



UNIVERSITÀ POLITECNICA DELLE MARCHE
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Corso di Laurea in Medicina e Chirurgia

**Aritmie Fetali: un aggiornamento
sull'attuale sorveglianza e gestione**

**Fetal Arrhythmias: an update on current
surveillance and management**

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ABSTRACT

Le aritmie cardiache fetali sono comuni anomalie che si manifestano generalmente con un ritmo irregolare. Sebbene molte irregolarità siano benigne e generate da ectopie atriali isolate, che si risolvono spontaneamente nel corso della gravidanza, in alcuni casi possono provocare l'insorgenza di tachicardia, bradicardia o ritmo irregolare, il quale necessita di essere distinto da un blocco atrioventricolare di secondo grado.

Le tachiaritmie e le bradiaritmie sono alterazioni del ritmo cardiaco rare, infatti si riscontrano in circa il 2% delle gravidanze, ma necessitano comunque di una immediata diagnosi e gestione poiché, se sostenute, possono portare ad una compromissione emodinamica fetale, un parto prematuro o una morte fetale endouterina. Per ridurre il rischio che tali eventi prognosticamente sfavorevoli si verifichino, ad oggi, c'è la possibilità di eseguire una terapia in utero.

La tachicardia sopraventricolare (TSV) e il Flutter Atriale (AF) sono le più comuni tachiaritmie fetali. Queste alterazioni del ritmo cardiaco necessitano una diagnosi precoce al fine di attuare il trattamento farmacologico transplacentare più appropriato, prima che insorgano alterazioni emodinamiche fetali, come l'idrope e l'anasarca, che pongono seriamente a rischio la gravidanza e rendono più difficile la gestione terapeutica della patologia cardiaca stessa.

Digossina, Flecainide e Sotalolo sono i farmaci più comunemente utilizzati, sia singolarmente che in associazione. La Digossina è il farmaco antiaritmico maggiormente impiegato come terapia di prima linea delle tachiaritmie. La nostra esperienza e la letteratura hanno però evidenziato come la somministrazione della sola Digossina sia terapeuticamente meno efficace nei feti idropici rispetto alla Flecainide e al Sotalolo. In presenza di anasarca e idrope è infatti fortemente raccomandato l'uso della sola Flecainide o l'uso di Digossina e Flecainide, o di Digossina e Sotalolo o di Flecainide e Sotalolo.

Fondamentale oltre alla terapia farmacologica è anche la sorveglianza sia del feto che della madre, che ad oggi prevede l'esecuzione dell'Ecografia, dell'Ecocardiografia, della Cardiotocografia fetale, dell'Elettrocardiogramma (ECG) e degli esami ematici materni, ad intervalli temporali differenti in base alla risposta al trattamento. L'ECG materno viene eseguito per verificare l'effetto che i farmaci antiaritmici utilizzati hanno sull'attività cardiaca della madre, mentre gli esami ematici materni vengono svolti per controllare che i livelli sierologici dei farmaci rimangano entro il range terapeutico.

Sebbene la TSV e il AF siano le più comuni cause di terapia in utero, nessuno dei farmaci antiaritmici utilizzati è mai stato valutato per i suoi effetti sulla madre e sul bambino in uno studio clinico randomizzato.

In assenza di tali prove, non c'è ancora un consenso condiviso sull'ottimale gestione e sorveglianza delle tachiaritmie.

Il blocco atrioventricolare completo (CAVB) è la causa più comune di bradiaritmia fetale e, nella maggior parte dei casi, alla base di questa alterazione del ritmo cardiaco vi è una patologia autoimmune materna. La gestione della CAVB può essere impegnativa, poiché ad oggi sono disponibili poche opzioni farmacologiche e con scarsa efficacia terapeutica. Negli ultimi anni sono in atto molteplici studi in aperto per verificare se il trattamento preventivo con l'idrossiclorochina nelle gravidanze ad alto rischio di sviluppare CAVB isolato sia efficace e giustificato, considerando che il rischio fetale di insorgenza del blocco atrioventricolare è dell'1-2% nelle donne con anticorpi anti-Ro/La.

Anche in questo tipo di aritmie, fondamentale è la diagnosi precoce mediante il monitoraggio ambulatoriale del cuore fetale.

La prognosi del CAVB fetale isolato può essere migliorata dal trattamento transplacentare con Desametasone e β -stimolazione quando la frequenza cardiaca fetale è < 55 bpm. Qualora invece la frequenza cardiaca fetale è > 55 bpm e la diagnosi di blocco atrioventricolare immuno-mediato viene fatta entro 7 giorni dall'insorgenza, è utile la somministrazione del Desametasone o delle immunoglobuline intravenose. Se la diagnosi viene invece fatta dopo 7 giorni dall'insorgenza, si preferisce non attuare un trattamento farmacologico ma solo

uno stringente monitoraggio ecocardiografico. Questi approcci terapeutici alternativi richiedono però ulteriori studi per verificare con maggiore attendibilità la loro efficacia.

Fondamentale, anche in questo, oltre alla terapia farmacologica è la sorveglianza materno-fetale, che ad oggi prevede l'esecuzione dell'Ecografia, dell'Ecocardiografia, della Cardiotocografia (CTG) fetale e degli esami ematici materni, per controllare i livelli anticorpali, ad intervalli temporali differenti in base alla risposta al trattamento.

Questo studio mira a sviluppare, in seguito all'esperienza del Dipartimento di Ostetricia e Ginecologia del Presidio Salesi dell'AOU degli Ospedali Riuniti di Ancona e ad una approfondita analisi e comparazione della letteratura scientifica, nuovi e appropriati protocolli di gestione terapeutica e di sorveglianza per i tre tipi di aritmia fetale più frequentemente riscontrati durante la gestazione.

1. INTRODUCTION

In recent years, the collaboration between pediatric cardiologist specialized in fetal medicine and the maternal fetal specialist has been strongly consolidated for the study of fetuses with structural heart disease, arrhythmias or cardiovascular dysfunctions. This has led to new multidisciplinary standards of care and new therapeutic possibilities, still evolving, for a specialized management of fetal heart medicine.

Depending on gestational age and degree of fetal activity, the normal fetal cardiac rhythm is characterized by a regular heart rate ranging between 100 and 180 beats/min (bpm) with a normal 1:1 atrio-ventricular (AV) electromechanical relationship during each cardiac cycle. Accordingly, fetal cardiac arrhythmias may present as an irregular heart rate, as an abnormally slow or fast heart rate, or as a combination of irregular rhythm and an abnormal heart rate.

These rhythm disturbances can be caused either by generation or propagation anomalies of electrical impulses, due to ischemia, inflammation, electrolyte disturbances, stresses, cardiac structural abnormality, or gene mutations.

Fetal arrhythmias accounted for 2% of unselected pregnancies and for as 16.6% of high-risk pregnancies from 21 gestational weeks to term. In 90% of cases, are transient rhythm irregularities in structurally normal heart with benign nature and resolve spontaneously. However, in 10 % of cases, persistent bradycardia (< 100

bpm) and sustained tachycardia (> 180 bpm) may cause low cardiac output, fetal hydrops, preterm delivery and higher perinatal morbidity and mortality. This includes supraventricular tachycardia (SVT), atrial flutter (AF) and complete AV block as the major fetal arrhythmias mechanism.

The outcome of affected fetuses is influenced by numerous variables including, arrhythmia characteristics, gestational age at diagnosis, heart defects and choice of treatment. Therefore, a prompt diagnosis and a correct treatment, are crucial for fetal well-being and represent a challenge that involves a team of specialists on fetal cardiac ultrasound.

In this article, through an in-depth analysis and comparison of the scientific literature, we aim to provide a logical approach to manage fetal arrhythmias with an update on current protocols of diagnose surveillance and treatment.

Inside are described three clinical cases treated by the Department of Obstetrics and Gynecology of the Salesi Presidium of the AOU, Ospedali Riuniti of Ancona.

2. HOW TO ASSESS FETAL CARDIAC RHYTHM

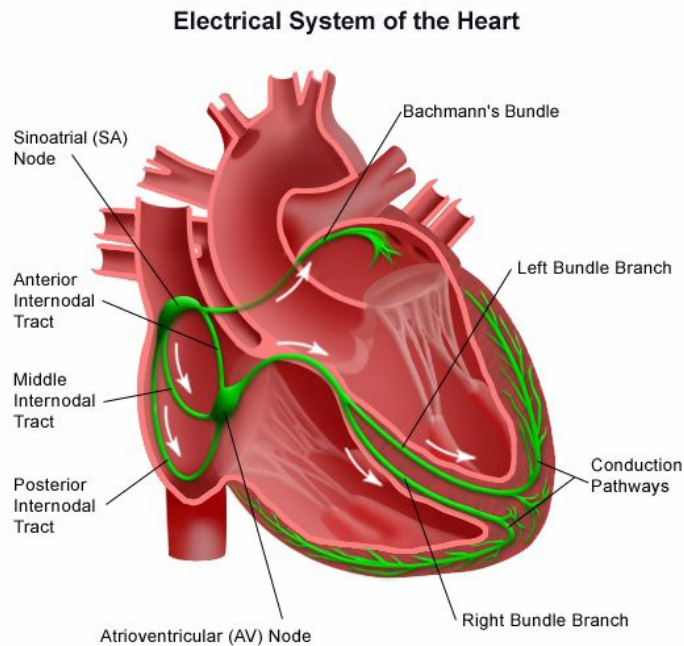


Fig. 1

Treatment of fetal arrhythmias relies on accurate diagnosis. Therefore, a basic understanding of normal rhythm is essential. Contraction and relaxation result from electric 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 ensures that ventricular contraction follows atrial contraction leading to a 1:1 AV relationship.

Fetal heart is characterized by a reduced systolic and chronotropic reserve and a

restrictive pathophysiology, for which heart rates lower than 55 bpm or higher than 200 bpm can rapidly determine heart failure.

To study cardiac rhythm, simultaneous recording of atrial and ventricular activities is needed. Ultrasound-based techniques are the main tools available prenatally to determine fetal well-being, assess cardiac structures and define the nature of rhythm.

M-mode echocardiography is commonly used. It is based on placing a line of ultrasound beam across cardiac structures to register mechanical results of electrical activation. Typically, M-mode and two-dimensional echocardiography, with the help of Doppler and Color Doppler ultrasound, is applied on the four-chamber view to record atrial and ventricular motion.

Limitation are image resolution and fetal position.

In an effort to detect lower grade AV block, attention has focused on the measurement of the mechanical PR interval by Doppler techniques, including *pulsed wave (PW) Doppler or tissue-Doppler*. In PW Doppler PR interval is measured between the onset of the A-wave (atrial systole) and the onset of the ejection outflow Doppler (ventricular systole) aligning the gated PW-Doppler cursor simultaneously across an inflow and outflow, traditionally the left ventricular inflow-outflow tract area (mitral-aortic). Alternative site include ascending aorta-superior vena cava and right pulmonary artery-pulmonary vein.

Although useful, AV time intervals are derived from flow and the accuracy of the measurements are influenced by myocardial intrinsic properties, ventricular loading conditions, fetal heart rate and the speed of pulse wave propagation.¹

Color and PW tissue Doppler are also described but not widely used.

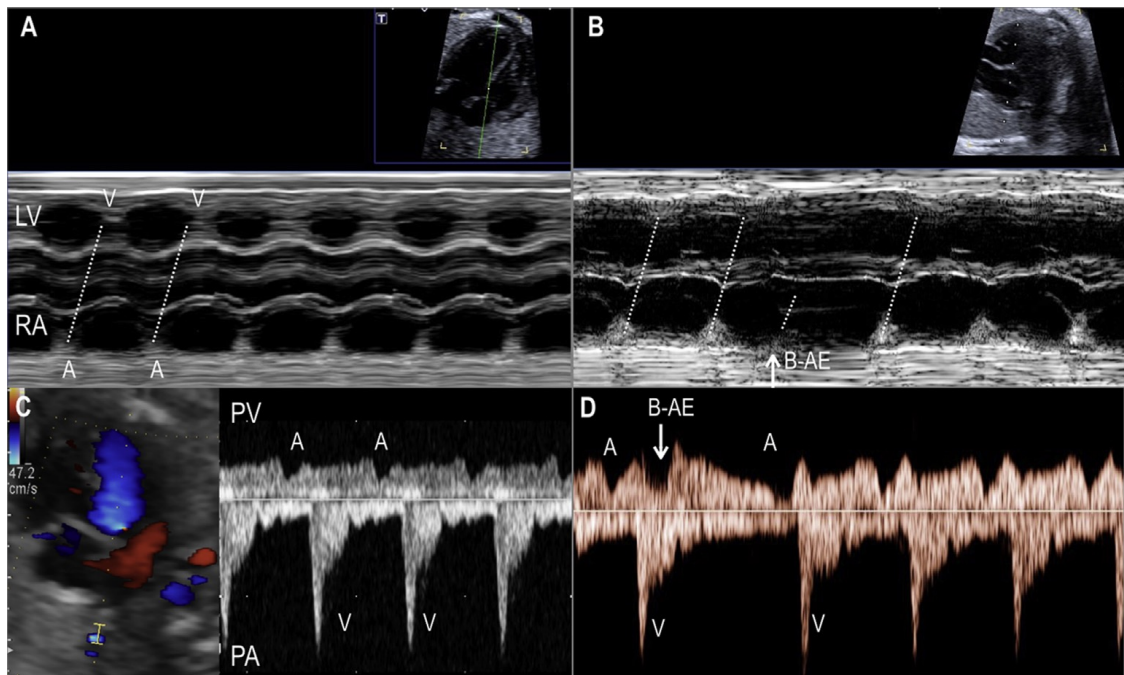


Fig. 2 - M-Mode [A;B] and simultaneous pulsed-wave Doppler signal [C,D] across the pulmonary artery (PA) and vein (PV). Images [A,C] depict normal sinus rhythm, and image [B,D] show a blocked atrial ectopic (B-AE). Note the regular interval between atrial signals during sinus rhythm and an early signal (arrow) characteristic of atrial ectopic. A/V = atrial/ventricular systole; LV = left ventricle; RA = right atrium. [2]

Fetal electrocardiography (f-ECG) (Fig.3) and fetal magnetocardiography (f-MCG) (Fig.4) 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 constitute part of routine clinical practice. To date signal

processing has improved, although f-ECG signal-to-noise ratio remains a limitation, especially around 27 - 36 weeks.² F-MCG is superior but requires a shielded environment and has high maintenance costs.

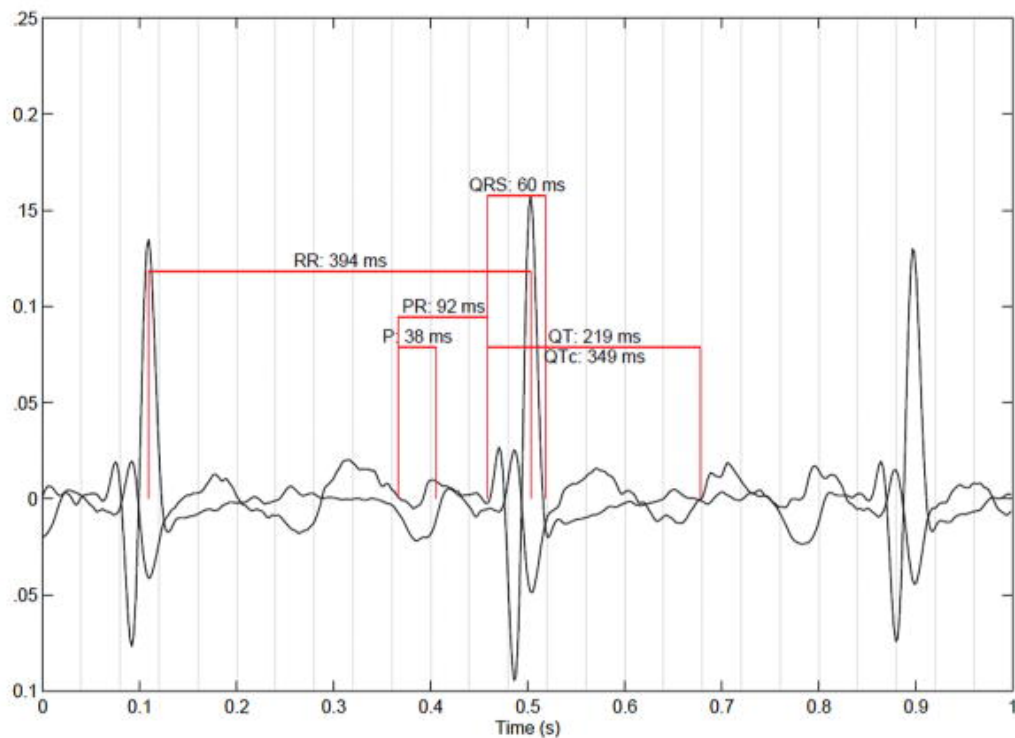


Fig. 3 – fECG [3]

fMCG can be performed in many fetuses after 20 weeks' gestation, but is less reliable before this gestational age. Recordings are usually performed over 1–2 h in 5–10 min epochs.⁴

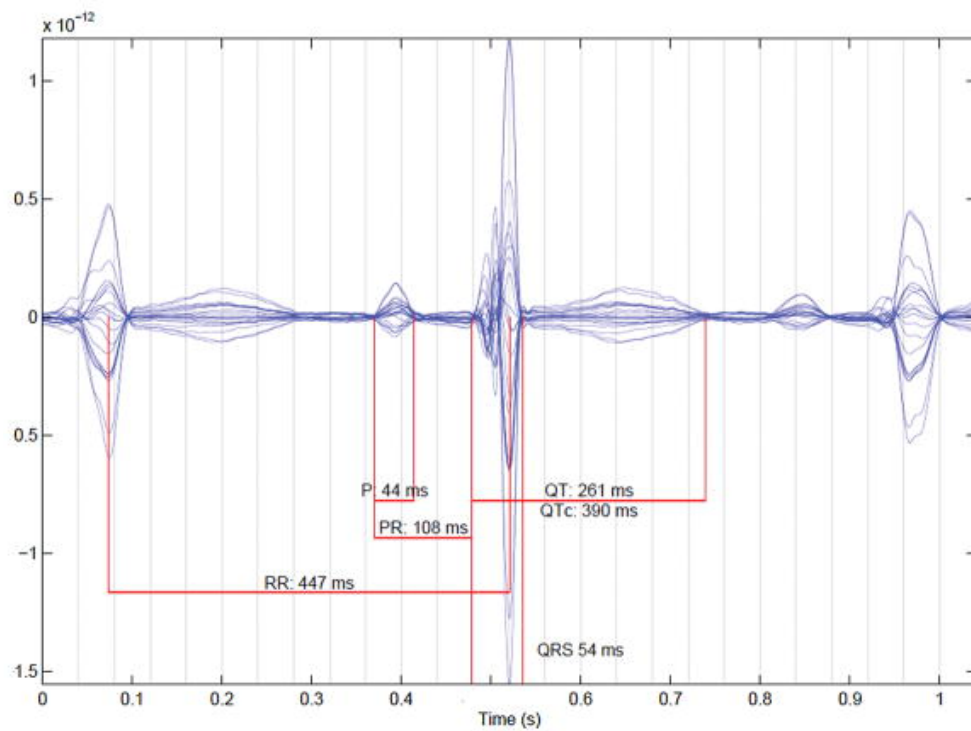


Fig. 4 – fMCG [3]

Another way to detect fetal heart rate involves using *Cardiotocography* (CTG) (Fig.5). CTG registers baseline FHR and FHR variability by Doppler as well as registering uterine contractions. The use of CTG is usually limited to > 30 weeks' gestation. However, CTG technology functions poorly during fetal tachycardia or AV block. It is best used to trend certain treatments such as the response to transplacental medications and as an adjunct to biophysical profiles for fetal assessment when sinus rhythm is the predominant rhythm.³

3. EPIDEMIOLOGY

Fetal arrhythmias account for 0.6 – 2 % of all pregnancies and account for 10 to 20% of referrals to fetal cardiac center. The majority (85-90%) of these abnormalities resolve on their own and are not detected at the time of evaluation or consist of atrial ectopic, and only less than 10% have sustained tachyarrhythmias and bradyarrhythmias that persist over time and need treatment. Although fetal arrhythmias account for a small percentage some of these persistent fetal arrhythmias, especially when associated with structural heart defect, congestive heart failure, or hydrops fetalis, may be associated with a poor prognosis and even cause fetal death.

Hidden sustained fetal arrhythmias may contribute to a high rate of fetal demise (3 – 10%), hydrops and prematurity³ as it causes an increase in central venous pressure and a decreased cardiac output.

Fetal arrhythmias go into differential diagnosis with hypoxemic bradycardias during labor, tachycardia due to maternal hyperpyrexia infections (chorioamniotitis and cytomegalovirus), MAF, anemia, thyrotoxicosis and maternal medication.⁵

The main fetal arrhythmias are: supraventricular tachycardia (SVT), atrial flutter (AF) and complete AV block.

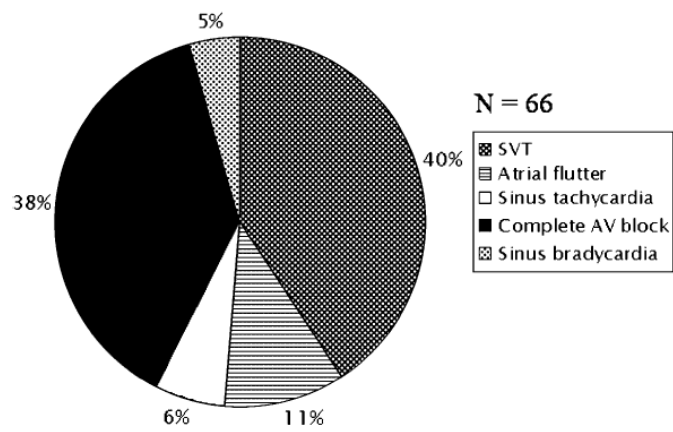


Fig. 5 – Distribution of major fetal bradyarrhythmias and tachyarrhythmias seen at the Hospital for Sick Children during the last 5 years (2000-2004). SVT, supraventricular tachycardia; AV, atrioventricular. [25]

4. FETAL RHYTHM IRREGULARITIES

Irregular fetal heart rhythm, often described as extrasystoles, constitute a large proportion of referrals due to arrhythmias. They occurs in sinus rhythm with atrial or, less frequently, with ventricular premature contractions (PVCs), which are clinically benign if brief and isolated and are commonly identified during the third trimester. If an extrasystole follows every sinus beat, it is termed bigeminy, if it follows every third beat, it is termed trigeminy, and if it follows every fourth beat, the rhythm is quadrigeminy. Premature atrial contractions (PACs) are extra beats in which the ectopic focus originates in the atria, and premature ventricle contractions (PVCs) are those that originate in the ventricles. (*Fig. 6*)

In utero, the prevalence of PAC to PVC is 10:1 and PACs are difficult to distinguish from PVCs. A premature ventricular beat is not preceded by an atrial contraction (no A wave). The PACs may be followed by a ventricular contraction (V wave) when conducted to the ventricles, or not, in cases of blocked PACs. Indeed, in non conducted PAC there is a longer compensatory pause and this feature would be helpful for differentiating PVCs from PACs.

Fetal extrasystoles are associated with congenital cardiac defects in approximately 1% of cases, and fetal echocardiogram is recommended. The most common heart defects are cardiac malformations, myocardial diseases, and intracardiac tumors.

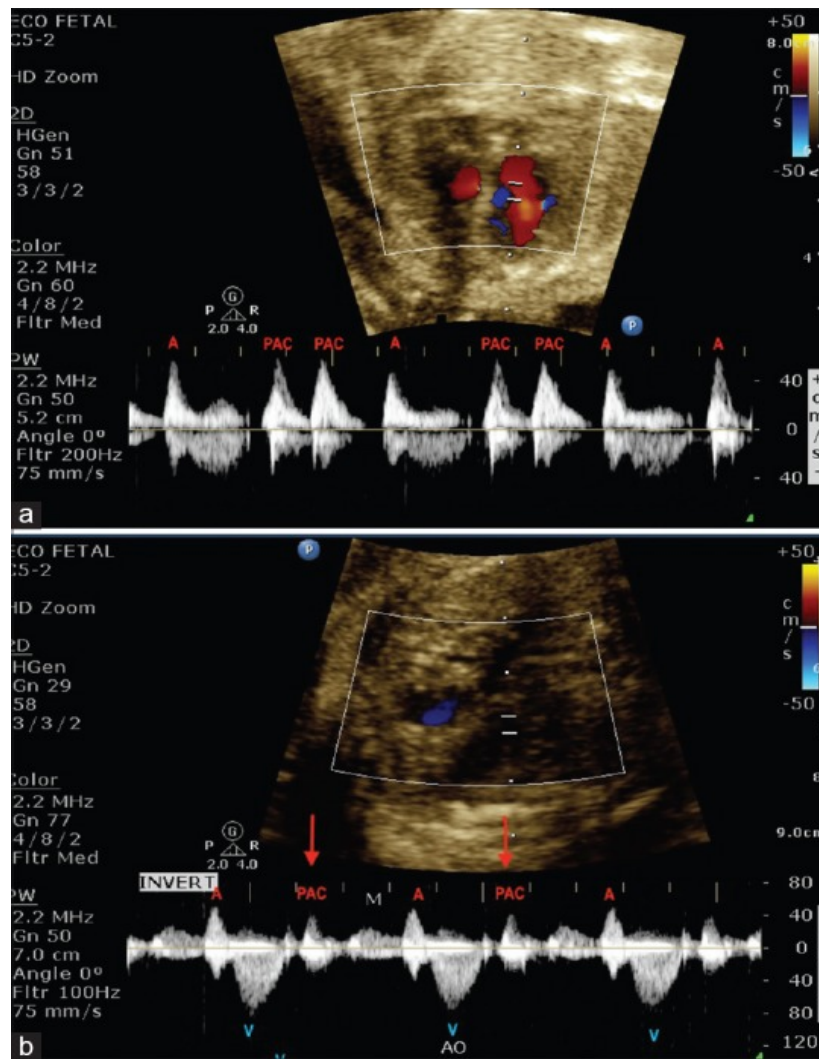


Fig. 6 - Blocked atrial bigeminy frequently has a variable atrial rhythm, with a shorter AA time interval, between the conducted and following blocked atrial beats (a), alternating with a clearly longer AA time interval between the blocked and following conducted beat (b). [5]

4.1 MANAGEMENT

In general, isolated PACs or PVCs do not require antiarrhythmic therapy, and in the majority of cases, they resolve spontaneously before delivery. However, risk stratification is important because in a small minority of cases, around 2 – 3%, the extrasystoles are multiples (couplets), which increase the risk for a sustained SVT

in $\approx 10\%$. At the specialist level, if isolated ectopics are confirmed and occur occasionally, the patient can be discharged. If ectopics are frequent 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.

The bigeminal blocked PACs, also known as blocked atrial bigeminy (BAB), often produce a low ventricular fetal HR, ranging from 70 to 90 bpm. It has not been associated with hydrops, and no treatment is required. BAB is frequently misdiagnosed as second-degree AV block (AVB) and should be correctly identified to avoid management mistakes.

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; therefore, a neonatal ECG and a 24 h-ECG recording are advisable.

5. TACHYARRHYTHMIAS

Fetal tachycardia is defined as $HR > 180$ bpm. Based on its persistence, it can be classified as *sustained* when the arrhythmia is present for more than 50% of the examination time or *intermittent* when periods of tachycardia alternate with predominantly normal HR. Persistent tachyarrhythmias may be well tolerated or, at the other end of the spectrum, may lead to congestive heart failure, dilated cardiomyopathy, nonimmune hydrops, polyhydramnios, neurological pathology and even death. Fetal hydrops has been associated with a mortality risk of up to 35%, compared with 0 - 4% in cases without significant heart failure.

The fetal heart structure is often normal, but CHD may be present.

According to the electrophysiological levels of the heart, the tachyarrhythmias are subdivided into:

- 1) Supraventricular Tachycardia (SVT);
- 2) Atrial Flutter (AF);
- 3) Sinus Tachycardia;
- 4) Ventricular Tachycardia (VT).

SVT is the most common form of fetal tachycardia (70% – 75%), whereas VT is the rarest.

Tachycardia	Rhythm	AR	AV conduction	VR	AV interval
Re-entrant SVT	Regular	220-300	1:1	220-300	VA < AV VA >70<100 ms
Atrial ectopic tachycardia	Irregular (or chaotic)	>160-250	1:1	Variable	VA > AV VA >100 ms
Atrial flutter	Variable	350-500	2:1, 3:1, 4:1	Variable VR < AR	
JET	Regular	180-240	<1:1 or 1:1	180-240	VA ≥ AV >100 ms
VT	Variable	Variable VR > AR	<1:1 or 1:1	180-300	VA < AV
ST	Regular	180-200	1:1	180-200	AV=VA

SVT: Supraventricular tachycardia, JET: Junctional ectopic tachycardia, VT: Ventricular tachycardia, ST: Sinus tachycardia, AR: Atrial rate, VR: Ventricular rate, AV: Atrioventricular interval time, VA: Ventriculoatrial interval time

Fig. 7 – The characteristics of the main types of tachycardia [5]

5.1 SUPRAVENTRICULAR TACHYCARDIA

The term ‘supraventricular tachycardia’ encompasses tachycardias with three different mechanisms including:

1. *AV re-entrant tachycardia (AVRT)* related to retrograde fast accessory pathway conduction;
2. *Permanent junctional reciprocating tachycardia (PJRT)* related to retrograde
3. Slow accessory pathway conduction;
4. *Atrial ectopic tachycardia (AET)* due to an atrial focus with enhanced automaticity.

SVT mechanisms may be quite accurately differentiated based on their arrhythmia

pattern including the AV and ventriculo-atrial (VA) relationship. However, the differentiation of AVRT, PJRT or AET by fetal echocardiography can be difficult and it is not required prenatally since it is no evidence that it affects the results of therapy.

AVRT accounts for 90% of fetal and neonatal forms of SVT. During typical orthodromic AVRT, there is normal AV conduction through the AV node, while an accessory pathway conducts retrograde from the ventricles to the atria. As the retrograde atrial activation occurs shortly after the ventricular activation, this yields a short VA time interval on Doppler or M-mode echocardiography. Other features of short VA SVT include intermittent or sustained episodes of regular fast heart rates between 180 and 300 bpm and 1:1 AV conduction. The onset and termination of AVRT is sudden. After birth, antegrade accessory pathway conduction (Wolff-Parkinson-White syndrome) is found in 10% of cases with fetal SVT.

Atrial ectopic tachycardia (AET) and *permanent junctional reciprocating tachycardia (PJRT)* are less common but more resistant to treatment compared with short VA SVT. Typically, these are long VA tachycardias (VA : AV ratio > 1), with FHR usually ~180 - 220 bpm. AET may have 1:1 or variable AV conduction, whereas PJRT shows 1:1 conduction. In PJRT, the retrograde (VA)

conduction occurs through a slow conducting accessory pathway. This results in sustained long VA tachycardia of about 220 bpm with a 1:1 AV relationship. In AET, an atrial focus exceeds the normal pacemaker activity of the sinus node. AET is mainly sustained due to multiple runs of fast heart rates between 200 and 250 bpm. The tachycardia may have a gradual onset and offset, and variable second-degree AV block may occur.

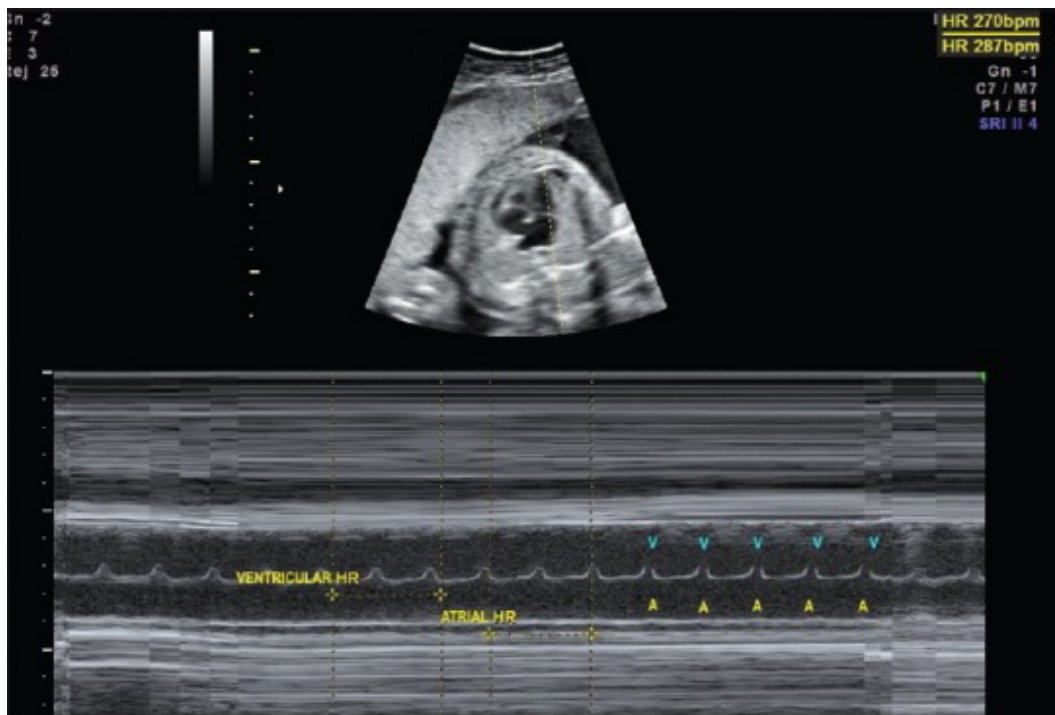


Fig. 8 – Re-entrant supraventricular tachycardia with HR of 287 bpm M-mode tracing showing the 1:1 atrioventricular conduction. A, Atrium wave; V, Ventricular wave; HR, Heart rate. [5]

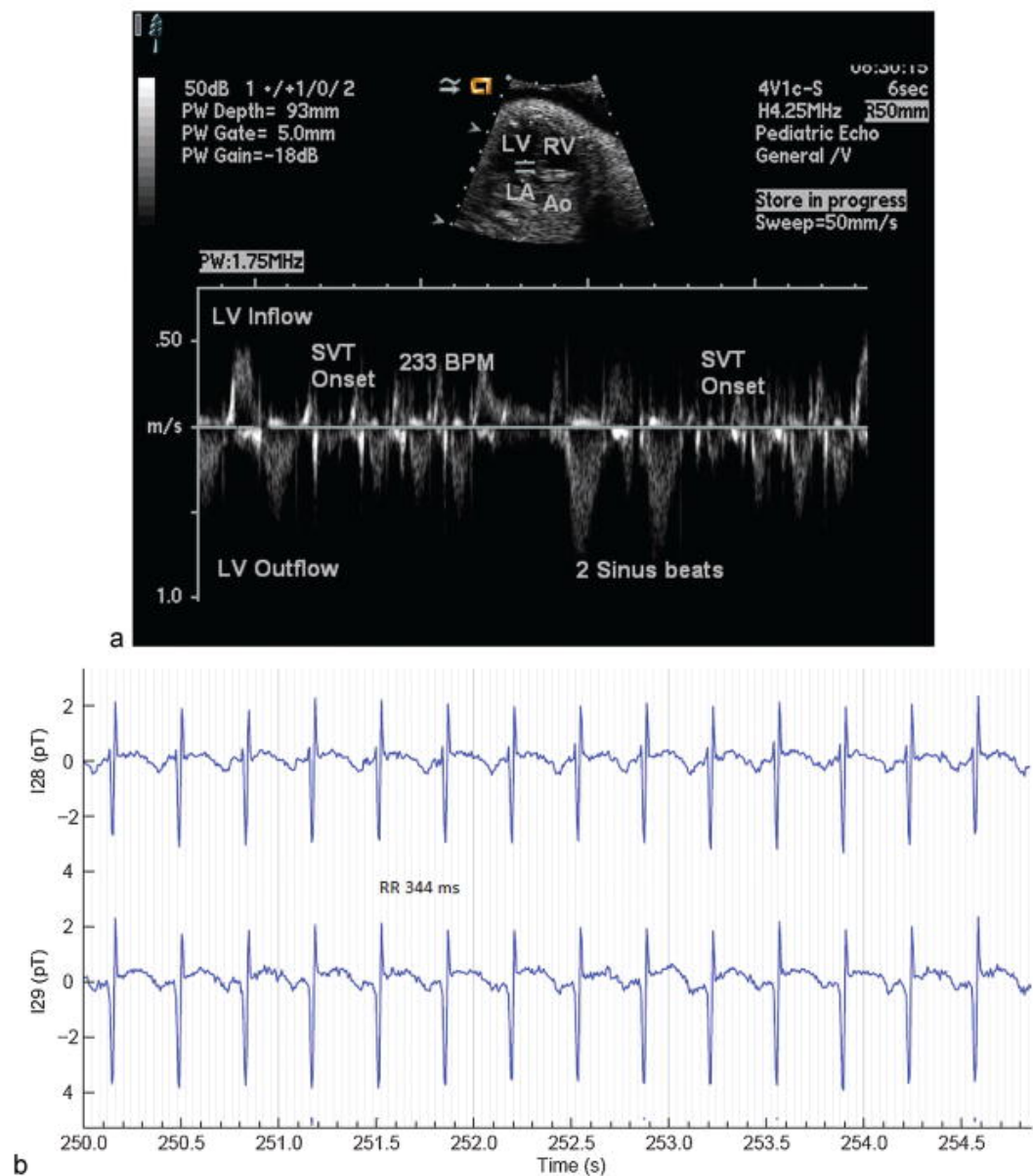


Fig. 9 – SVT measured (a) echocardiography and (b) by fMCG, fetal magnetocardiography. [8]

Supraventricular tachycardia generally occurs between the 24th and 32nd week of gestation.

The risk of complications, such as especially heart failure and hydrops, are closely related to the duration of the tachycardia.

5.2 ATRIAL FLUTTER

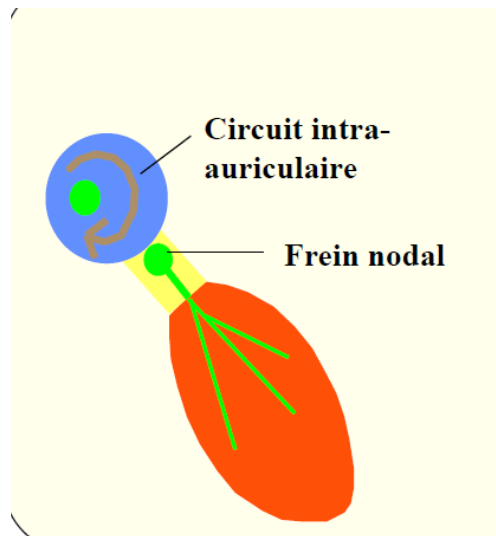


Fig. 10 – Atrial Flutter [9]

Atrial Flutter (AF) is caused by a circular macro-reentrant pathway within the atrial wall and the AV node is not a part of the reentry circuit. It occurs at a frequency of 25 – 30 % among all types of tachyarrhythmia. AF is observed only in the third trimester, which is probably related to the large atrial size achieved at 27 – 30 weeks of gestation, with high vulnerability to atrial extrasystoles. Atrial rates range between 300 and 550 bpm which is sufficiently fast so that 1:1 AV is not occurring, due to a physiological block at AV node. AF can be associated with myocarditis, SSA/SSB isoimmunization, and congenital heart diseases (CHDs). Ebstein's anomaly is a type of CHD in which atrial dilatation secondary to tricuspid regurgitation may cause AF.

AF can also alternate with periods of AVRT in the same fetus.

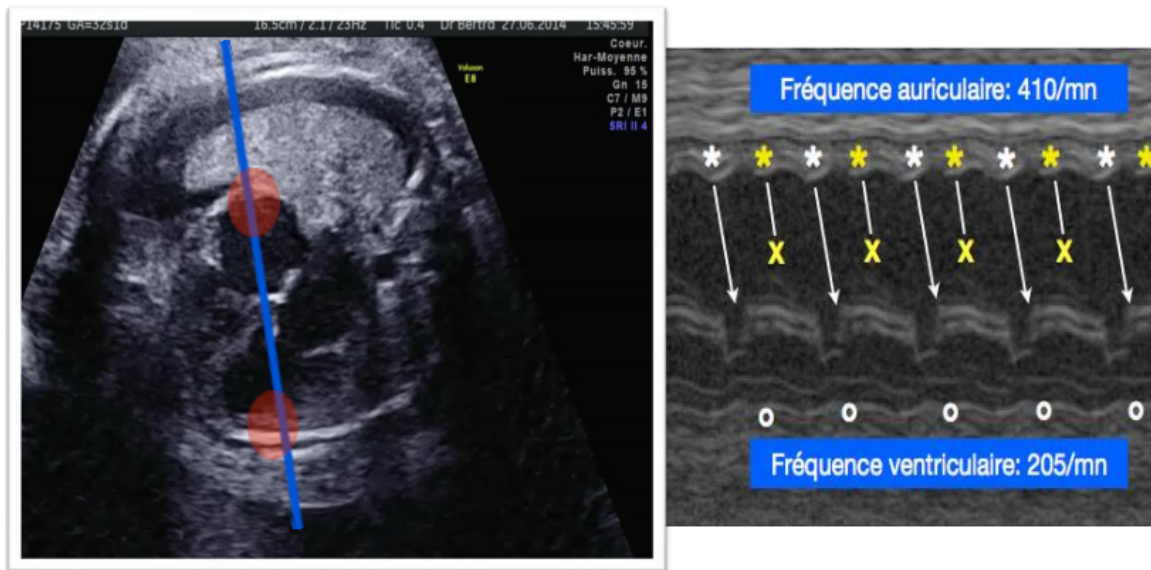


Fig. 11 – Atrial Flutter in M-mode [9]

Atrial Flutter are characterized by a:

- FHR > 400 bpm;
- Fixed ventricular FHR;
- AV block 2:1, 3:1 or higher;
- Majority through the accessory conduction pathways;
- 40% present hydrops.⁶

If flutter or AV Block is caused by an autoimmune disease, with positive anti-Ro antibodies, the use of steroids is necessary for the management of the underlying disease and, eventually, for the resolution of the arrhythmia.

5.3 SINUS TACHYCARDIA

Sinus tachycardia (ST) is characterized by fetal HR > 180 bpm but < 200 bpm with normal atrium-ventricular (AV) conduction, so there are similar atrial and ventricular rates with some variability. Sustained ST is usually related to fetal distress and pregnancy conditions such as thyrotoxicosis, anemia, fetal hypoxia, maternal medication (β -agonists), and infections such as chorioamniotitis and cytomegalovirus.

Generally, no specific antiarrhythmic therapy is indicated. Indeed, the underlying cause of ST should be identified and treated.⁵

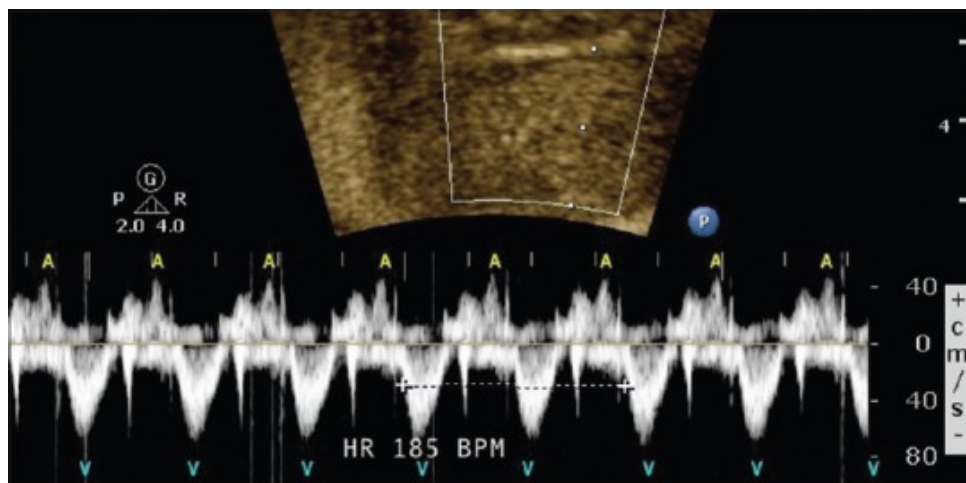


Fig. 12 – Sinus Tachycardia with 1:1 AV relationship at a rate of 185 bpm. [5]

5.4 VENTRICULAR TACHYCARDIA

VT is extremely rare during fetal life and is rarely detected in utero. In general, there is an AV dissociation relationship, with ventricular rates ranging from 180 to 300 bpm in excess of atrial rate. However, in a few cases of VT in which there is a retrograde 1:1 VA conduction, the ventricular and atrial rates are similar (1:1), making it almost impossible to differentiate these types of VT from SVT by fetal cardiac ultrasound. In VT, the Doppler wave velocities of the umbilical cord are low and the VA interval is shorter ($VA < AV$). The electrophysiological mechanism of this tachycardia is an ectopic ventricular focus due to inflammation (cardiomyopathy) or abnormalities of the myocardial oxygen supply. Myocardial hypoxia in fetuses is related to myocardial hypertrophy secondary to VA valves stenosis or from cardiac tumors such as hamartomas. Furthermore, VT is associated with long-QT syndrome, a genetic ion channel disease. This condition should be strongly suspected when the tachycardia occurs in combination with periods of bradycardia and AV heart block. However, the prenatal measurement of QT interval is only possible by fMCG.⁵

Intermittent fetal tachycardia with no heart defects usually do not need drug therapy, but require follow-up.

5.5 MANAGEMENT of TACHYARRHYTHMIAS

Fetal supraventricular tachyarrhythmia (SVA), including AF and SVT, are the leading cause of fetal heart failure, prematurity and perinatal death. Therefore a prompt diagnosis and treatment is required.

As already mentioned, management option upon a new diagnosis of fetal SVT include observation, drug therapy and postnatal cardioversion. Several factors influence the management and treatment:

- **Type of SVA**: SVT or AF;
- **Duration**: Perinatal mortality increases the longer the fetus remains in incessant tachyarrhythmias, reaching the rate of 35 % if hydrops is present;
- **Gestational Age**: for the advanced gestational ages (> 37 weeks) delivery is the preferred option, since the prematurity related risks are overcome;
- **Hydrops**: the presence of hydrops is associated to a higher perinatal morbidity and mortality and to a different choice of treatment due to a larger volume of distribution.
- **Maternal health**.

Not all tachycardias require treatment. If *intermittent* and with no hemodynamic compromise, treatment may be unnecessary. However, close FHR monitoring is needed to establish the frequency and duration of tachycardia. Inpatients are

submitted to multiple observation over 24 - 48h; while outpatients monitoring is carried out 1 - 3 times a week and intermittent scans.

If tachycardia is *incessant or hemodynamic compromise* is evident (hydrops, cardiomegaly, or AV valve regurgitation), treatment should not be delayed.

Prior to 37 weeks, transplacental pharmacological treatment to obtain a normal rhythm is the preferred option because the hazard associated with preterm delivery outweighs the risks of drug therapy. After 37+0/7 weeks, primary delivery by caesarean section is often elected. Cardioversion prior to birth will also facilitate vaginal delivery by allowing the interpretation of the fetal heart rate tracings during labor.

According to different type of SVA, the proarrhythmic properties and the risks of pharmacologic treatments available, it would be useful to address the woman to a series of clinical, laboratory and instrumental exams before starting treatment:

- whole blood count;
- electrolyte;
- creatinine and kidney function testing;
- liver function testing;
- thyroid-stimulating hormone (TSH);
- more specific exams to exclude or confirm underlying disease, such as:
anti-A and anti-B serum, HSV IgG e IgM, VZV IgG e IgM, Ab anti-

Borrelia, alpha-fetoprotein, ANA, ENA, Anti-DNA, Anti-SM, Anti SSA-SSB, Anticardiolipin, anti- β_2 -glycoprotein 1, Anti-TPO, Anti-TG;

- ECG;
- Echocardiography.

Then is necessary a thorough cardiac history and physical examination aimed at identifying any potential cardiac disease, but also investigate family history and execute genetic screening.

It is also important to check the patient is taking drugs that have QT lengthening as a side effect and therefore can predispose to the development of fetal arrhythmias, such as metoclopramide or chlorpromazine, that are commonly prescribed antiemetic medication.

To date, maternal transplacental of SVA is the option of choice. If it fails, direct administrations, such as intraumbilical, intraperitoneal, or intramuscular injection of antiarrhythmic agents can be considered as alternative approaches. Intraumbilical administration of antiarrhythmic agents can be performed under ultrasound guidance, but with somewhat technical difficulty, especially when the fetus is in an unfavorable position. This direct treatment is indicated in cases of tachyarrhythmia with hydrops fetalis as an adjunctive to the higher dose of transplacental therapy.⁴

Among the hemodynamic consequences, the most negative one that could be

encountered is fetal hydrops, a sign of cardiac failure, which is diagnosed when ≥ 2 abnormal fetal fluid collections, such as pericardial and pleural effusion, ascites, and skin edema, regardless of the amount of effusion present. The extent of the hydrops is defined by obstetric ultrasound.

Progression of hydrops can be rapid at earlier gestational age, at higher ventricular rates, and for incessant tachycardias. With complex and unusual types of tachycardia, defining the mechanism is important because it can impact the choice of therapy. Finally, there can be a poor response to transplacental treatment.

Precisely the possible adverse effects of these drugs on maternal cardiac activity require that patients begin inpatient therapy with checks of serum levels of drugs, every 3 - 5 days, and of the ECG, first once a day and then once a week, when the drug's effects and levels have stabilized. Subsequently, when the therapy is able to control the fetal arrhythmia, the signs of heart failure disappear and no abnormalities are observed in the maternal ECG, it can be decided to continue the therapy in the home setting, with periodic ultrasound, cardiotocographic (CTG) and electrocardiographs to be decided on the basis of what is detected in the individual tests, generally at least once a week.

Periodic fetal heart check with echocardiographic ultrasound is very important in the control of arrhythmia, to assess whether the activated treatment can manage the arrhythmia and avoid the appearance of pathological signs that may be caused

by arrhythmia.

The goal of treatment is to bring the heart rate back to a sinus value and obtain a good control of the arrhythmia in the shortest possible time, before heart failure and therefore hydrops appears.

The effectiveness of therapy is also associated with the time that elapses before treatment is started, because fetuses left in incessant tachycardia tend to develop hydrops.

Furthermore, therapy outcome also depends largely on the amount of drug that crosses the placenta, which is subject to the altered maternal pharmacokinetics and pharmacodynamics in pregnancy. Various physiologic changes during pregnancy influence maternal pharmacokinetics. In addition, the fetal plasma concentration is also influenced by changes in the fetus itself.⁷

Wacker-Gusmann et al.³ noticed that correction of underlying maternal electrolyte abnormality (Ca^{2+} , Mg^{2+} and K^{+}), as well as vitamin D deficit, can facilitate pharmacoreversion of tachycardia and maintenance of sinus rhythm.

Also, the choice of the appropriate drug and the route of administration to reach a rapid therapeutic level in the fetus and the early diagnosis of maternal and fetus complications determine the success of intrauterine antiarrhythmic treatment of the fetus.

So, fetal therapy is sometimes difficult and often unsuccessful.

To date, the effectiveness of transplacental treatment is observed in 70-80% of cases, but mortality is higher than 50% in fetuses in which tachyarrhythmias have already caused the development of hydrops.

Among the hemodynamic consequences, fetal hydrops is a consequence of heart failure, which is diagnosed when ≥ 2 abnormal fetal fluid collections, such as pericardial and pleural effusion, ascites, and skin edema, regardless of the amount of effusion present.

Progression to hydrops can be rapid at earlier gestational age, at higher ventricular rates, and for incessant tachycardias. With complex and unusual types of tachycardia, defining the mechanism is important because it can have an impact on the choice of therapy. Finally, there can be a poor response to transplacental treatment.

5.6 TREATMENT of TACHYARRHYTHMIAS

The rationale to offer transplacental therapy for fetal SVA is to achieve rapid and lasting cardioversion, to prevent or treat fetal heart failure, and to follow the pregnancy to continue to term with the delivery of a healthy child. Digoxin, Flecainide and Sotalol are the most commonly used. Digoxin is widely accepted as first-line antiarrhythmic drug for fetal SVA. However, it is less effective in

hydropic fetuses, compared to Sotalol and Flecainide. Amiodarone or direct fetal drug administration are mainly reserved for therapy-resistant SVA because of increased risks of maternal and fetal adverse events.¹⁰ Nevertheless, the choice of treatment is still a contentious. None of the drugs used has ever been evaluated for their effects on the mother and her child in a Randomized Clinical Trial (RCT). There is, however, considerable non-randomized experience in the transplacental treatment of fetal SVT with several antiarrhythmic agents, including Digoxin, Flecaïnide (class Ic), Sotalol and Amiodarone.

- **Digoxin** actions are given by the Na^+/K^+ ATPase pump block at the level of the cardiac striated muscle fiber cell and that improves the contractile activity of the myocardium. The increase of the force of contraction determines a reduction of the duration of the systole and increase of the maximum tension of the cardiac wall. Digoxin also has a parasympathomimetic effect, and it causes vagal stimulation; this involves negative chronotropic and dromotropic actions. Particularly marked is the lengthening of the refractory period of AV node and therefore it is used for the management of Supraventricular Tachyarrhythmias and Atrial Flutter.¹¹

This drug causes changes in cardiac action potential and ECG (“digitalis effects”), where PQ elongation, QT shortening, ST segment depression and

T wave inversion or biphasic T wave will be observed. These can occur as adverse effects in the mother: premature beats, atrial tachycardia, accelerated junctional rhythm/tachycardia, ventricular tachycardia, ventricular fibrillation, sinus bradycardia, AV block and sinus pause. Digoxin is contraindicated in selective atrioventricular nodal blocks that may facilitate 1:1 anterograde conduction via bypass tract given that, in the setting of rapid atrial arrhythmias, could result in ventricular fibrillation.¹²

Other side effects notified: nausea, anorexia, headache, visual disturbances, central nervous system (such as dizziness) and mental/cognitive disturbance.

Hypokalemia, hypercalcemia or hypomagnesemia may predispose patients to digoxin toxicity, so initial laboratory testing for electrolytes and renal function should be performed, and electrolyte abnormalities should be corrected.¹³

Digoxin therapy generally begins with an intravenous dose and then switch to oral administration.

Digoxin loading dose is 1 mg per 24 h intravenous in 2/3 divided dose to be infused in 1 hour; then the maintenance dose is 0.125 – 0.250 mg twice daily orally.

The therapeutic plasma concentration is between 0.50 – 2 ng/ml, beyond

which the possibility of side effects and toxicity increase ¹¹; so it is necessary to periodically re-check the serum levels of the drug to verify that are not higher than 2 ng/ml, if this occur it is necessary to remodel the therapy.

The time window of control of the serum levels varies according to the previously detected values, the pharmacological doses administered, the changes in maternal electrolytes and in the maternal ECG trace. The measurement of maternal serum levels of digoxin should be performed at least 6-8 hours after the last dose to allow adequate time for equilibration of digoxin between serum and tissue.

Although maternally administrated digoxin has been considered as the first-line agent for cardioversion of fetal SVT, digoxin is less effective in fetal SVT complicated by hydrops fetalis secondary to poor transplacental transfer. ¹³

In the absence of hydrops, oral digoxin is well absorbed and transferred to the fetus, to reach fetal serum concentration that are close to those in maternal serum within 3-5 days. ¹⁰

- **Flecainide** inhibits Na^+ channels, slowing conduction and increasing refractoriness of all cardiac tissues. This drug can also depress the automatism of the NSA and the conduction of the NAV or any accessory

pathways. On the ECG, flecainide markedly lengthens PS, widens the QRS and stretches QT.

Flecainide is used for the treatment of supraventricular tachyarrhythmias in the absence of structural and ischemic damage of the heart tissue; indeed “Cardiac Arrhythmia Suppression Trial” demonstrated that flecainide was associated with increased mortality and nonfatal cardiac arrest in patients with recent myocardial infarction.¹³

The therapeutic plasma concentration is between 0.20 – 0.70 mcg/ml, beyond which the possibility of side effects increases; at maternal serum concentration > 1 mcg/ml, increase the risk of toxicity that is suggested by an increase in QRS duration of 50% and prolongation in PR interval of 30%.^{11 - 14}

Infrequent maternal side effects include blurred vision, nausea, constipation, dizziness and headache.¹⁰ Maternal flecainide toxicity is managed with supportive care and aggressive intravenous bicarbonate administration

Peak plasma levels are reached after 2 – 3 hours and steady-state levels are achieved within three to five days, with a half-life ranging from 7 to 23 hours.¹⁵

Patient with impaired renal or hepatic function require dose monitoring and

dose reduction, because flecainide undergoes to hepatic oxidative metabolism and its metabolites are excreted mostly in the urine.¹⁶

For the management of fetal SVT, flecainide can be used alone or in combination with other drugs, such as digoxin; generally when used alone the oral dosage is up to 100 mg two/three time a day, while if used in combination the dosage is often 100 mg per day, i.e. 50 mg every 12 hours. In the different studies observed, Flecainide has excellent bioavailability in hydropic fetuses and thus achieve a higher rate of arrhythmia control. Which, in some cases, results in hydrops resolution and less mortality.

- **Sotalol** is both an I_{Kr} channel and β -blocker, with β -blockade as the main effect. The combined effects decrease heart rate, and prolong action potential duration and tissue refractoriness throughout the heart. Possible maternal ECG changes upon sotalol initiation include P and QRS widening, first-degree atrioventricular block, and a lengthening of the entire QT interval.¹³ The toxicity of the drug is related to its actions of elongation of the action potential resulting in possible maternal new bundle branch block or bradycardia.

Some experts may recommend mandatory inpatient monitoring with continuous ECG for up to three days.¹⁷

Moreover, this drugs is excreted predominantly by the kidneys and so

caution should be taken in patients with renal impairment.

This drug is contraindicated in or must be used with extreme caution in patients with maternal history of asthma, decompensated heart failure, maternal prolonged QT interval and maternal bradycardia.^{13 - 17}

There did not seem to be a correlation between sotalol blood concentrations and the occurrence of conversion to sinus rhythm. The levels at which the drug proved to be effective were only slightly higher than those that did not result in conversion, indicating a large difference in sensitivity to the drug. The suggested Sotalol dose for treatment of fetal SVT ranges from 80 to 160 mg twice daily. To minimize the possible risk of maternal adverse events and/or intrauterine death, a dosage scheme with an initiation dose of 80 mg of Sotalol two/three times daily, a stepwise increase by 80 mg every three days, and a maximum daily dose of 480 mg given in three divided doses has been suggested.

The therapeutic plasma concentration is between 0.60 – 2.5 mg/L, beyond which the possibility of side effects increases, such as marked prolongation of the corrected QT interval.¹⁷

Sotalol is well absorbed and transferred to reach a fetal steady state level like maternal plasma level.

Evaluating several studies, it can be stated that Sotalol seems to be more

efficacious than other drugs in fetal Atrial Flutter, but it is often used as a second-line treatment in combination with digoxin or flecainide for the management of persistent supraventricular tachycardias unresponsive to first-line therapy.

- **Amiodarone** exerts multiple effects on ion channels in the various cardiac districts; the most significant is the I_{Kr} block with consequent lengthening of the duration of the action potential. Moreover, is able to determine a blockage of the Na^+ and Ca^+ channels. Exactly this last effect combined with the non-competitive β -blocking activity, could explain the slowing of heart rate and conduction through NAV.

On ECG, Amiodarone causes prolongation of PR, QRS and QT.

This drug has a relatively low bioavailability with slow absorption. Its half-life is extremely prolonged (30 - 60 days), so that the steady state is reached only after a few weeks or months of treatment, making dosage adjustments complex if necessary. Therapeutic monitoring is of little help due to difficulties in establishing correlations between plasma concentrations and therapeutic effects.¹¹

Cardiovascular signs of amiodarone toxicity include sinus bradycardia, intraventricular conduction defects, and high-grade heart blocks. Moreover, Amiodarone prolongs the QT interval and can cause prominent

U waves and biphasic T waves. It has also been associated with torsades de pointes, especially in the setting of hypokalemia.

Another serious adverse effect includes amiodarone pulmonary toxicity, manifested as pneumonitis with symptoms of nonproductive cough, dyspnea, weight loss, and fever with associated finding of diffuse interstitial infiltrates on chest radiograph.

Iodine content and its structural similarity to thyroxine, amiodarone can lead both to hyperthyroidism and hypothyroidism. Other less common side effects include neurologic (tremor, ataxia, and peripheral neuropathy) and gastrointestinal (nausea, constipation, anorexia, cholestasis, and hepatitis) complications.

Prior to initiation of amiodarone, a baseline assessment that includes an ECG, a chest radiograph, thyroid and liver laboratory studies, and pulmonary function tests could be considered. Heart rate, thyroid studies, and liver transaminase levels should be observed at time of amiodarone loading.¹¹⁻¹³

Maternal administration of Amiodarone, a class III antiarrhythmic agent, has been shown to be an effective treatment for fetal SVT in the setting of hydrops fetalis or ventricular dysfunction.

Given that maternal administration of Amiodarone has been associated with

transient neonatal hypothyroidism in up to 17% of exposed fetuses, and mild neurological abnormalities, its use is thus usually reserved for treatment of severe, refractory, maternal, or fetal arrhythmia.

If Amiodarone is chosen as treatment modality, maternal electrolytes and ECG could be monitored daily during loading and serially during maintenance therapy.¹³

Orally administered amiodarone seems to be safe and effective treatment for drug-refractory fetal tachycardia, specifically reentrant supraventricular tachycardia, junctional ectopic, or ventricular tachycardia, even when accompanied by hydrops fetalis or ventricular dysfunction.

In the study of Strasburger and al. amiodarone has been shown to be useful in the treatment of fetal SVT when there is failure of flecainide and sotalol therapy.¹⁸

The suggested Amiodarone dose for treatment of fetal SVT ranges 1660 - 2400 mg/day two to four times daily usually halved every 24 hours, maintenance dose 200 – 400 mg/day twice daily.^{13 - 19}

Amiodarone can be used as a first or second-line treatment alone or in combination with other drugs, especially digoxin, for all fetuses, whether they have hydropic or not.¹⁹

This drug is poorly effective in terminating atrial flutter.

However, virtually all antiarrhythmic agents may have potential to provoke or to exacerbate existing arrhythmias. This risk increases with toxic drug levels, maternal heart disease, ventricular arrhythmia and hypokalemia.

Digoxin, Flecainide and Sotalol can be the first-line treatments of most common fetal tachyarrhythmias: Tachycardia Supraventricular, Atrial Flutter and Tachycardia Ventricular. Amiodarone and combined therapies are reserved for refractory fetal tachycardia.

Maternal administration of digoxin has traditionally been the treatment of choice in the earlier years of fetal SVT therapy, but because questions have since been raised about the effectiveness of this drug, especially in hydropic fetuses, a variety of newer drugs and other methods have been applied to treat fetal tachycardia. Digoxin is praised for its safety and efficacy, but maternal higher doses are required to maintain a therapeutic serum level especially in the presence of hydrops fetalis.

Multiple studies point out that digoxin has positive inotropic and negative chronotropic properties, and is more effective for non-hydropic fetuses with SVT, because in presence of fetal hydrops, maternal-fetal digoxin transfer is poor and effective fetal drug levels may not even be obtained at near-toxic maternal

levels.⁴⁻⁶⁻²⁰⁻²⁻²²

Digoxin monotherapy showed a lower effective rate than combined digoxin and flecainide/sotalol for the treatment of fetal tachycardias.

Flecainide is an effective first-line treatment for fetal SVT with a high successful rate of 88,2%, low side effect and relatively easy utilization.²³

Flecainide is highly effective in achieving sinus rhythm in hydropic and nonhydropic fetuses with SVT, refractory SVT or SVT with signs of heart failure. Oral flecainide (100mg three time daily) is reserved for those cases unresponsive to sotalol and digoxin.²⁴

Flecainide was preferred in converting SVT to normal sinus rhythm or in slowing AF to well-tolled ventricular rates.²⁵ The conversion rate to sinus rhythm of flecainide for short VA SVT was higher than digoxin (96% versus 69%). For long VA SVT, the conversion rate to sinus rhythm did not differ significantly between the two drugs.

In nonhydropic fetuses, the successful rate of flecainide was higher than digoxin and a same trend was observed in hydropic fetuses, while the successful of combined flecainide with amiodarone was 100%; but, in choosing this therapeutic line, it is always necessary to consider the side effects of amiodarone.

The intrauterine or neonatal mortality rate in hydropic fetuses treated with flecainide was much lower than that treated with digoxin.⁴

For hydropic fetuses, flecainide or amiodarone as first-line therapy is effective for converting SVT to sinus rhythm. Amiodarone alone or combined with digoxin as second-line therapy obtained an effective rate of 50% in converting to sinus rhythm.

Surely, we can assert that Flecainide is more effective than digoxin, especially when hydrops is present: when hydrops is present, the bioavailability of digoxin decreases, leading to lower blood concentration this drug compared with nonhydropic fetuses.^{20 - 21}

Amiodarone was successful in reverting SVT in patients who were not responding to flecainide treatment as well.²⁶

So, for hydropic fetuses, the sequence of the drug effects is flecainide with amiodarone (100%) > flecainide alone (86%) > digoxin (38%).²⁰

As previously mentioned, it is very important to achieve good control of the heart rate and the disappearance of the hydrops in the shortest possible time. This goal changes according to the treatment chosen and the condition of the fetus at the time therapy is started.

Even today, the first-line therapy in fetal tachyarrhythmias, without hydrops, involves the use of digoxin, which must lead to cardioversion and return to sinus rhythm within 3 days of starting treatment, if this does not occur it is necessary to

pass to a second-line treatment by adding the administration of flecainide.

The median time to obtain conversion to Sinus Rhythm with only digoxin is 3 – 5 days in a range of 1 – 21 days.

The median time to conversion to Sinus Rhythm is 11.5 days (range 3 – 14 days) with a combination therapy of flecainide and digoxin, while the median time to heart conversion is 3 days (range 1 – 7 days) with flecainide monotherapy.⁴⁻²⁷⁻²⁸

All the therapy will be judged ineffective if the fetal arrhythmia does not disappear or improve 3 or more days after the start of the highest sotalol dose.

If therapy starts only with digoxin, a median time conversion to SR is 5 days; if it uses only flecainide, time conversion is 3 days; while, with sotalol time conversion is 12 days.

Certainly, evaluating various studies it can be stated that the conversion time to a sinus rhythm also depends on the presence and extent of the hydrops: using a therapy with digoxin and flecainide we realize that this conversion time increases as the presence increases of the hydrops.

Instead, if therapy starts with digoxin and then flecainide is added, the resolution of fetal hydrops is observed after a median of 11 days (range 3 – 32 days) after conversion to sinus rhythm and 19 days (range 11 – 39 days) after initiation of flecainide therapy.⁴⁻²⁸

The time to conversion to sinus rhythm for Sotalol varied from 1 to 35 days.⁴

In some cases, SVT episodes may recur during treatment which are usually managed with immediate administration of 50 mg of Flecainide to try to return to a fetal sinus rhythm.

Sotalol was earlier thought to be drug of choice for fetal SVT because it is efficient in treating arrhythmia in infants, but in some studies, have been reported fetal deaths caused by this drug and this suggest a proarrhythmic effect of this drug. Therefore, Sotalol is now being used as a first-line and second-line therapy with digoxin for the treatment of Short VA SVT or AF respectively in hydropic and nonhydropic fetuses, then it is used alone as first-line therapy of Long AV SVT.⁴ Surely, Sotalol is more effective for prenatal AF termination than digoxin or flecainide, whereas flecainide and digoxin were superior to sotalol in converting SVT to a normal rhythm and in slowing both AF and SVT rates.

For AF persisting for 5 days, flecainide use achieved a much better heart rate control than sotalol. With combined flecainide and digoxin therapy, conversion to sinus rhythm occurred within 5 days (range 0–14 days).⁴

Refractory AF in fetuses with hydrops fetalis may show response to intramuscular injection of digoxin and/or amiodarone by restoring sinus rhythm and by improving hemodynamic status.²⁹

Our experience concerns 2 cases of TSV both with marked hydrops, characterized by the presence of pleural and pericardial effusions, ascites and subcutaneous edema.

In the first patient, whose TSV (HR of 270-290 bpm) was diagnosed at 30 + 6 GW in association with the transposition of the great vessels of the heart to an intact septum, management was performed immediately with:

- Digoxin: 0.250 mg and 0.125 mg per daily;
- Flecainide: 100 mg per daily (50 mg x 2).

Drug dosages were changed multiple times to achieve good heart rate control and stay within the therapeutic range of serum pharmacological levels, also because the patient developed minimal electrocardiographic alterations definable “digitalis effects” which required a control and evaluation of the maternal ECG, first daily and then every two days.

With this combined therapy control of tachycardia was achieved within 3 days of starting treatment while complete disappearance of the anasarca was achieved in approximately 5 weeks.

However, several episodes of supraventricular tachycardia with HR of 230-250 bpm occurred during management, immediately controlled with the administration of 50 mg of flecainide and conversion to sinus rhythm.

In the second patient, the diagnosis of TSV was made at 21 + 6 GW and was

initially managed with digoxin alone (0.250 mg twice daily).

After 6 days of treatment, however, it was also necessary to add sotalol because the fetus had a refractory TSV with HR of 240 bpm. The dose of sotalol used was 200mg divided into 3 daily administrations.

After the addition of sotalol, cardioversion was achieved in 48 hours with subsequent good control of HR; while the complete disappearance of the effusions and subcutaneous edema took about 5 weeks.

In both cases the fetal outcome was good even if after birth the newborn of the first case was subjected to multiple cardiac surgery to correct the transposition of the great vessels.

Our experience underlines even more how in the presence of hydrops, cardioversion of TSV and reabsorption of anasarca are obtained more quickly by immediately starting the combined administration of 2 drugs, such as digoxin and flecainide or digoxin and sotalol.

Both patients underwent all the clinical, laboratory and instrumental tests described previously with therapy started in the hospitalization regime followed by the specific follow-up.

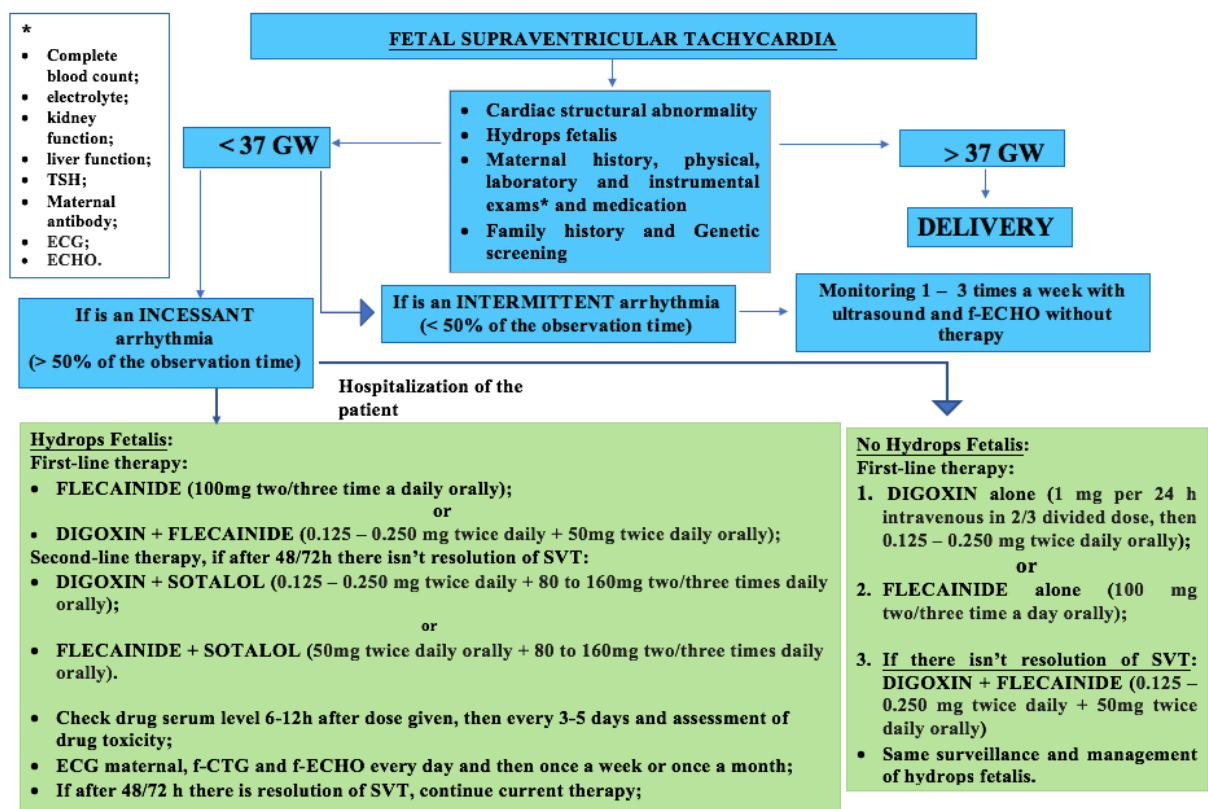


Fig. 13 – Management Supraventricular Tachycardia

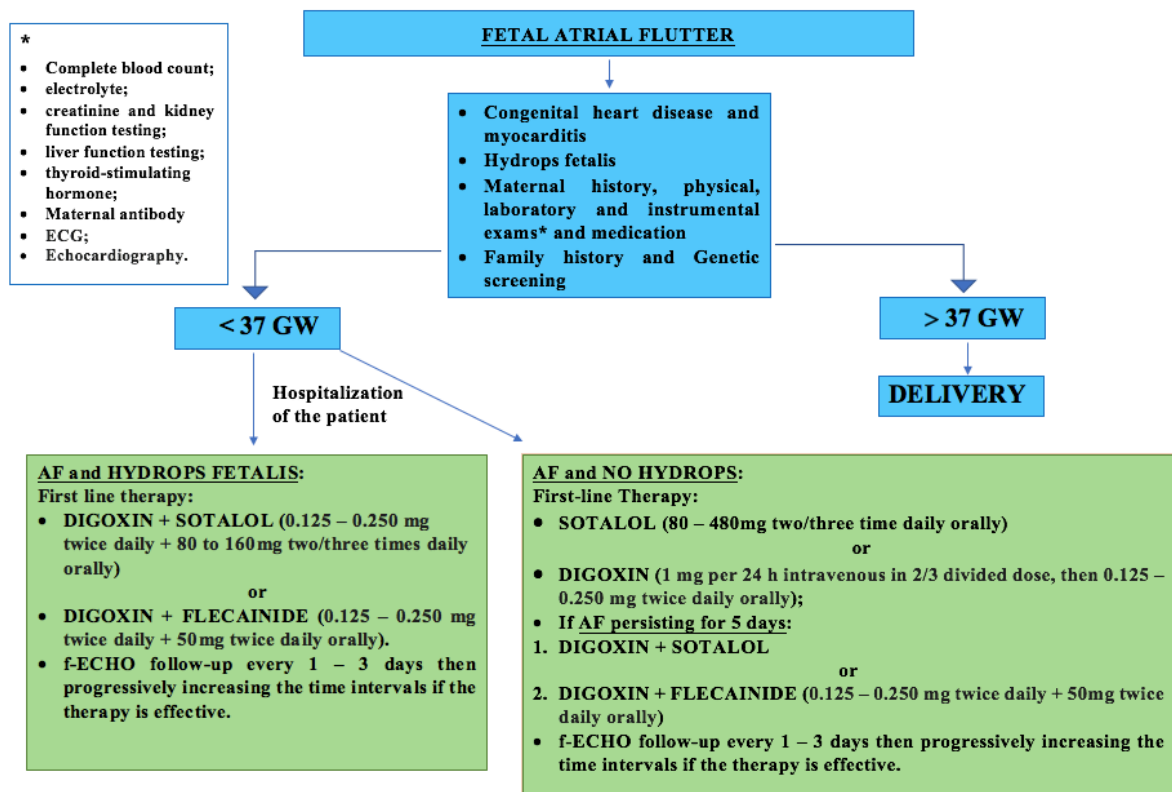


Fig. 14 – Management Atrial Flutter

6. BRADYARRHYTHMIA

The standard obstetric definition of fetal bradycardia has been a sustained FHR < 110 bpm over at least a 10 minutes period.³

Brief episodes of sinus bradycardia that last less than 1-2 min are frequent and benign findings, particularly during the first and second trimesters.

These are transient fetal decelerations due to vagal stimulation by cord compression, that resolve rapidly with less pressure in maternal abdomen. No treatment is required. Less common, are persistent bradycardia, that even if intermittent, requires prompt diagnosis and management to preserve fetal well-being.

A prolonged or persistent decrease in heart rate < 100 bpm may be observed during symptomatic sinus bradycardia, atrial bigeminy with blocked premature beats, and high degree AV block. As the ventricular rate may be comparable among these rhythm anomalies, ultrasound imaging is used for their diagnostic-differentiation.²⁵

Persistent fetal bradycardia is relatively rare. The basic mechanisms include congenital displaced atrial activation, acquired damage of the SA node, ion channel dysfunction, and secondary suppression of the SN rate. SN rates can be suppressed due to atrial isomerism, inflammation and fibrosis in a normal SN, viral myocarditis or collagen vascular disorders (SSA/Ro and/or SSB/La

antibodies), maternal treatment with beta-blockers, sedatives, or other medications, rare metabolic disorders (e.g. Pompe disease), or sinus bradycardia due to idiopathic origin, neck stretch, or other autonomic causes.⁴

6.1 BRADYCARDIA WITH 1:1 AV CONDUCTION – SINUS BRADYCARDIA, SINUS NODE DYSFUNCTION AND LOW-ATRIAL BRADYCARDIA

The most common cause of persistent bradycardia with 1:1 AV conduction is sinus bradycardia. Only occasionally may indicate low atrial rhythm, which is characteristic of left atrial isomerism.

Sinus bradycardia is characterized by a heart rate between 90 and 130 bpm or less. Transient sinus bradycardia is often seen during echocardiographic examination due to compression of the fetal umbilical cord. Causes of prolonged sinus bradycardia include fetal distress secondary to fetal hypoxia and acidosis, 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. Runs of ventricular tachycardia and 2 : 1 AV block are additional findings that suggest fetal long QT syndrome.²⁰

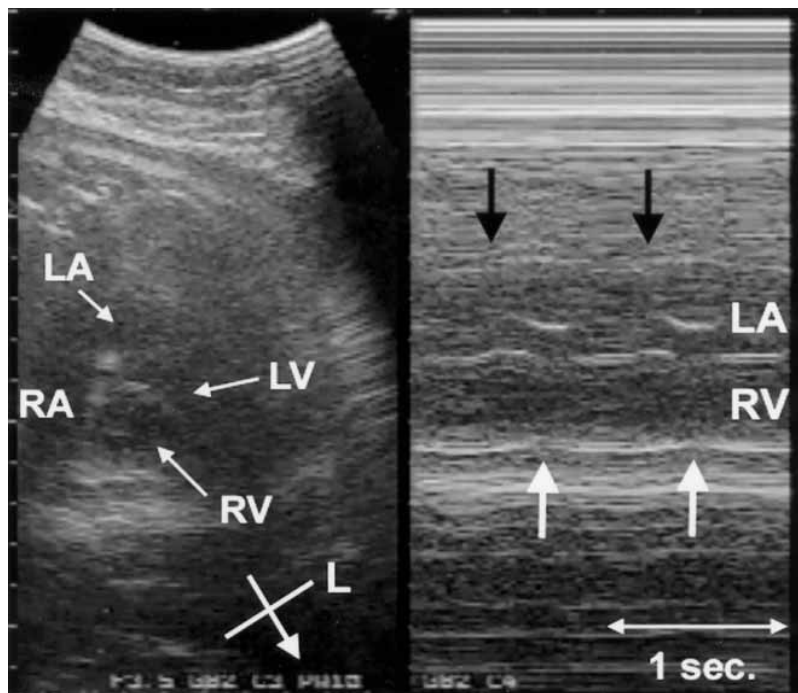


Figura 15 – Fetal Echocardiogram and M-mode echocardiography revealed 1:1 atrioventricular conduction with a slow ventricular contraction rate of about 70 bpm. [30]

Fetal bradycardia with 1:1 atrioventricular conduction seems to have a good prenatal and postnatal prognosis when the cardiac structure is normal. This bradycardia may have several advantages compared with bradycardia with heart block. One to one synchronized atrioventricular contraction has a clear hemodynamic advantage over non-synchronized contraction with heart block.³⁰

In *low-atrial bradycardia*, short PR interval is present in the ECG. Low-atrial mechanisms are seen in left atrial isomerism due to the absence of the SN.

Fetal sinus and low-atrial bradycardias usually demonstrate HR reactivity even in the presence of serious underlying conditions; however, this reactivity may be blunted due to a reduction in the autonomic influences.⁷

Anyway, low atrial bradycardia does not cause hemodynamic compromise and does not need treatment.

6.1.1 MANAGEMENT

Neither sinus nor low-atrial bradycardia requires specific treatment and are not generally associated with hemodynamic compromise at the time of birth; however, since 40% of fetuses with sinus bradycardia have associated long-QT syndrome, neonatal ECG screening is recommended considering this condition's inherent autosomal-dominant transmission.⁵

Before birth, monitoring fetal well-being at 4 - 6 weeks is advisable. Since perinatal outcome depends on etiology, 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. 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.

6.2 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 to regular bradycardia, FHR $\sim 70 - 80$ bpm and it may be confused with second- or third-degree AV block. Because both are characterized by higher atrial than ventricular rates. This differentiation is essential as bradycardia secondary to blocked premature beats resolves spontaneously without treatment, while complete AV block (CAVB) is an irreversible and potentially life-threatening disorder. Timing of atrial (A) contractions is essential in the differential diagnosis. In AV block, however, the time interval between consecutive atrial impulses hardly varies while every second event occurs prematurely in atrial bigeminy and trigeminy.

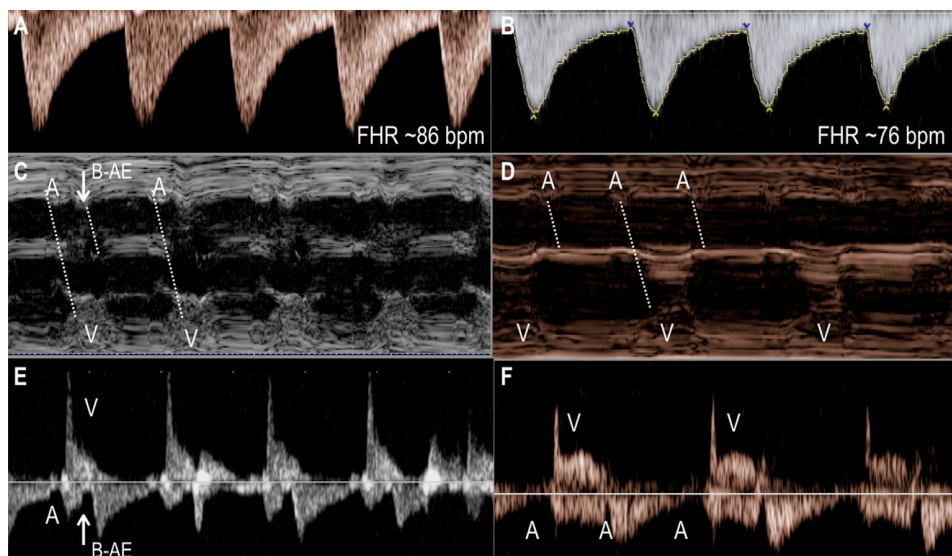


Fig. 16 - Different dysrhythmias causing regular bradycardia at a similar rate and arterial Doppler [A,B], depicted on M-mode [C,D], and pulmonary vessel Doppler [E,F].

*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 $\frac{1}{4}$ atrial/ventricular systole; (B-AE) $\frac{1}{4}$ blocked atrial ectopics; FHR $\frac{1}{4}$ fetal heart rate, bpm $\frac{1}{4}$ beats per minute. [2]

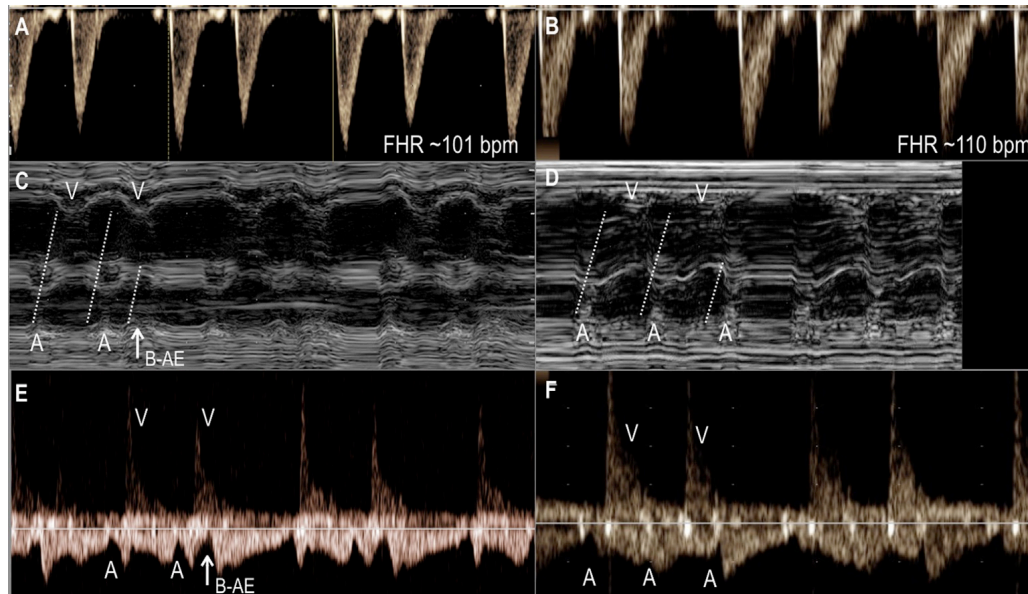


Fig. 17 - Different dysrhythmias causing irregular bradycardia at a similar rate and arterial Doppler [A,B], depicted on M-mode [C,D], and pulmonary vessel Doppler [E,F]. Images [A,C,E] show blocked atrial trigeminy. Note the irregular atrial activity: two beats are conducted, but the early ectopic signal 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 $\frac{1}{4}$ atrial/ventricular systole; (B-AE) $\frac{1}{4}$ blocked atrial ectopics; FHR $\frac{1}{4}$ fetal heart rate, bpm $\frac{1}{4}$ beats per minute. [2]

6.2.1 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. In one study, all cases of blocked bigeminy resolved spontaneously², whereas others report tachycardia in 14% of cases. 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.

6.3 FETAL ATRIOVENTRICULAR BLOCK

Atrioventricular Block (AVB) refers to prolongation or blockage of AV conduction of a normal sinus beat thorough the AV node.

Atrioventricular block (AVB) refers to prolongation or blockage of AV conduction of a normal sinus beat through the AV node.

There are three grades of heart block:

- First-degree AVB: is characterized by a prolonged AV conduction time but all impulses are conducted. It simply reflects a delay of conduction.

AV intervals increase with gestation and decrease with increased HR.

First degree atrioventricular block, however, is not always seen before onset of second-degree or third-degree atrioventricular block.

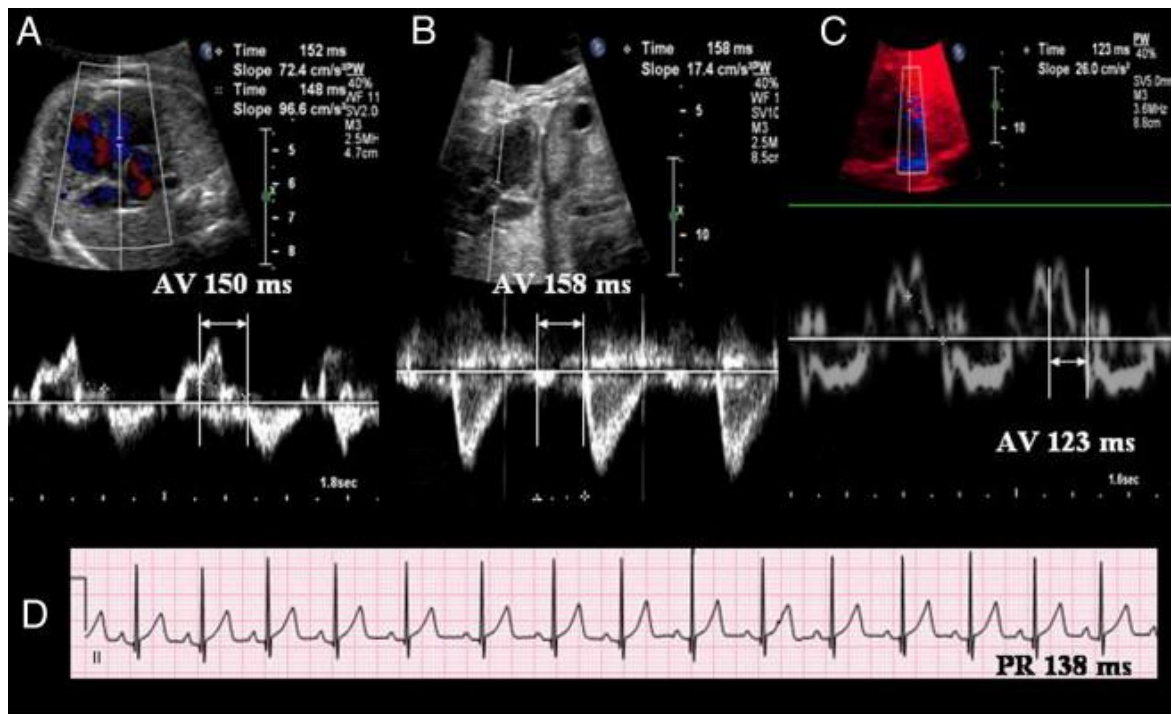


Fig. 18 – BAV I degree. [36]

- Second-degree AVB (incomplete): is extremely rare. It is a failure to conduct some atrial impulses to the ventricles.

Two subtypes are distinguished:

- *Type I (Mobitz I or Wenkebach phenomenon)* there is a progressive lengthening of AV conduction until an isolated impulse is blocked. The rhythm is irregular but FHR is usually normal.
- *Type II (or Mobitz II)* is characterized by a sudden block of an isolated impulse without prior lengthening of the AV conduction time. 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.

- Third-degree AVB (complete block - CAVB): is a condition where there is no AV conduction, and the atria and ventricles beat independently. It accounts for nearly 40% of major fetal arrhythmias referred to the authors' institution. Significant bradycardia is only seen with high second- or third-degree AV block. A HR < 60 bpm is strongly indicative of CAVB; patients with BAB have a HR of 65 – 90 bpm which is frequently intermittent, and 2:1 AVB results in a HR of 60 – 75 bpm. The fetal heart compensates to the evolving heart block by increasing its stroke volume. If the heart fails to adapt, fetal hydrops develops with a high risk of fetal or neonatal death. Of the survivors, most required pacemaker implantation during the first year of life.

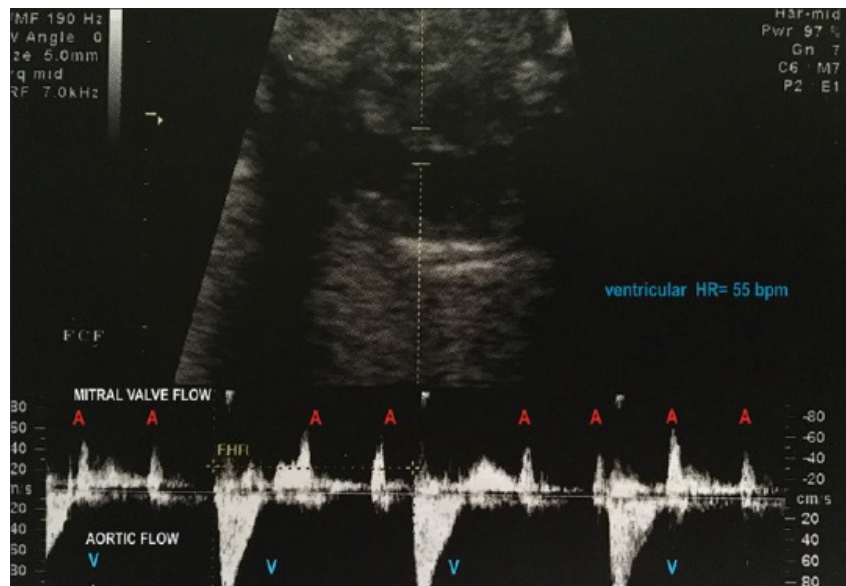


Fig. 19 - Complete Atrioventricular block in a hydroptic fetus with 55 ventricular heart rate and 121 atrial heart rate. [5]

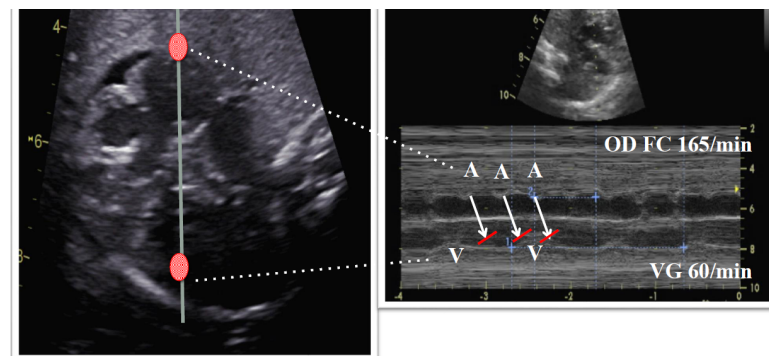


Fig. 20 – Complete Atrioventricular block with atrio-ventricular dissociation. [9]

Congenital AV block occurs in 1 in 15,000 to 1 in 20,000 live births.

Etiology may be autoimmune, linked to Congenital Heart Disease (CHD), or unknown.

Approximately half of all AVB cases are caused by associated CHD, and the remaining cases are often immune-induced arrhythmias and undetermined etiology.

The main forms of structural heart disease associated with AV Block are: Transposition of the great vessels (TGA), left isomerism and complete atrioventricular canal (AVC). The prognosis is generally poor with a combined fetal and neonatal mortality > 80%, especially when it is a complete - block. In one series, 60% were liveborn and neonatal mortality approached 80% (left isomerism 90%; AV discordance 25%).

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). Regression of nonimmune II-AVB has also been reported, although some may represent spontaneous resolution of ectopic-related bradycardia.²

The majority of AVB in structurally normal hearts is secondary to immune-mediated etiology. This type of block is named *Isoimmune atrioventricular block*.

The main autoantibodies responsible of AVB are: antinuclear antibodies, Anti-DNA, Anti-Ro (SSA), Anti-La (SSB), Anticentromer antibodies, anticardiolipids antibodies, Anti-RNA and Lupus Anticoagulant. Those produced against the 48 kDa SSB/La peptide and 52 kDa and 60 kDa SSA/Ro peptides seem to be the most damaging to the fetal and neonatal conduction system. Transplacental transfer of maternal autoantibodies, anti-Ro (SS-A) and/or anti-La (SS-B), 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. The evidence is emerging that, in addition to conduction disease, 10 - 15% of the affected offspring will have a life-threatening cardiomyopathy.

Immune-mediated AV block typically develops after 16 - 18 weeks of gestation, peaks at 20 - 24, and most (82%) occur before 30 weeks. The prognosis in AV block is better than that in CHD cases, but fetal demise is still ~ 6 - 10%.

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%), but recurrence risk is considerably higher (16-19%) and may be related to antibody levels.

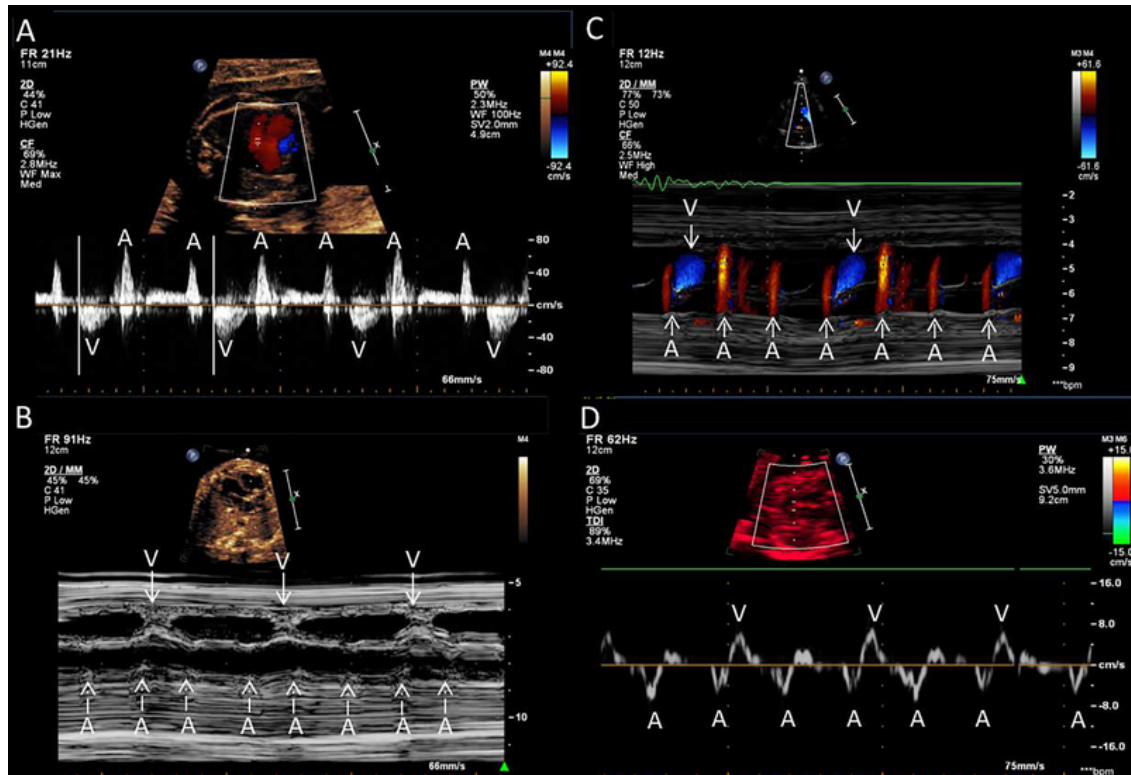


Fig. 21 – Prenatal evaluation for Complete Atrioventricular Block. A: Pulsed Wave Doppler. B: M-mode. C: Color Doppler M-mode. D: Doppler Imaging. [37]

6.3.1 MANAGEMENT

Management option upon a new diagnosis of fetal AV Block include observation, drug therapy and postnatal pacemaker implantation.

Care decisions are largely influenced by heart function, atrial and ventricular rate, AV Block characteristics, gestational age, fetal-maternal health, presence of maternal antibodies, presence or not of hydrops and willingness of the mother to undergo treatment.

It is necessary to study the family history and perform genetic screening.

Very important is to exclude and possibly treat maternal serum levels of electrolytes disorders, Vit D deficiency, hypomagnesemia, hypocalcemia or hypokalemia. It is also important to know if woman takes any medications that lengthen QT interval (ondansetrone, Pitocin, azithromycin, antidepressants, etc.).

Of course, it is necessary to investigate and research if there is an immune cause at the base of the blockade.

The management require weekly fetal echocardiograms with M-mode technique, tissue Doppler and pulsed wave Doppler.

Surely important is that antibody-exposed fetuses should undergo weekly echocardiograms between 16 and 24 weeks of gestation to assess AV chronology and control fetal condition.

Generally, first degree AV Blocks are not subjected to treatment, but are checked with a stringent echocardiographic follow-up to verify its evolution; surely require steroids therapy the second and third degree AV Blocks.

In all the different forms of AVB an echocardiography must be performed every 1 – 3 days and then progressively the control interval is increased if there is an improvement or disappearance of the arrhythmia.

6.3.2 TREATMENT

The treatment of fetal block involves close observation for signs of fetal compromise or distress. Decision on early delivery should be based on a risk-benefit analysis for both mother and fetus. In general, delivery is recommended for near-term fetuses.

The management of fetal block has undergone several advances.

Studies have been published on the use of therapies to prevent development of AV block in high risk pregnancies.

Among the therapeutic possibilities, there are: hydroxychloroquine, Intravenous immunoglobulin and plasmapheresis.

Hydroxychloroquine (Plaquenil) is an immune modulator with anti-inflammatory effects (antimalarial agent); Plaquenil is generally used to treat systemic lupus erythematosus and it inhibits several TLR pathways suggested to be important in the macrophage induced fibrosis and inflammation seen in immune mediated Congenital Complete Heart Block. A retrospective, case controlled study demonstrated a trend towards a lower incidence of rhythm or functional cardiac complications in fetuses exposed to hydroxychloroquine compared to those who were not.¹ Studies are still underway to evaluate the real efficacy of a preventive therapy with hydroxychloroquine and to define more appropriate pharmacological management. In summary, there is insufficient robust evidence

to suggest that prophylactic maternal therapy alters the incidence or recurrence rate of congenital complete AV block in the high risk population. Furthermore, despite an increased incidence of complete AV block in asymptomatic women, until more robust scientific evidence is available, most clinicians will continue to refer women with positive antibody to fetal cardiology surveillance during the second trimester to monitor for the development and progression of AV block.³⁵

Beta-adrenergic drugs, steroids and immunoglobulin are reported to be effective transplacental treatments for fetal AVB (given orally or intravenously to the mother) of fetal therapies (umbilical cord).

β -agonists, such as terbutaline, salbutamol and isoprenaline, are used to increase low fetal ventricular rates and to improve myocardial contractility, independently of the immune-mediated or structural complete heart block. β -agonists are typically used when heart rate is $< 50 - 55$ bpm.

Orally administered Salbutamol typically increases fetal HR by $5 - 10$ bpm.

The suggested Salbutamol dose for treatment of fetal AV Block is 10 mg three times a day orally. However, this therapy is often poorly tolerated by the mother due to the appearance of acceleration of heartbeat associated with the physiological tachycardia of pregnancy.

In utero, Terbutaline is normally well tolerated but maternal resting heart rates around 100 to 120 bpm and benign maternal ectopy have commonly found. Other

side effects are palpitations and tremor. Unfortunately, although terbutaline may increase fetal rates and prolong pregnancy, no studies have shown a survival benefit.

Moreover, fetal pacing has not been shown to be successful in improving survival or prolonging gestation; therefore, at present this treatment is experimental and not recommended as part of standard care.⁵

In the presence of isolated fetal myocardial-endocardial fibroelastosis (EFE), maternal intravenous immunoglobulin is administered at two to three weekly intervals prenatally.¹

Immune-mediated AV block may benefit from in utero treatment with fluorinated steroids (dexamethasone, prednisolone, betamethasone), or intravenous immunoglobulin.

Dexamethasone is believed to reduce fetal bradycardia related to maternal autoimmune disease. Dexamethasone is the steroid of choice because it is not metabolized by the placenta in vivo and is available to the fetus in the active form. Transplacental treatment with high-dose Dexamethasone is attempted has successfully reversed the fetal complete AV block into first degree.²⁰

The suggested Dexamethasone dose is 4 – 8 mg daily by intramuscular way. Benefits of this drug include reduction of inflammation, reversal or stabilization of incomplete block and improvement or resolution of hydrops or endocardial

fibroelastosis. Important complications of dexamethasone that have been reported include growth restriction, oligohydramnios, ductal constriction, maternal diabetes mellitus and central nervous system side effects. In case of steroid-induced oligohydramnios, the amniotic fluid volume should be carefully monitored throughout gestation and Dexamethasone reduced to 2 mg daily at approximately 30 weeks gestation.

Given the significant risks and limited data on benefit, extensive maternal counseling should be undertaken before the initiation of dexamethasone, and the drug should be discontinued if significant maternal or fetal side effects develop.³⁵

Pregnant women who perform this therapy should undergo periodic glycemia and blood pressure checks.

Despite these potential complications, a trial of dexamethasone for second-degree AVB, or first-degree AVB with additional cardiac finding of inflammation, may be considered to prevent progression to complete AV Block.⁵

Once a fetus has developed Complete Atrio-ventricular Block (CAVB), it is generally found to be irreversible. Thus, pharmacological therapy for CAVB is aimed at limiting further immune mediated damage through the use of corticosteroids, and at times augmenting cardiac output via beta-stimulation of heart rate. A large multinational, multicenter retrospective study of patients with second degree heart block or CAVB found no difference in mortality between

those treated with corticosteroids +/- beta stimulation versus untreated populations. Despite these generally negative findings, corticosteroid +/- beta stimulation may prove to be advantageous in certain CAVB subsets such as those with fetal hydrops or those treated during emergent CAVB. Thus, ongoing investigation is important to identify CCHB patients who may possibly benefit from optimal pharmacotherapy.³⁷⁻³⁹⁻⁴⁰

Alternative therapeutic strategies to fetal corticosteroids such as plasmapheresis and intravenous gamma globulin (IVIG) are aimed at reducing circulating levels of maternal autoimmune antibodies and decreasing placental transmission. These treatments may also accelerate maternal IgG catabolism. Both IVIG and plasmapheresis have been demonstrated to be safe in women with autoimmune diseases, but are expensive, difficult to administer, and can lead to hemodynamic compromise as well as risks of immunosuppression. Unfortunately, however the variable results and lack of reproducibility of studies performed with this therapy, potentially in part secondary to a low number of subjects, do not currently provide sufficient evidence for use as a primary therapy to prevent CAVB.³⁷

At date, however, the indications for treatment of complete AV block are controversial.

Preterm delivery is often necessary in the presence of AVB; this should be taken into consideration as soon as the first signs of decompensation appear, provided

that the gestational age is at least 28 weeks.

About the modalities of delivery in the presence of complete AVB, it is always advisable to have a full birth, as there is no possibility to adequately monitor the fetus during labor.

Optimal fetal management with AVB requires close synergy between obstetricians, neonatologists and pediatric cardiologists.

Treatment of the newborn with BAV essentially depends on the degree of blockage and associated symptoms.

In subjects with advanced second degree and third degree congenital BAV, pacemaker implantation is recommended in the neonatal period when heart rate is < 55 bpm in the presence of a structurally normal heart or < 70 bpm in the presence of congenital heart disease.

Pacemaker implantation can also be considered in patients with long QT syndrome and 2 : 1 AV block or third degree AV block.

To date, there are many therapeutic possibilities for atrio-ventricular blocks but none of these have proved to be the most effective.

For this reason, very often if AV block is found during a pregnancy, no type of treatment is often applied, but a stringent echocardiographic follow-up is performed to follow the progress of the fetal clinical picture.

In light of this, studies are being carried out to use a preventive therapy based on Plaquenil in immune-mediated AVBs. Up to now it has been observed that this type of treatment can reduce the risk of the fetus developing a BAV by 7.5% in women who have autoantibodies. Unfortunately, the scientific evidence about the effectiveness of this preventive treatment is scarce and therefore it cannot yet be used widely.

However, we can say that in presence of a second or third degree AV block, regardless of etiology: if the HR is > 55 bpm not is necessary pharmacological treatment, while if HR is $< 50 - 55$ bpm is administered Salbutamolo 10 mg three times a day, orally, in hospitalization.

If HR is > 55 bpm and the BAV has appeared for more than 7 days, only observation and monitoring are performed; if it has appeared less than 7 days, therapy with corticosteroids or immunoglobulins is performed.

If the patient is more than 28 GW and we are faced with a severe form of BAV, it is preferred to carry out the delivery.

6.3.3 FETAL SURVEILLANCE OF ANTI-Ro/ANTI-La-AFFECTED PREGNANCIES

Detecting the onset of fetal heart block in SSA/Ro-positive mothers is a tremendous challenge.

Initially, for mothers who are known to be anti-Ro and/or anti-La positive, weekly echocardiograms were thought to be adequate to detect a gradual AV interval prolongation and eventual block. Unfortunately, there are no reliable markers that predict which fetus of an anti-Ro/La-antibody-positive woman will develop immune-mediated cardiac complications. Some fetuses with normal AV intervals can develop complete atrioventricular block in a matter of days with no preceding first-degree block. By contrast, when first-degree atrioventricular block is seen, it rarely progresses to more substantial block. This feature is a highly specific marker for SSA/Ro or SSB/La exposure, although it is poorly sensitive.³⁰

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, but levels are not usually available. A small case series also suggests treatment benefits if block is recognized within 24 h, suggesting a potential role for increasing HR monitoring. Until a consensus is achieved, surveillance (scans and HR monitoring) from 16 weeks is tailored to individual cases and intensified if there is a previously affected child.²

Our experience concerns one case of immuno-mediated AVB of high grade with a HR of 55-65 bpm.

The diagnosis of BAV was performed at a gestational age of 21 + 2 Weeks during a control ultrasound. After all the necessary laboratory tests were performed, high titer anti-Ro-SSA antibodies were found.

At 23 + 2 GW is detected the presence of a minimal pericardial effusion, mainly anterior, of 1.9 mm.

The patient was subjected from 23 + 2 GW to a combined therapy of:

- Dexamethasone: 4mg daily;
- Intravenous immunoglobulins: 1gr / Kg 1 time every 2 weeks, in hospital.

During the treatment, monitoring was performed with echocardiography and CTG every 3 - 5 days and periodic tests to check the serum levels of immunoglobulins, which however have always remained at a high titer despite the therapy.

Cardioversion was never found in echocardiographic and CTG controls, with the persistent presence throughout pregnancy of high-grade BAV with HR of 55-60 bpm; while the pericardial effusion underwent a progressive reabsorption, with complete disappearance at 35 + 2 GW.

Due to the persistence of the AV block, was planned a cesarean delivery at 36 + 1 GW with the need for immediate implantation of the cardiac pacemaker.

At 36 GW, however, is found intrauterine fetal death.

Our experience underlines how unfortunately still today the therapeutic possibilities in the presence of a high-grade AV block are few and with unsatisfactory results.

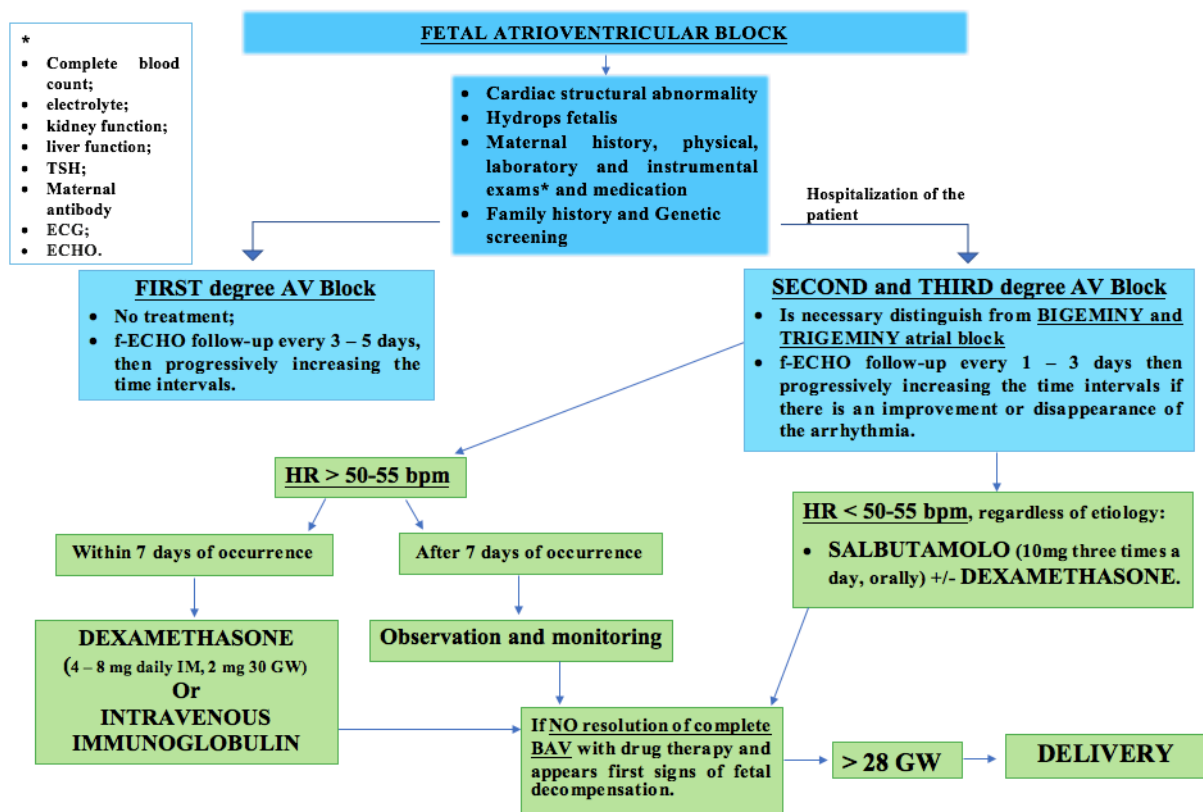


Fig. 22 – Management Atrioventricular Block

6.4 LONG-QT SYNDROME

Congenital long QT syndrome accounted for 15-17% of fetal bradycardias <110 beats/min in fetuses with a normal cardiac structure.

The most common fetal presentation of long QT syndrome is fetal bradycardia, but the syndrome can also be associated with intermittent or persistent Torsades de Pointes-type ventricular tachycardia (VT), or a second-degree AV block. The mechanism of long QT syndrome relies on a delayed repolarization of cardiac ventricular myocytes as the repolarization current decreases and the depolarization current increases. Presumably, Torsades de Pointes (TdP), the characteristic arrhythmia of long QT syndrome, is initiated by early afterdepolarizations. Also sinus bradycardia is a manifestation of fetal long QT syndrome and is reported to be more common than TdP and 2° AV Block.

The fMCG may be the most reliable tool for the prenatal diagnosis of long QT syndrome, but this condition should be differentiated from fetal bradycardia and decreased heart rate variability. A 27-week fetus with bradycardia along with hydrops fetalis, second-degree AV block, and ventricular tachycardia is diagnosed with long QT syndrome.

Maternal electrolyte abnormalities, especially hypomagnesemia and hypocalcemia, as well as drugs and anesthetic agents that lengthen the QT interval, should be avoided.⁵

6.4.1 MANAGEMENT

If long QT syndrome is confirmed or suspected in the fetus, close observation and avoidance of drugs that lengthen QT interval is recommended. Of course, is very important that electrolyte and vitamin D deficiency are corrected.⁸

Early-onset long QT syndrome should be treated with combined beta-blockers and mexiletine at the start of therapy. In cases where Long QT syndrome involves the onset of VT / TdP and drug treatment is unable to control these abnormalities, it is necessary to implant a cardiac defibrillator in the fetus.

Intrauterine treatment of fetal long QT syndrome can suppress the lethal VTs and postpone delivery, thus avoiding implantable cardioverter defibrillator or pacemaker implants in a premature infant.⁴¹

7. CONCLUSION

Fetal arrhythmias are common abnormalities usually manifesting as irregular rhythm. Although most irregularities are benign and caused by isolated atrial ectopics, in a few cases they can trigger tachycardia, regular bradycardia (< 100 bpm) or irregular rhythm that requires differentiation from second-degree AV block.

Tachyarrhythmias and bradyarrhythmias are less common but they need urgent attention because if sustained may lead to hemodynamic compromise and may require in utero therapy.

Supraventricular Tachycardia (SVT) and Atrial Flutter (AF) are the most common fetal tachyarrhythmia and often respond to transplacental treatment with a favorable outcome. Digoxin, flecainide and sotalol are the most commonly drug used. Digoxin is widely accepted as a first-line antiarrhythmic drug. However, it is less effective in hydropic fetuses compared to flecainide and sotalol.

Although fetal AF and SVT are the most common causes of intended in-utero fetal therapy, none of the drugs used has ever been evaluated for their effects on the mother and her child in a Randomized Clinical Trial. In the absence of such evidence, there is still no consensus on their optimal management.

Complete Atrioventricular Block (CAVB) is the common cause of fetal bradyarrhythmia. Management of CAVB may be challenging, with few

therapeutic options available.

Preventive treatment of pregnancies at risk of isolated CAVB appears to be unjustified based on a 1 – 2 % fetal risk in women with anti-Ro/La antibodies. The results of an open-label trial of hydroxychloroquine to prevent autoimmune AV block are awaited. Ambulatory fetal heart monitoring may contribute to the early detection of AV block. The outcome of isolated fetal CAVB may be improved by transplacental treatment with dexamethasone and β -stimulation at heart rates < 55 bpm. This alternative treatment approaches require further study. This study aims to develop adequate and specific management and therapeutic protocols for the three types of fetal arrhythmia that are most frequently encountered during gestation, based on scientific evidence currently available. These protocols are summarized in the three flow charts inserted above.

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