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Fetal dysrhythmias

Julene S. Carvalho, MD, PhD, FRCPCH, Consultant Fetal & Paediatric Cardiologist and Professor of Practice, Fetal Cardiology [a, b, c, *]

[a] Royal Brompton and Harefield NHS Foundation Trust, Sydney Street, London, SW3 6NP, UK
[b] Fetal Medicine Unit, St George's University Hospital, Blackshaw Road, London, SW17 0QT, UK
[c] Molecular and Clinical Sciences Research Institute, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK

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A B S T R A C T

Fetal dysrhythmias are common abnormalities, usually manifesting as irregular rhythms. Although most irregularities are benign and caused by isolated atrial ectopics, in a few cases, rhythm irregularity may indicate partial atrioventricular block, which has different etiological and prognostic implications. We provide a flowchart for the initial management of irregular rhythm to help select cases requiring urgent specialist referral. Tachycardias and bradycardias are less frequent, can lead to hemodynamic compromise, and may require in utero therapy. Pharmacological treatment of tachycardia depends on the type (supraventricular tachycardia or atrial flutter) and presence of hydrops, with digoxin, flecainide, and sotalol being commonly used. An ongoing randomized trial may best inform about their efficacy. Bradycardia due to blocked bigeminy normally resolves spontaneously, but if it is due to established complete heart block, there is no effective treatment. Ongoing research suggests hydroxychloroquine may reduce the risk of autoimmune atrioventricular block. Sinus bradycardia (rate <3rd centile) may be a prenatal marker for long-QT syndrome.

* Corresponding author. Royal Brompton Hospital, Sydney Street, London, SW3 6NP, UK.
E-mail address: j.carvalho@rbht.nhs.uk.

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Introduction

Fetal dysrhythmias are abnormalities of fetal heart rate (FHR) and/or rhythm (regular or irregular), often detected on antenatal visits or during an ultrasound examination. Once recognized, further evaluation is needed.

Most dysrhythmias present as irregular rhythm ("skipped" or "missed beats") in structurally normal hearts, have a benign nature, and resolve spontaneously. In a small proportion, this requires a closer follow-up. A risk stratification protocol helps identify cases that require specialist assessment. Tachycardias and bradycardias require urgent evaluation, and diagnosis can be challenging.

Assessment of fetal dysrhythmias is usually based on ultrasound to determine fetal well-being, assess cardiac structures, and define the nature of rhythm disturbance with confidence to decide whether in utero treatment is needed. In this review, we aim to provide a logical approach to diagnose fetal dysrhythmias and an update on current management.

Assessing fetal cardiac rhythm

Treatment of fetal dysrhythmias relies on accurate diagnosis; thus, basic understanding of normal rhythm is essential. Contraction and relaxation result from myocardial electrical stimulation, which starts in the natural pacemaker (sinus node). Normal sinus rate varies but is broadly between 120 and 160 bpm. The impulse generated initiates atrial contraction and travels toward the atrioventricular (AV) node and subsequently through the specialized tissue in the ventricles (bundle of His, right and left bundles, and Purkinje fibers), thus activating the ventricular myocardium. A slight physiological delay (AV delay) ensures that ventricular contraction follows atrial contraction leading to a 1:1 AV relationship.

To study cardiac rhythm, simultaneous recording of atrial and ventricular activities is needed. Ultrasound-based techniques are the main tools available prenatally. Other methods are not widely available. A brief appraisal of such techniques is presented below.

M-mode echocardiography is commonly used. It is based on placing a line of ultrasound beam (M-mode line) across cardiac structures to register mechanical results of electrical activation. Typically, M-mode is applied on the four-chamber view to record atrial and ventricular motion (Fig. 1). Limitations are image resolution and fetal position. Pulsed-wave Doppler signal was traditionally used in the left ventricular inflow–outflow tract area (mitral-aortic) [1]. Alternative sites include ascending aorta–superior vena cava [2] and pulmonary artery–vein [3] (Fig. 1). Color and PW tissue Doppler imaging have also been described [4–6] but are not widely used.

Fetal electrocardiography (f-ECG) and fetal magnetocardiography (f-MCG) allow measurements of cardiac time intervals, especially QRS complex and QT interval. Both techniques rely on extracting fetal electrical activity from a combined fetomaternal signal. However, despite being available for many years, neither constitutes part of routine clinical practice. Signal processing has improved, but f-ECG signal-to-noise ratio remains a limitation, especially around 27–36 weeks [7]. f-MCG is superior but requires a shielded environment and has high maintenance costs [8].

Rhythm irregularities

Irregular fetal heart rhythms, often described as "missed" or "skipped" beats, constitute a large proportion of referrals due to dysrhythmias [9]. In the majority, the underlying diagnosis is isolated atrial ectopics occurring in structurally normal hearts (Fig. 1). Ventricular ectopics and/or associated congenital heart disease (CHD) is less common. Most ectopics resolve spontaneously and may no longer be seen when a scan is performed [9,10]. However, in a minority, rhythm irregularities may represent a significant dysrhythmia, including conduction abnormalities in ~2.5% [11]. There is a relatively small risk ($\leq$5%) of ectopics triggering episodes of tachycardia [12,13], while persistent atrial bigeminy with blocked ectopics can lead to prolonged episodes of bradycardia.

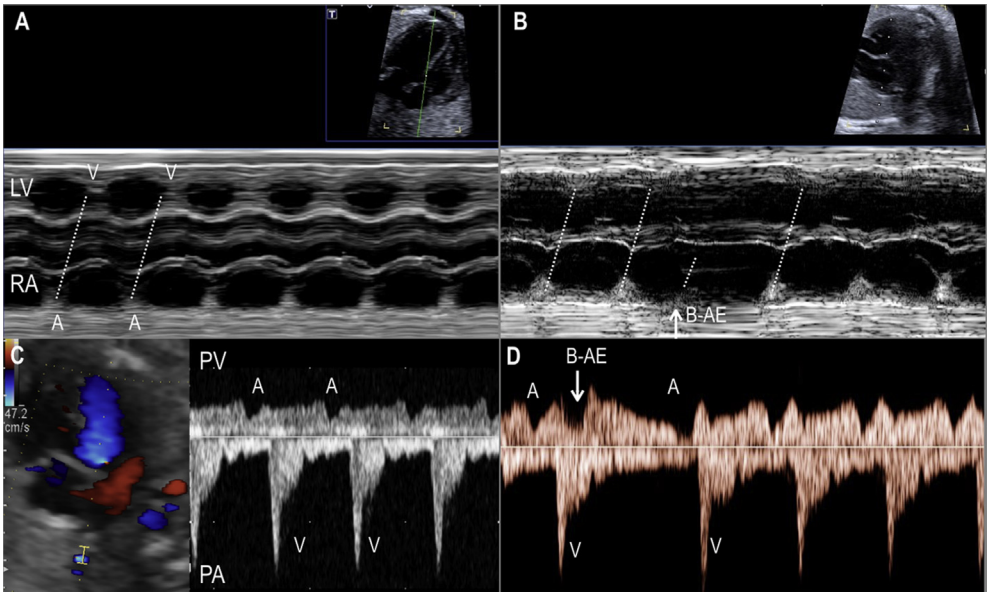

Fig. 1. M-mode [A,B] and simultaneous pulsed-wave Doppler signal [C,D] across the pulmonary artery (PA) and vein (PV). Images [A,C] depict normal sinus rhythm, and images [B,D] show a blocked atrial ectopic (B-AE). Note the regular interval between atrial signals during sinus rhythm and an early signal (arrow) characteristic of atrial ectopic. A/V = atrial/ventricular systole; LV = left ventricle; RA = right atrium.

Management

Most irregular rhythms require no intervention, and pregnant women can be reassured. However, risk stratification is important. A flowchart to help this is shown in Fig. 2. It relies on recording FHR and an obstetric scan focused on fetal well-being and cardiac screening views.

If either is abnormal, women can be referred promptly. At the specialist level, if isolated ectopics are confirmed and occur occasionally (i.e., rhythm is mostly regular), the patient can be discharged. If ectopics are frequent (i.e., rhythm is mostly irregular/"chaotic") or occur as couplets/triplets (two/three together), ambulatory FHR surveillance by Doppler at 1- to 2-week intervals is advisable. Further scans can be performed at the local or tertiary level to monitor for small risk of tachycardia. This possibility should be considered and fetal surveillance intensified, if there is cardiomegaly, AV valve regurgitation, small effusions, or unexplained polyhydramnios, even if FHR is normal. Prolonged periods of blocked bigeminy reduce FHR to ~70–80 bpm and needs differentiation from 2:1 AV block [14–16] (Fig. 3), whereas conducted bigeminy or blocked trigeminy leads to an irregular pattern that can mimic variable second-degree AV block (Fig. 4) [16]. Monitoring for the development of tachycardia in these cases is advisable.

A neonatal ECG can be performed if irregular rhythm persists after birth. If couplets, triplets, and chaotic rhythms are identified prenatally, the risk of tachycardia seems to extend to the neonatal period [17]; therefore, a neonatal ECG and a 24 h-ECG recording are advisable.

Tachycardias

Fetal tachycardias are defined as FHR >180 bpm, but persistent rates ~160–180 bpm may also be abnormal. They are potentially life threatening due to the development of ventricular dysfunction and heart failure, although the fetus may tolerate intermittent tachycardia. The diagnosis may be straightforward, but tachycardia, even if persistent, may remain undetected and may only be recognized when the fetus is hydropic. The fetal heart structure is often normal, but CHD may be present.

The most common are supraventricular tachycardia (SVT, ~3/4 of cases) and atrial flutter (AF) [18,19]. They can also originate from the sinus node, AV junction, or ventricles. The diagnosis relies

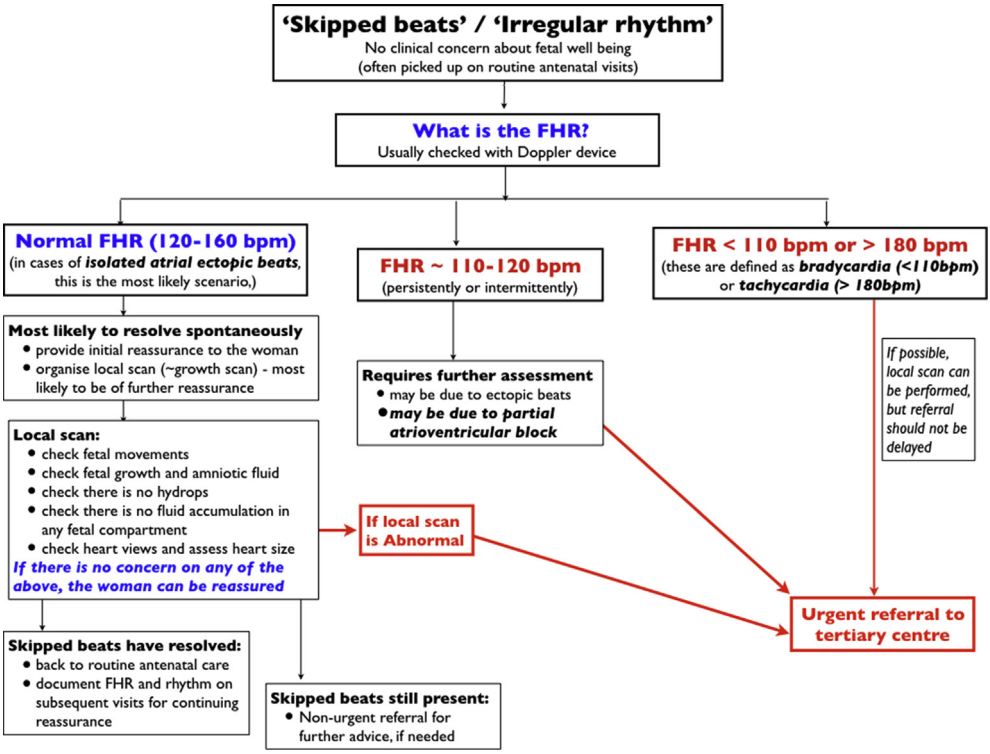

Fig. 2. Suggested flowchart for the initial management of irregular rhythms. FHR = fetal heart rate, bpm = beats per minute.

mainly on echocardiography, with careful analysis of atrial and ventricular contractions, their rates, and temporal relationship. FHR and rate variability may aid but are not diagnostic.

Supraventricular tachycardia and atrial flutter

AV re-entry tachycardia (AVRT) accounts for 90% of fetal and neonatal forms of SVT [18], which is associated with an accessory pathway between atria and ventricles that creates an extra circuit for the electrical impulse. Atrial ectopics often trigger the tachycardia. Following antegrade conduction through the AV node toward the ventricles, the impulse travels faster and retrogradely from the ventricle to atrium through the accessory pathway. This antegrade–retrograde conduction perpetuates the circuit. AVRT rate is 220–240 bpm but can reach ~280 bpm. Rate relates to the accessory pathway properties and is relatively fixed with no variability [20]. Typically, AVRT has a short ventriculo-atrial (VA) interval, representing a short VA tachycardia (VA:AV ratio <1) (Fig. 5).

AF often occurs later in pregnancy [18]. It results from intra-atrial circuits, often initiated and terminated by premature atrial contractions [8]. Atrial rates are faster (300–500 bpm) than ventricular rates due to a physiological block at AV node [12]. Typically, the pattern is 2:1 (atrial rate ~440–450 bpm; ventricular rate ~220-225 bpm), but AV node blockage can vary. At slower atrial rates, 1:1 AV conduction may occur, leading to much faster ventricular rates. AF can also alternate with periods of AVRT in the same fetus [8].

Other tachycardias

Atrial ectopic tachycardia (AET) and permanent junctional reciprocating tachycardia (PJRT) are less common. AET may have 1:1 or variable AV conduction, whereas PJRT shows 1:1 conduction. Typically, these are long VA tachycardias (VA:AV ratio > 1), with FHR usually ~180–220 bpm [18,20]. AET relates

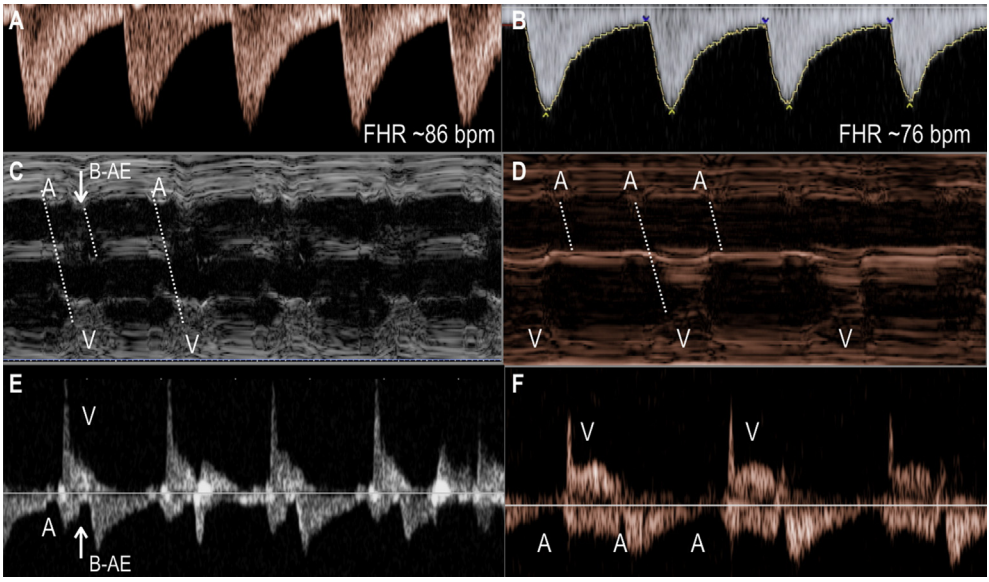

Fig. 3. Different dysrhythmias causing regular bradycardia at a similar rate and arterial Doppler [A,B], depicted on M-mode [C,D], and pulmonary vessel Doppler [E,F]. Images [A,C,E] show blocked atrial bigeminy. Note the irregular atrial activity: one is conducted, but the early ectopic signal is blocked. Images [B,D,F] show 2:1 heart block. Note that the atrial signal is regular: one is conducted, and the other is not. A/V = atrial/ventricular systole; (B-AE) = blocked atrial ectopics; FHR = fetal heart rate, bpm = beats per minute.

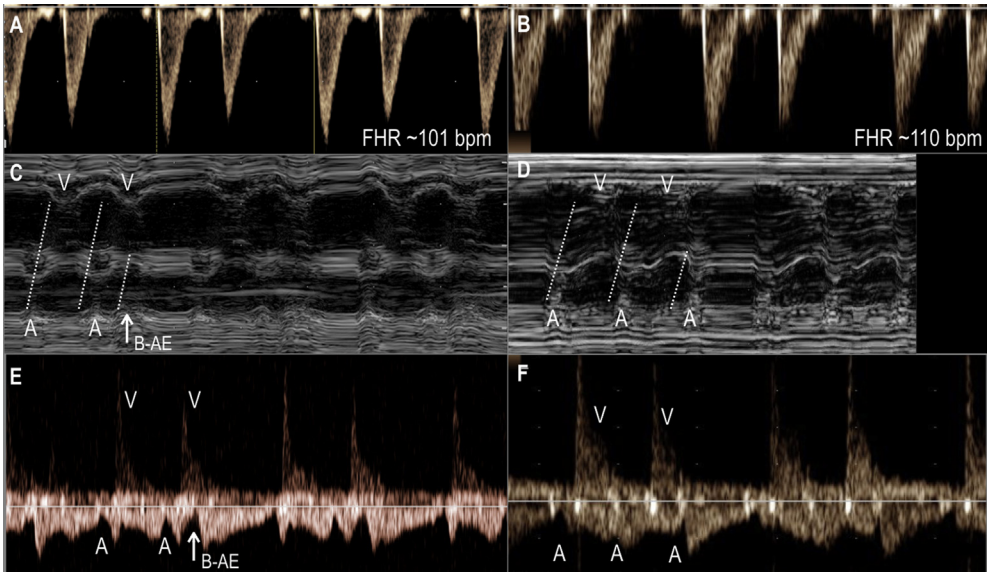

Fig. 4. Different dysrhythmias causing irregular bradycardia at a similar rate and arterial Doppler [A,B], depicted on M-mode [C,D], and pulmonary vessel Doppler [E,F]. Images [A,C,E] show blocked atrial trigeminy. Note the irregular atrial activity: two beats are conducted, but the early ectopic signal is blocked. Images [B, D, F] show 3:2 heart block. Note that the atrial activity is regular: two are conducted, but one is not. A/V = atrial/ventricular systole; (B-AE) = blocked atrial ectopics; FHR = fetal heart rate, bpm = beats per minute.

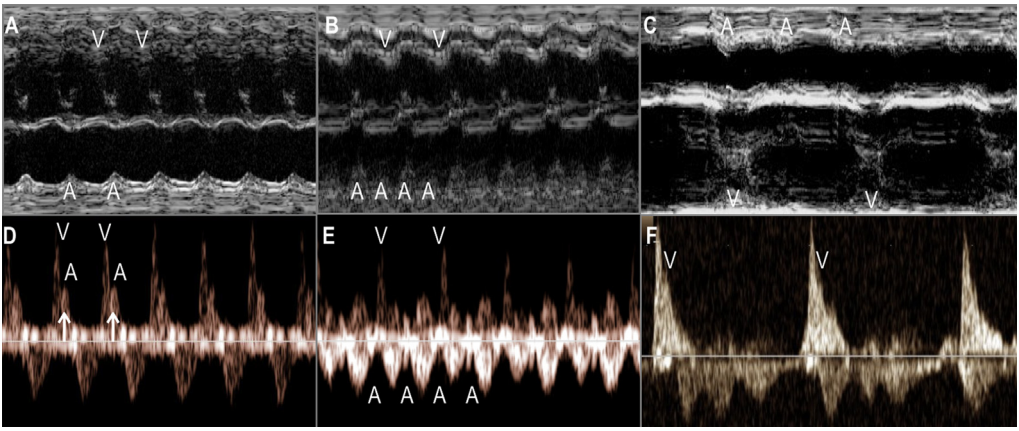

Fig. 5. Examples of supraventricular tachycardia with 1:1 conduction and a short VA interval, where the arrows show flow reversal during atrial contraction [A,D]; atrial flutter with typical 2:1 conduction [B,E], and complete AV block with diagnostic AV dissociation [C,F], depicted on M-mode [A,B,C], and Doppler in pulmonary vessels [D,E,F]. A/V = atrial/ventricular contraction.

to increased atrial automaticity [12]; there may be higher heart rate variability and a warm-up phenomenon. JPRT is mediated by a slow conducting pathway near the coronary sinus, allowing VA conduction [21]. PJRT is usually incessant, may be difficult to treat, and may lead to tachycardia-related cardiomyopathy [12].

Sinus tachycardia is common. If persistent, maternal fever or beta-stimulation, stress, and infection need to be considered as the underlying disease. Rates may be mildly elevated (160–180 bpm) or as high as 200 bpm. Heart rate variability is usually preserved [12]. AV conduction is 1:1, and VA interval is long. Treatment is targeted at the cause, if identified. Ventricular tachycardia (VT) is rare. It starts in the ventricles and typically has no retrograde conduction, causing AV dissociation, with ventricular rate (180–300 bpm) faster than the sinus rate. Long-QT syndrome is an important cause of VT, often alternating with bradycardia due to 2:1 AV block. Other associations are cardiac tumors (e.g., rhabdomyomas) and cardiomyopathy. Rarely there is VA conduction, simulating AVRT. Junctional ectopic tachycardia (JET) is one of the rarest fetal tachycardias [22], often incessant, with little FHR variability and not well-tolerated despite rates rarely exceeding 200 bpm. It results from increased AV node automaticity, which depolarizes the ventricles only, causing AV dissociation and simulating VT. Intermittently, however, atrial and ventricular activation may occur almost simultaneously, leading to 1:1 AV relationship with a very short VA interval, which helps differentiating from VT [22,23]. JET has also been associated with maternal autoantibodies; in these cases, it is intermittent and alternate with AV block [23,24].

Management

Fetal tachycardia is an emergency requiring urgent cardiac and obstetric assessment. Depending on the mechanism, hemodynamic consequences, fetal well-being, and the woman's choice, management options are no intervention, drug therapy, or delivery.

Not all tachycardias require treatment. If intermittent (<50% of the time) and with no hemodynamic compromise (e.g., no hydrops, no cardiomegaly, or no AV valve regurgitation), treatment may be unnecessary. However, close FHR monitoring is needed to establish the frequency and duration of tachycardia. Multiple observations as inpatient over 24–48 h may help. Outpatient monitoring may involve checks 1–3 times a week and intermittent scans.

If the tachycardia is incessant (>50% of the time) or hemodynamic compromise is evident, treatment should not be delayed. Choices are pharmacological therapy or delivery depending mainly on gestational age. If there is significant polyhydramnios, spontaneous labor and delivery may be inevitable.

Risks and benefits of treatment and the life-threatening nature of tachycardia should be discussed. Inpatient treatment is preferable. Baseline maternal ECG, serum electrolyte levels, and liver and renal function should be determined. If serum levels are available, doses can be adjusted accordingly.

Pharmacological therapy

Digoxin, flecainide, sotalol, and amiodarone are relatively safe, but side effects including arrhythmogenic ones are reported. Transplacental transfer is preferred, but adequate fetal concentration is influenced by the presence of hydrops. Digoxin has poor transfer in hydropic fetuses, limiting its use as monotherapy. Direct fetal treatment (cordocentesis, intramuscular, intraperitoneal, or intra-amniotic) is an option for severely hydropic or refractory cases, usually combined with oral medication. Digoxin and amiodarone are the preferred drugs. Dose is based on fetal weight, but a 25% increase is recommended to account for placental circulation [25].

Most supraventricular tachyarrhythmias are treated successfully. Survival rates are ~80–90% [18,19,26,27], hydrops being the most important determinant of outcome. Fetal response also relates to tachycardia type and medication used. In the largest retrospective series treated with digoxin, flecainide, or sotalol (n = 111, 1998–2008), SVT was better controlled than AF. Conversion rates were slower for incessant tachycardia and hydrops [18]. Overall mortality was 5% (hydrops = 17%; nonhydrops = 0%). Hydrops was associated with faster ventricular rates; therefore, if rapid conversion cannot be achieved, rate reduction is also important. Compared to sotalol, termination rates for SVT after 5 days were better with flecainide (59%) and digoxin (57%) than with sotalol (38%). Similarly, time to convert half of SVT cases was shorter for digoxin (3 days) and flecainide (4 days) than for sotalol (12 days). Conversely, in AF cases, sotalol was better, converting 50% of cases in 12 days and achieving sinus rhythm in 29% by day 5, but flecainide had better rate reduction if tachycardia persisted.

These three drugs remain as the first choice in more recent studies, with variable efficacy reflecting variability in protocols and patient population. Sotalol (±digoxin, 2004–2008) had an overall response of 85% among 21 cases of SVT or AF, with 52% conversion and 33% rate control [26]. Many converted in <5 days, but hydrops-related mortality was ~38%. In another study, sotalol monotherapy converted 70% and 50% of nonhydropic and hydropic fetuses, respectively [28]. For many years (1987–2012), comparison of two centers showed flecainide to be superior to intravenous digoxin, with clear mortality difference in hydropic cases (flecainide = 0%, digoxin = 47%). Flecainide also converted 96% of short VA SVT compared to digoxin (69%), with shorter median response time (3 versus 8 days) [27]. Two other studies also report good response to flecainide as the first choice of monotherapy, with and without hydrops [29,30]. In one, high doses (400 mg/day) converted 72% of hydropic fetuses with SVT, with median time of 3 days [29], whereas in the other, conversion or rate reduction was achieved in 87% using conventional doses [30]. A more aggressive approach using dual therapy (flecainide and digoxin) for all tachyarrhythmias is reported [19]. Of 27 treated fetuses (2001–2009), 81% converted and rate control was achieved in 15%, but perinatal mortality was still ~13% despite dual therapy.

These reports suggest a trend to use flecainide, a finding in line with a recent systematic review indicating flecainide to be superior in AVRT treatment [31]. However, all studies are retrospective. Depending on multiple variables, it remains unclear whether sotalol and digoxin also have a place as first-line therapy, in isolation or combined with other medications. Hydropic fetuses remain a high-risk group. Interpretation of drug efficacy in such cases is hindered, as treatment failure and mortality is often linked to "severe hydrops," but systematic information about the degree of hydrops is often lacking in successfully treated cases. A randomized controlled trial is ongoing and may provide some answers (www.fasttherapytrial.com). Drug availability also impacts the choice of medication. Digoxin is available worldwide, but flecainide and sotalol are not.

Amiodarone is considered as second-line option in drug-refractory tachycardia with hydrops. It was successfully injected into the umbilical vein nearly three decades ago [32] and is still considered safe [25]. Intramuscular fetal injection of digoxin is also an alternative [33]. Transplacental amiodarone is also used successfully, often combined with digoxin [34,35].

Standard oral dose for flecainide is 100 mg, 8 hourly. It has adequate placental transfer even in hydrops. Therapeutic trough levels often reach the normal range (200–1000 μg/L) in 3 days. Maintenance doses are 200–300 mg/day (maximum 400–450 mg/day). In one study, levels did not correspond to response, median ~450 μg/L in responders and nonresponders [36]. Digoxin, given orally

or intravenously, requires a loading dose, but regimes vary. The following is used in the ongoing RCT: loading dose = 2 mg (0.5 mg 12 hourly, or 0.5 mg 8 hourly in hydrops), followed by maintenance, adjusted according to serum levels taken 12 h after the third or fourth dose. Levels are aimed at 1.0–2.0 ng/ml but higher in hydrops (1.5–2.0 ng/ml). Digoxin, as a direct intramuscular fetal injection, was effective at a dose of 88 μg/estimated fetal weight, repeated at 12–24 h interval, maximum 3 doses [33]. Sotalol has quick placental transfer, reaching desirable levels even in hydropic fetuses. Side effects are dose related. It prolongs QT interval, and hence, maternal ECG should be monitored. Initial recommended dose is 240 mg/day, 8 or 12 hourly but higher in hydrops (320 mg/day, 12 hourly). After a few days, dosage is titrated according to response, maximum of 480 mg/day [18]. Amiodarone has poor placental transfer (10%–40%), worse in hydrops, but it accumulates in fetal compartments due to long half-life. Loading and maintenance doses vary [20,34,35], A suggested regime includes a loading dose with 1200 mg/day for 5–7 days (orally or 24 h intravenous infusion) followed by a maintenance dose of 600–800 mg/day (200 mg 6 or 8 hourly) [20]. Recommended doses for direct fetal therapy are 2.5–5 mg/kg estimated fetal weight [20].

Information about the treatment of VT and JET is limited. Magnesium sulfate (intravenous loading dose of 2–4 g, followed by 1–2 g/h), lidocaine (intravenous loading dose of 1–1.5 mg/kg followed by 1–3 mg/min), and oral propranolol (40–80 mg 8 hourly) have been used for VT. Amiodarone, sotalol, and flecainide may also be effective [17]. If associated with long QT, beta-blockers are preferable and drugs that prolong QT interval (e.g., sotalol) should be avoided. Treatment for fetal JET has included sotalol, digoxin, and flecainide [23].

Bradycardias

Bradycardia is often associated with fetal distress, but its incidental finding requires further assessment. Transient episodes during scanning are common because of vagal stimulation by cord compression and resolve rapidly with less pressure to maternal abdomen. However, persistent bradycardia, even if intermittent, requires diagnostic workup so that management is appropriate.

The obstetric definition of bradycardia according to the guidelines of the American College of Obstetricians and Gynecologists is FHR <110 bpm. However, gestational age-specific nomograms indicate variability [37], with the third centile corresponding to rates of ~135 and 130 bpm at 25 and 35 weeks, respectively. This helps prediction of familial long-QT syndrome [38]. Setting a higher threshold of ~115 bpm for irregular rhythms also helps in the identification of some forms of AV block [16] (Fig. 2).

Bradycardia of 70–80 bpm has different management implications depending on the underlying electrophysiological mechanism. Thus, accurate diagnosis is paramount and based on the detailed evaluation of regularity pattern of atrial and ventricular contractions and their temporal relationship.

Bradycardia with 1:1 AV conduction

Persistent bradycardia with 1:1 AV conduction, not associated with fetal distress, is rare. This is almost invariably sinus bradycardia but may occasionally indicate low atrial rhythm, which is characteristic of left atrial isomerism. Sinus bradycardia may be a manifestation of sinus node dysfunction, congenital long-QT syndrome, or circulating maternal autoantibodies. Baseline FHR < third percentile is a potential marker for long-QT syndrome albeit with low sensitivity [37].

Management

Parental 12-lead ECG, family history, and maternal autoantibody status should be obtained. History of important arrhythmias, sudden death, or recurrent fetal loss may indicate an underlying genetic cause. Sinus bradycardia is well tolerated prenatally and does not require treatment. Monitoring fetal well-being at 4–6 weeks is advisable. Perinatal outcome depends on etiology. Neonates need a 12-lead ECG. Further family/genetic tests can be performed depending on history.

A positive family history and evidence of intermittent 2:1 AV block/VT are strong indicators of fetal long-QT syndrome. The QT interval can be measured by f-MCG, if available. The value of steroids to treat autoimmune sinus bradycardia is unknown. In these cases, we observed progressive decrease in

baseline FHR as pregnancy advanced. Low atrial rhythm can be transient or progress to heart block, which in itself carries a guarded outlook, especially if associated with major CHD.

Bradycardia related to atrial ectopics

When atrial ectopics occur regularly generating bigeminy (one normal beat and one ectopic) or trigeminy (two normal beats and one ectopic), overall ventricular rate may fall. Blocked atrial bigeminy leads to regular bradycardia, FHR ~70–80 bpm. It cannot be distinguished from 2:1AV block on the basis of FHR alone and accounted for nearly half of bradycardia with rates <110 bpm [14]. Timing of atrial (A) contractions is essential in the differential diagnosis (Fig. 3), which is often straightforward but, at times, may simulate 2:1 AV block. Careful measurements are needed, and f-MCG can be used for this [15]. When atrial bigeminy is conducted or if there is blocked atrial trigeminy, the rhythm is irregular, FHR ~100–115 bpm and ought to be distinguished from partial forms of AV block [16] (Fig. 4).

Management

Following a positive diagnosis of atrial ectopics causing bradycardia, the pregnant woman can be reassured. Treatment is not required, but FHR monitoring is needed because of the small risk of tachycardia (Fig. 2). In one study, all cases of blocked bigeminy resolved spontaneously [10], whereas others report tachycardia in 14% of cases [14].

Because of the potential risk that emergency cesarean section is performed unnecessarily, especially if FHR is <100 bpm, it is important that the pregnant woman and all professionals looking after her understand its benign nature. Maternal awareness of normal fetal movements is important, and other means of assessing fetal well-being need to be in place.

Heart block

Heart block refers to prolongation or blockage of AV conduction of a normal sinus beat through the AV node. Severity varies, with first-degree block (I-AVB) simply reflecting delayed conduction. FHR reflects the pacemaker rate, and the AV interval must be measured. In second-degree block (II-AVB), AV blockage occurs intermittently. There are two types of AV blockage: in type I (Mobitz I or Wenckebach phenomenon), there is progressive lengthening of the AV interval until a blockage occurs. The rhythm is irregular, but FHR is usually normal. In type II (or Mobitz II), some beats are conducted and some are blocked. A 2:1 AV conduction is common, causing regular bradycardia, with a ventricular rate of ~60–80 bpm. However, the ratio of AV conduction may vary (e.g., 3:2), with rate and rhythm pattern also varying accordingly. Both types of II-AVB need differentiation from atrial ectopics (Figs. 3 and 4). In complete or third-degree block (III-AVB), there is no AV conduction at all so that atria and ventricles beat independently (Fig. 5). Congenital AV block occurs in 1 in 15,000 to 1 in 20,000 live births. Etiology may be autoimmune, linked to CHD, or unknown.

AV block associated with CHD accounts for many cases, most occurring with left isomerism and less with AV discordance. The prognosis is generally poor [39,40] with high fetal and neonatal mortality [40]. In one series (n = 59), 60% were liveborn and neonatal mortality approached 80% (left isomerism = 90%; AV discordance = 25%) [39].

In isolated nonimmune AV block, prognosis seems better. Of 26 congenital cases, 16 had III-AVB. In 10 cases with partial block, mean progression time to III-AVB was 2.8 years. No deaths or cardiomyopathy was observed (mean follow up ~11 years) [41]. Regression of nonimmune II-AVB has also been reported [39,42], although some may represent spontaneous resolution of ectopic-related bradycardia [43].

Autoimmune AV block is due to the transplacental transfer of maternal autoantibodies, anti-Ro (SS-A) and/or anti-La (SS-B), that target the fetal ribonucleoproteins “Ro” and “La” located in the conduction system, thereby causing inflammation, fibrosis, and irreversible damage. The process can also target myocardial cells. AV block typically develops after 16–18 weeks of gestation, peaks at 20–24, and most (82%) occur before 30 weeks [44]. The prognosis in AV block is better than that in CHD cases, but fetal demise is still ~6%–10% [42,45]. Presentation <20 weeks, hydrops, impaired function, and FHR <50 bpm are recognized risk factors. Risk of fetal block in affected women is

relatively low (2%–3%) [46], but recurrence risk is considerably higher (16–19%) [44] and may be related to antibody levels [47].

Management of autoimmune AV block

Treatment aims to reduce or prevent myocardial and conduction abnormalities, reduce levels of maternal antibodies, or augment FHR. Options include maternal steroids, beta-sympathomimetic agents, intravenous gamma globulin (IVIG), and plasmapheresis [48,49]. Established autoimmune III-AVB is irreversible [44].

In utero pacing has limitations. Dedicated pacing wires developed over a decade ago had limited clinical use and no survivors. Developments in minimally invasive micro-pacemakers [50] and ex-utero intrapartum treatment [51] may have a future role. More exciting is the possibility of prevention. Studies suggest that sustained fetal exposure to hydroxychloroquine reduces AV block recurrence to 7.5% [52]. Results of a prospective open-label clinical trial (PATCH: Preventive Approach to Congenital Heart Block with Hydroxychloroquine) are awaited.

Fluorinated steroids aim to reduce inflammation. The most used steroid is dexamethasone (4–8 mg daily, tapered to 2 mg toward the end of pregnancy) despite its unproven efficacy regarding AV block, cardiomyopathy, or survival [53–55]. However, recent small series observations suggest a beneficial effect if treatment (dexamethasone and/or IVIG) is started within 24 h [56]. As randomized trials are lacking and fetal/maternal side effects occur [48], treatment may be considered only in compromised fetuses or recently developed AV block.

Beta-agonists (salbutamol and terbutaline) are used to increase FHR if < 50–55 bpm. Increase of 5–10 bpm with salbutamol (10 mg 8 hourly; maximum = 40 mg/day) or terbutaline (2.5–7.5 mg 4–6 hourly; maximum = 30 mg/day) is reported [48]. Maternal tremor and palpitations are side effects that tend to settle; hence, doses can be titrated up.

Immunoglobulins and plasmapheresis have also been used. Repeated maternal injections of IVIG aim to reduce the effects of antibodies on the fetal heart. Two prospective multicenter trials used 400 mg/kg at 3-week intervals at 12–24 weeks, in women with previously affected children but failed to prevent recurrence [57,58], which may have been dose related. Higher doses (1 g/kg, plus steroids) may potentially improve outcome [59]. Plasmapheresis aims to reduce maternal levels of antibodies. A potential effect on II-AVB combined with IVIG and betamethasone is reported in a small prospective study [60]. Larger controlled trials are needed.

Fetal surveillance of anti-Ro/anti-LA-affected pregnancies

Intensive surveillance with weekly AV interval measurements aiming to treat partial block to prevent III-AVB has been suggested. However, the PRIDE study did not support this strategy [46]. Fetuses with I-AVB, treated or untreated, did not progress to III-AVB. Importantly, III-AVB occurred without previous partial block. In another prospective study, I-AVB reverted with dexamethasone but no controls [61]. Conversely, of 150 fetuses followed up serially, 15 developed partial blocks, none were treated, and AV interval normalized in all but one [62]. Notably, altered myocardial contractility may also prolong the AV interval [63].

Although current studies do not support weekly monitoring of the AV interval for all pregnancies at risk, targeted surveillance, stratified by antibody levels >100 U/mL, seems safe [64], but levels are not usually available. A small case series also suggests treatment benefits if block is recognized within 24 h [56], suggesting a potential role for increasing FHR monitoring [65]. Until a consensus is achieved, surveillance (scans and FHR monitoring) from 16 weeks is tailored to individual cases and intensified if there is a previously affected child.

Summary

Irregular rhythms due to atrial ectopics are the most common fetal dysrhythmia and usually resolve spontaneously. However, they can constitute a diagnostic challenge during routine obstetric care. In a few cases, ectopics can trigger tachycardia; hence, risk stratification is important for appropriate fetal monitoring. Conversely, ectopics can cause regular bradycardia (<100 bpm) or irregular rhythms that require differentiation from second-degree AV block. Accuracy in diagnosis is important, as

management implications differ. Less common dysrhythmias such as tachycardias and AV block can be life threatening. Tachycardias need urgent attention. If sustained, they can lead to fetal hydrops. SVT and AF often respond to transplacental treatment. Flecainide, digoxin, and sotalol are commonly used. An RCT to assess the efficacy of these drugs is ongoing. Hydrops increases morbidity and mortality for tachycardias and bradycardias. Management of complete AV block may be challenging, with few therapeutic options available. The results of an open-label trial of hydroxychloroquine to prevent the recurrence of AV block are awaited. Ambulatory fetal heart monitoring may contribute to the early detection of AV block.

Conflict of interest

None.

Practice points

What we know
- Fetal dysrhythmias, mainly atrial ectopics, are common, often benign but can cause bradycardia and trigger tachycardia.
- Tachycardias require urgent assessment, as it can lead to hemodynamic compromise, hydrops, and death.
- SVT with 1:1 AV conduction and AF are the most common tachycardias. Transplacental treatment is successful in the majority.
- Bradycardia due to ectopic beats is well tolerated.
- Bradycardia due to heart block is often associated with maternal autoantibodies.
- There is no proven effective in utero treatment for heart block.

What we do not know
- Best drug to treat all fetal tachycardias.
- Best practice to survey pregnancies affected by anti-Ro/anti-La antibodies.
- How to treat/manage partial AV block.
- How to pace the fetal heart.

Research agenda

- Randomized trial to treat fetal tachycardia (www.fasttherapytrial).
- Risk stratification of fetuses at risk of long-QT syndrome.
- Early recognition and treatment of emerging heart block (www.heartsoundsathome).
- In utero pacing for established complete heart block.

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