in the fetus. In one case it rapidly and effectively terminated incessant tachycardia in a 28-week hydropic fetus, with cardioversion being achieved within 15–30 s. Sinus rhythm was maintained with digoxin and flecainide.[81] It has also been used as a diagnostic tool to differentiate between fetal AVRT and atrial flutter.[82]

Direct fetal therapy, i.e. direct injection of drugs into the fetal circulation, is a last resort in severely hydropic fetuses with tachycardia resistent to transplacental therapy. Injections of amiodarone, digoxin, verapamil and adenosine have been reported into various fetal sites, including – most commonly – the umbilical vein, the fetal heart, the fetal peritoneum and muscle.[9,10,82–85]

Fetal bradycardias

Transient, benign episodes of sinus bradycardia are frequently encountered in the first and second trimesters of pregnancy. However, heart rates persistently $<$100 bpm require further evaluation, the differential diagnosis usually being accomplished by FE.

Sinus bradycardia and blocked ectopics

There is 1:1 AV conduction in sinus bradycardia. Underlying causes include a preterminal fetus and sinus node dysfunction but, more importantly, this might be the only manifestation of long-QT syndrome. A positive family history of the condition, or the presence of VT or 2:1 AV block in the same fetus, helps to establish this diagnosis.[52,53]

If blocked atrial ectopic beats are regular and sustained, as in atrial bigeminy, ventricular rates are typically around 70–80 bpm (Figure 2). This is well tolerated by the fetus, requires no treatment and is almost always self-limiting; however, it can last for days or weeks. Follow-up is advisable, usually for reassurance, but a small number of cases might develop tachyarrhythmia.[39] Blocked ectopics should be distinguished from heart block.

Atrioventricular block

AV block is associated with normal atrial activity and a disturbance of electrical conduction between atria and ventricles. First-degree block has a prolonged AV interval, which is the basis of the diagnosis (see above). It cannot be detected by routine scans because the heart rate is normal. Second-degree block can be type I or II. In type I

(Wenckebach) there is progressive lengthening of AV conduction time until one impulse is blocked. This gives an irregular rhythm but heart rate might be normal. In type II (Mobitz II), some beats are conducted and others are blocked without prior lengthening of the AV interval. AV conduction is usually 2:1 (Figure 5) and less often 3:1. In third-degree or complete AV block (CAVB), there is complete interruption of AV conduction so that atria and ventricles beat independently.

Complete AV block is rare, occurring in 1 in 15 000–22 000 live births.[86] Close monitoring is required because fetal hydrops might develop. This is the most important marker of adverse outcome, followed by the association with complex CHD.[87] In these cases, many fetuses have left atrial isomerism and, less often, congenitally corrected transposition of the great arteries. The occurrence of AV block in the first trimester is a marker for left isomerism and has a high mortality.[88]

In the absence of CHD, heart block is mainly due to the transplacental passage of maternal IgG antibodies, most often anti-Ro (SS-A) or anti-La (SS-B) type, which injure the conduction tissue, with subsequent fibrous replacement.[89] Commonly, heart block develops >18 weeks of gestation and peaks at 20–24 weeks. Most cases (82%) occur <30 weeks.[90] The risk of AV block in women with known antibodies was 2% in a prospective study[91] but might be as high as 7.5%.[90] The recurrence risk was found to be 16%.[90]

The prognosis for autoimmune-mediated CAVB is better than if associated with CHD but there still is significant mortality of 18–43%.[11,90,92,93] Risk factors for adverse outcome are fetal hydrops, endocardial fibroelastosis, premature delivery and heart rate <55 bpm.[11,92,93] Most survivors require pacemaker implantation in the first year of life.[93] Various therapies have been tried in autoimmune-related CAVB, including maternal dexamethasone, β-agonists and plasmapheresis, aiming to prevent myocardial inflammation, augment fetal heart rate and reverse cardiac failure. Treatment of fetuses with partial AV block aims to prevent progression of the disease process.

Fluorinated steroids (dexamethasone and betamethasone) cross the placenta better than prednisone and should be used if treatment is considered. There have been isolated reports on possible positive effects of steroids in fetal AV block but no definitive data from prospective studies or clinical trials. Recently, institutional policy to use steroids and beta-stimulation was reported to improve outcome of fetal

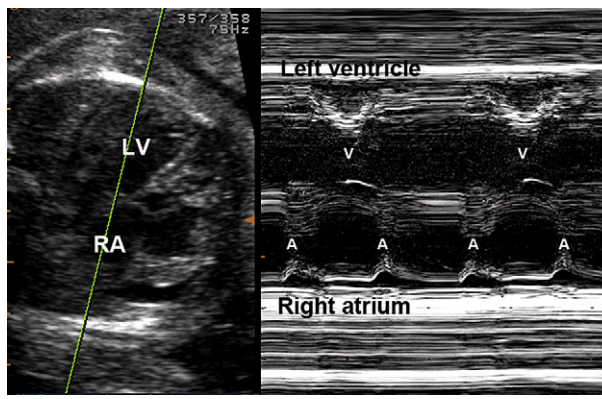

Figure 5. Example of bradycardia due to 2:1 heart block recorded with free-angular M-mode cursor. A, atrial contraction; LV, left atrium; RA, right atrium; V, ventricular contraction.

CAVB[94], but this treatment protocol has raised questions that only large randomized prospective studies can answer.[95] However, an attempt to run a European multicentre study[96] was abandoned due to poor enrolment. The use of steroids can be justified in cases of partial heart block but there is no firm evidence they are an effective form of treatment. Additionally, there are concerns regarding steroid treatment antenatally. Repeated doses have been shown to impair fetal growth and decrease brain weight in animal studies.[97] Conversely, no negative effect was found on the neuropsychological development of children who were exposed to anti-Ro and anti-La antibodies and to very high doses of dexamethasone.[98]

Sympathomimetics (terbutaline, salbutamol) have been used to increase fetal heart rate with variable success.[11,87,94,99] Maternal plasma exchange and administration of maternal immunoglobulin or azathioprine are other experimental therapy options that aim – primarily – to reduce maternal auto-antibody titres. Direct fetal pacing has been attempted in isolated cases without reported survivors. The development of a new endocardial lead for direct fetal pacing could make this feasible in the future.[100]

SUMMARY

Fetal dysrhythmias are common and often due to ectopic beats, which are benign and do not require treatment. However, a small number of fetuses might have important and life-threatening conditions associated with bradycardia or tachycardia. Therapy for persistent tachyarrhythmias should be started promptly. Transplacental therapy is the preferred route and is often effective to treat or prevent heart failure. Flecainide, digoxin and sotalol are commonly used and relatively safe; there is no clinical trial evidence as to the drug of first choice. Prenatal therapy for bradycardia due to heart block is empirical. Steroids such as maternal dexamethasone and sympathomimetics have been used but there are no prospective, controlled studies on their effectiveness. If hydrops develops, fetal morbidity and mortality are high.

Practice points

- Rhythm disturbances are diagnosed in at least 2% of pregnancies during routine scanning.
- Most fetal dysrhythmias are intermittent extrasystoles that have little clinical relevance and require no treatment.
- Less than 10% of referrals have prolonged or persistent tachy- or bradyarrhythmias that require therapy.
- Persistent tachycardia and heart block are associated with increased fetal and perinatal mortality, requiring close fetal surveillance.
- Fetal echocardiography allows correct diagnosis of the dysrhythmia, its underlying mechanism and exclusion of structural abnormalities.
- Prognosis is governed by the type of arrhythmia, the association with structural cardiac anomaly and the co-existence of intrauterine cardiac failure.
- Presence or absence of hydrops fetalis is the most important factor in determining the outcome of tachyarrhythmias and heart block.
- The most common types of tachyarrhythmia are re-entry supraventricular tachycardia and atrial flutter.

- Persistent fetal tachycardias should be treated promptly with anti-arrhythmic drugs given either transplacentally or via direct fetal route.
- Well-tolerated and relatively safe anti-arrhythmic drugs are available for the successful treatment of fetal tachycardias.
- Second- and third-degree (complete) AV block should be distinguished from blocked atrial bigeminy as management and prognosis differ.
- The treatment of fetuses with immune-mediated heart block with steroids remains debatable.

Research agenda

- Efficacy of preventive treatment to influence progression of immune-mediated atrioventricular block.
- Efficacy of transplacental treatment (steroids, β-agonists) for immune-mediated complete heart block.
- Controlled trials on efficacy and on the maternal and fetal safety of drugs used to treat fetal tachycardia.
- Investigation of potential long-term effects of prolonged in-utero exposure to high-dose steroids used to treat heart block.
- Long-term neurodevelopmental outcome of fetal hydrops associated with life-theatening dysrhythmias.
- Further development of transabdominal ECG, transesophageal ECG and MGC.
- Direct fetal cardiac pacing.

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