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# Arrhythmias in Pregnancy

Marius Craina[1], Gheorghe Furău[2], Răzvan Nițu[1], Lavinia Stelea[1],
Dan Ancușa[1], Corina Șerban[1], Rodica Mihăescu[1] and Ioana Mozoș[1]
[1]*"Victor Babeş" University of Medicine and Pharmacy, Timişoara,*
[2]*"Vasile Goldiş" Western University of Arad,*
*Romania*

## 1. Introduction

Pregnancies, as well as the post-partum period, are characterized by important metabolic changes. A lot of physiological changes affect the circulating blood volume, peripheral vascular compliance and resistance, myocardial function, heart rate and the neuro-hormonal system. These changes are well known in normal pregnancies, due to thorough examination and intense study; however there are still some questions related to the differences between women with and without structural diseases. Tocolitic medication used in pregnancy can cause cardiac complications in a healthy woman.

The presence of cardiovascular diseases in pregnancy must not be ignored because:

* Cardiovascular diseases are top causes of non-obstetrical maternal death (Sullivan, 1990).
* The modern possibilities of investigation improved diagnosis of cardiac diseases.
* The modern therapy can help women with cardiovascular diseases to have a good pregnancy outcome. Until recently, pregnancy was forbidden in those women.
* Women with repaired congenital heart defects. These women will have an increased risk of arrhythmias during pregnancy (Tateno, 2003). These types of patients usually have fragile hemodynamics and need additional therapy in most of the cases.

## 2. Physiological changes during pregnancy

The antepartum period is characterized by three main changes: an increased blood volume and heart rate and a reduction in the systemic vascular resistance. The increased blood volume can be estimated by examining ventricular diastolic volume and pressure. The increase starts gradually in the 6th week of gestation and by the end of the pregnancy it will reach 50% more than in the pre-pregnant state (Lind, 1985). However, this value is not constant. Studies have shown that there are increases from 20% to 100% above pre-pregnant blood volume (Pirani, 1973). It has been demonstrated that the blood volume increases at least until mid-pregnancy. The period, when the blood pressure plateaus, is arguable: some studies consider that it plateaus in the third trimester (Rovinsky, 1965), others have found a continuous increase until term (Lund, 1967). Blood volume increases considerably in a twin pregnancy (Thomsen, 1994). The increase in the end-diastolic volume can be noticed after 10 weeks of gestation and it will peak during the third trimester (Campos O, 1996). Pregnancy is associated with "physiological anemia", as a consequence of hemodilution (there is a proportional greater increase in the

plasma volume than in the red blood cell mass, the latter being around 40% above pre-pregnancy levels) (Pirani 1973). Hypervolemia is caused by hormonal factors like: prolactin, placental lactogen, growth hormone, and estrogen or peptides like the prostaglandins. Considering women without heart disease, the cardiac filling pressures are not higher in women at term compared to women 11-13 weeks' postpartum (Clark, 1989). The vascular resistance differs from one pregnancy state to another. A fall in systemic vascular resistance has been described in the 5th week of gestation; a nadir between the 20th and 32nd week was followed by a slowly increase. The overall fall in the systemic vascular resistance occurs because of the changes in the resistance and flow in multiple vascular beds, such as the uteroplacental, renal, muscular, cutaneous and mammary bed. There are no changes in the hepatic or the cerebral blood flow. Variations in the renal and unteroplacental blood flow are primarily caused by positional changes (Jurkovic, 1991). For example, in the supine position in case of a pregnant woman, there is a compression of the inferior vena cava. An obstruction of the abdominal aorta and iliac arteries may also occur because of the uterus (Bieniarz, 1969). The resistance of these vascular beds is decreased due to the great amount of secreted vasodilators for example prostacyclin.

The systemic arterial pressure has a similar behavior: it decreases in the first semester and reaches its nadir at mid-pregnancy. Thereafter it increases and, in some cases, its level is higher than the pre-pregnancy level. The cardiac output is the most common measure of cardiac performance. Cardiac output, which is dependent on the heart rate and stroke volume, is gradually increasing by about 30-50% (Clark, 1989; and Rubler S, 1977) in the 5th week of gestation, reaching its peak at approximately the end of the second trimester (Robson, 1989) or in the third trimester (Bader, 1955). Afterwards, it is either constant until term or it decreases slightly near term. Although the amount of the oxygen in the blood is proportional with the cardiac output; there is no relation between the cardiac output and oxygen consumption, the last, increasing progressively by 20-30% at term (Elkus, 1992). Studies show different results when the ejection fraction is debated: some indicate that there are no alterations in the left ventricular ejection fraction (Katz, 1978 and Geva T, 1997), meanwhile other demonstrate increases in ejection fraction (Robson, 1989). This may be a result of the different loading conditions. The ratio of early to late diastolic flow velocity has been shown to be lower during the third semester compared with postpartum (Sadaniantz, 1992).

There is a wide individual variation of heart rate; however it usually increases by 10-20 beats; peaking in the late second trimester or early third trimester. Most pregnant women remain in sinus rhythm; but premature atrial and ventricular complexes may frequently occur.

Hemodynamic changes are also a cause of neurohormonal responses. The most important are the vasodilators: nitric oxide and prostaglandins, which cause, on one hand decreases in the peripheral resistance and, on the other hand, changes in the uterine and renal blood flow. Decreased cerebral blood flow activates the sympathetic nervous system. Conversely, plasma volume expansion suppresses catecholamine levels.

Neurohormones also activate the renin-angiotensin-aldosterone system that is responsible for the regulation of the salt and water homeostasis in the body (August, 1990). Pregnancy is characterized by increased levels of renin and angiotensin. The increased level of renin is not dependent on the extracellular volume.

Natriuretic peptides (also activated by neurohormones) are associated with cardiovascular and renal functions. The level of the two main natriuretic peptides (the atrial natriuretic-ANP and the brain natriuretic-BNP) is increased during pregnancy (Yoshimura, 1994). Their release is caused by atrial and ventricular distension.

During the peripartum period the hemodynamics will radically change, due to pain, anxiety and uterine contractions. For example, uterine contractions will increase the blood volume up to 500 mL (Ueland, 1969). The blood loss will be associated to the type of delivery. If in vaginal delivery there is a 10% blood loss; in caesarian delivery there may be a loss of up to 29% of the total blood volume (Ueland, 1976). Research has demonstrated that the circulation is not influenced by the placental separation. With every contraction the cardiac output increases up to 7-15%, consequently increasing the basal blood pressure. Early after delivery, cardiac output may continue to increase to as much as 80% above pre-labour values. Cardiac output will return to pre-labour levels about 1 hour post-partum. In labour the amount of the catecholamine increase. As a result, the heart rate will have high values. These values are not constant, and depend on many factors such as: position or anesthesia. Hemodynamic parameters need around 6 months to return to their normal values. Immediately after delivery, the cardiac output increases by as much as 80%, followed by a decrease in 24 weeks. Within the first 3 days after delivery the blood volume will decrease by 20%, however the hematocrit needs 2 weeks to be stabilized. Also, within 2 weeks after delivery the systemic vascular resistance increases by 30 % (Robson, 1987), and the heart rate will return to baseline levels. Stroke volume decreases for the first 24 weeks after delivery. Systolic and diastolic blood pressures remain unaltered from late pregnancy until 12 weeks post-partum (Campos, 1996).

## 2.1 Prevalence of arrhythmias in pregnancy

The elevated levels of estrogen and b-choral gonadotropine appear, from experimental models, to affect the expression of cardiac ion channels. By functioning in a proarrhythmic way, pregnancy gives rise to significant problems concerning the diagnosis and treatment of certain arrhythmias, especially when drugs and/or non pharmaceutical therapeutic methods are required (Mark, 2002).

Palpitations, fatigue and syncope are common in pregnancy. The sinus rate increases by about 10 beats/minute during pregnancy, and sinus tachycardia greater than 100 beats/min is common (Conti, 2005). Extrasystoles, intermittent sinus tachycardia and non-sustained arrhythmia are encountered in more than 50% of pregnant women are investigated for symptoms of arrhythmia (Gowda, 2003). Some arrhythmias occuring during pregnancy represent a recurrence of a pre-existing problem, but a substantial number of cases appear for the first time in pregnancy. Bradyarrhythmias presenting during pregnancy are rare with a prevalence of about 1–20 000, and are usually caused by sinoatrial disease or congenital complete heart block (Lee, 1995). Atrial fibrillation and flutter are rarely encountered during pregnancy unless organic heart disease or endocrine disorders are present. Episodes of such arrhythmias appearing for the first time during pregnancy require further evaluation for possible congenital heart disease, rheumatic valvular disease or hyperthyroidism (Leung, 1998).

## 3. Mechanisms of arrhythmia in pregnancy

The management of the arrhythmia is not different in pregnant women. However, hemodynamic conditions should be considered.

The cardiovascular system undergoes significant changes in adaptation to pregnancy, including an increased heart rate and cardiac output, reduced systemic resistance, increased plasma catecholamine concentrations and adrenergic receptor sensitivity, atrial stretch and

increased end-diastolic volumes due to intravascular volume expansion, as well as hormonal and emotional changes (Adamson, 2007). Pregnancies with abnormal uterine perfusion and subsequent pathological outcomes are paralleled by changes in ventricular repolarization, that precede clinical symptoms (Baumert, 2010). Repolarization of the ventricular myocardium might be affected in pregnancy due to changes in circulating hormones, electrolyte imbalances and increased sympathetic tone.

It is important to determine if the arrhythmia has clinical conequences such as deterioration of the underlying cardiac condition. Arrhythmogenic effects are linked to the type of arrhythmia. There is a high risk of maternal and fetal morbidity in women with repaired CHD (chronic heart diseases). Studies have demonstrated that simple tachyarrhythmia does not lead to death. However, death may occur if this type of arrhythmia is associated with structural diseases. New research suggests that women with cyanosis and CHD may experience still birth or miscarriage. In this situation, the best case scenario is a low birth weight infant.

## 4. Signs, investigations and diagnosis

### 4.1 Symptoms

Palpitations, the most common presenting symptom, are usually intermittent and only rarely indicate a serious problem. Patients with arrhythmia may also present with fatigue, breathlessness, peripheral edema and chest discomfort resulting from cardiac failure. Symptoms of thromboembolism may be the presenting feature of atrial fibrillation or atrial flutter. Patients complaining of palpitations, but without documented arrhythmia, have a low likelihood for having a life-threatening arrhythmia, and no further evaluation is warranted (Andreson, 1997). A history of previous heart disease increases the likelihood of life threatening arrythmias. Inquiry should be made about the family history, particularly with reference to cases of premature sudden death.

The severity of the symptoms allows the physician to judge whether the risks of therapy outweigh the benefits. The only difference in pregnancy is that the physician must consider the risk/benefit ratio for both the mother and the fetus. An arrhythmia that is hemodynamically compromising to the mother constitutes a major concern because of inadequate maternal, as well as placental, blood flow (Anderson, 1997).

### 4.2 Examination

The pulse may be abnormal during symptoms; the clinician should focus on looking for signs of heart disease that may be associated with arrhythmia, including scars from previous surgery, murmurs of structural heart disease and signs of cardiac failure. It is also important to look for systemic problems such as thyrotoxicosis that may cause arrhythmia. The diagnosis of heart disease in pregnancy is often difficult due to the anatomical and physiological changes in the cardiovascular system. Many symptoms and signs of normal pregnancy can mimic heart disease. Dyspnea is especially common, with 75% of women complaining of breathlessness by 31 weeks (Elkos, 1992). Orthopnea may also occur in the advanced stages of pregnancy and is due to pressure exerted on the diaphragm by the gravid uterus. Light-headedness and syncope can result from venocaval compression by the enlarged uterus causing supine hypotensive syndrome. Palpitations are common and are related to the increased heart rate and to women being more aware of their heart beat.

Abnormal findings which may warrant further evaluation include the following: (1) a laterally displaced apex beat (more than 2 cm beyond the mid-clavicular line) and (2) non-physiological murmurs such as diastolic murmurs, pan-systolic murmurs, late systolic murmurs, ejection systolic murmurs with intensities of grade 3 or more or those associated with ejection clicks. The radiation dose associated with a chest X-ray is very small (<0.005 rads) and the risk to the fetus is minimal with proper shielding. There should be no hesitancy in performing a chest X-ray when it is clinically indicated.

### 4.3 ECG
Several electrocardiographic changes have been described in pregnant patients (Gowda, 2003). Caution should be exercised when interpreting the electrocardiographic abnormalities in pregnant women, and must account for the normal physiological changes occuring in pregnancy. This may results in decreased PR, QRS, and QT intervals, but usually there is no change in the amplitude of the P wave, QRS complex, and T wave. There is an increase of the heart rate (about 10 beats/minute). The electrical axis shift can occur, more commonly leftward, due to rotation of the heart secondary to the enlargement of the gravid uterus. Premature atrial and ventricular contractions are common during pregnancy (Stein, 1999). Supraventricular tachycardia may occur as new onset paroxysmal supraventricular tachycardia or exacerbation during pregnancy, cause probably by the hyperdynamic state (Gowda, 2003). Wolf-Parkinson White (WPW) syndrome may first occur during pregnancy or the frequency of episodes may increase in women with previously diagnosed WPW syndrome. Atrial fibrillation and flutter are rare in pregnant patients and are secondary to congenital or valvular heart disease, electrolyte imbalances or metabolic disorders. Ventricular tachycardia raises usually the suspicion of underlying cardiovascular disease, but physical or physiological stresses may precipitate ventricular arrhythmias in pregnant women without structural heart disease. Bradyarrhythmias are uncommon in pregnancy.
A patient without previous heart disease will usually have a normal ECG between episodes of arrhythmia. Infrequently, a patient may have 12-lead ECG abnormalities indicative of primary 'electrical' disease, such as frequent ectopic beats or Wolff–Parkinson–White syndrome. A patient with previous heart disease may have an abnormal resting ECG, reflecting their condition and any surgical intervention they may have received in the past.
Arrhythmia symptoms are typically intermittent and a 12-lead ECG recording during symptoms may not be available. Prolonged ECG monitoring with either inpatient bedside monitoring or a portable Holter monitor may pick up an episode in a patient with frequent symptoms. Where symptoms are less frequent, it is appropriate for the patient to wear a cardiac rhythm event monitor for 7 days or longer, with a patient-activation function for use during episodes of symptoms. It is helpful for the patient to keep a diary of symptoms, which can then be related to the recorded rhythm. Most types of devices will also record asymptomatic episodes when the heart rate falls outside certain preprogrammed limits. The patient should be encouraged to pursue all her normal activities during the recording, in particular those activities that previously triggered her symptoms.

### 4.4 Echocardiography and Doppler
Echocardiography is of undisputed value in the diagnosis and follow-up of structural and functional heart disease, and should be considered an integral part of the investigation of any pregnant patient with arrhythmia. It is noninvasive and poses no risk to the fetus. It is the best way to exclude puerperal cardiomyopathy. Changes include slight increases in

systolic and diastolic left ventricular dimensions, moderate increases in the size of the right atrium, right ventricle and left atrium, progressive dilatation of the pulmonary, tricuspid and mitral valve annuli with functional regurgitation (Campos, 2009).

### 4.5 Genetic testing

Several cardiac conditions increase the vulnerability to arrhythmias and have a defined genetic basis. Although routine genetic testing for these conditions is not currently available for the evaluation of arrhythmia risk in pregnancy, a detailed family history should always be taken, and include specific questioning about premature sudden death. Counseling about the risk of transmission of these conditions to offspring is essential, and it is likely that there will be an increasing role for pre-implantation diagnosis of these conditions in affected families (Ueda, 2004).

### 4.6 Laboratory tests

Laboratory tests are not effective in diagnosis of syncope, but it can reveal some of its causes. Blood tests like complete blood count, electrolyte panel, and chemistry panel can lead to causes of arrhythmia. The blood test count is used to detect anemia or acute blood loss. Electrolyte panel may reveal the level of hydration. As far as the chemistry panel is concerned, thyroid stimulating hormone and serum drug levels should be assessed. Studies have shown that routine blood tests are not always necessary or fruitful (Olshansky, 2008). Besides blood tests, there are more precise diagnostic tests, like HUTT used by clinicians to assess patients who present syncope (Bendit et al. 1996). Used first by the NASA, HUTT emerged in cardiology in 1980 (NASA 1999, Baron-Esquivas et al 2003). The design of the HUTT was based on the following physiological mechanism: due to gravity, in a up-ward position, the blood will be displaced downwards. Consequently, the venous system will expand. The sympathetic system will increase the PVR and the skeletal muscle tone, the latter being an important component in maintaining the upright posture and also helping the venous blood to return to the heart and brain (Brignole, 2005). The role of the HUTT is to inhibit the skeletal muscle pump in the extremities that are responsible for the upright posture or orthostatic stress. In normal conditions; skeletal muscles contraction does not occur when venous pooling starts. However, individuals presenting excessive venous pooling, difficulty with PVR or sensitivity to diminish venous return, may experience difficulty in maintaining the upright posture on HUTT. The number of HUTT protocols varies, but the main idea is to induce venous pooling either through passive upright position or using vasodilators (protenerol, nitroglycerin, and adenosine) which inhibit the innate skeletal muscle pump. Guidelines (American College of Cardiology 1996) state that HUTT is efficient in cases such as: recurrent syncope or single episode in a high-risk patient; no evidence of the structural heart disease; structural heart diseases, as long as other causes have been excluded by the diagnostic testing. There are also conditions in which HUTT has proved to be inefficient. The most common are syncope episodes without injury and not in high risk setting and syncope with identified cause and identification of NCS would not alter therapy. There are some cases in which the use of HUTT is forbidden (syncope with ventricular outflow obstruction, critical mitral stenosis, and critical cerebral vascular stenosis).

## 5. Treatment

Due to the fact that physiological changes of pregnancy affect drug absorption as well as the metabolism in several ways, it may be difficult to obtain adequate therapeutic drug levels

and to avoid toxicity. This may explain why some women experience recurrence of symptoms of arrhythmia during pregnancy despite continuing therapy that had previously been effective (Tan, 2001).

Arrhythmias in pregnancy are treated conservatively. After determining the type of arrhythmia, the physician will evaluate for underlying causes. If symptoms are minimal, rest and vagal maneuvers may be used to help slow the heart rate. Vagal maneuvers include carotid massage, applying ice to the face, and the Valvsalva maneuver, which is the most successful in stopping tachycardias (Zu-Chi, 1998). When the arrhythmia causes symptoms or a drop in blood pressure, antiarrhythmic medications may be used. No anti-arrhythmic medication is completely safe during pregnancy; therefore medications are avoided during the first trimester, if possible, to limit risk to the fetus. Drugs with the longest safety record should be tried first. Propranolol, metoprolol, digoxin, and adenosine have been tested and shown to be well tolerated and safe during the second and third trimester (Ferrero, 2004).

When a cardiac disease is identified in a pregnant woman, we must keep in mind the following (ACOG, 1992):

- The blood volume and the cardiac output increase with approximately 50% at the beginning of the first trimester of pregnancy.
- There are big changes of the circulated volume and of the cardiac output during the birth and in the period after.
- The peripheral vascular resistance decreases in pregnancy and returns to minimum in the second trimester. After that it increases, up to 20% referred to normal, during late pregnancy.
- Hypercoagulability is present in pregnancy. This is very important, particularly in patients requiring anticoagulant therapy outside the pregnancy.

Pregnancies with any cardiac problem must be managed by a complex team, consisting of an obstetrician, a cardiologist and, if necessarily, an intensive therapy specialist and/or a fetal medicine specialist. The aforementioned are compulsory in order to obtain an excellent outcome both for mother and for the child.

## 5.1 Arrhythmia prevention

In pregnancy, risk of cardiac disease or arrhythmias should be eliminated by:

- *Making healthy lifestyle choices*

Living a "heart healthy" life is the best way to decrease the chances of developing heart disorders. Exercising regularly (brisk walking, running, bicycling, swimming) and eating healthy are the most important. According to the American Heart Association, a heart-healthy diet includes high amounts of fruits and vegetables (at least five servings a day) and of whole grain foods. It includes lean protein sources like fish, beans, and low-fat dairy products, derives most of its fat from unsaturated fats like olive oil, and avoids saturated fats, trans-fats, and cholesterol.

- *Maintaining a healthy weight*

It's important to balance the eaten calories with burned calories through daily activity and exercise. Obesity is linked to heart disease.

- *Smoking cessation and limiting the intake of caffeine or alcohol*

Tobacco contributes to as much as one-third of all cardiovascular disease. It is necessary to avoid or limit the intake of caffeine, alcohol, and other substances that may contribute to arrhythmias or heart disease. The American Heart Association recommends restriction of the use of alcohol to one drink a day for women and two a day for men (a drink equals 12

ounces of beer, 4 ounces of wine or 1 ounce of 100-proof spirits). A single episode of heavy consumption can trigger arrhythmias like atrial fibrillation. Stimulants, both legal and illegal, can contribute to the development of heart arrhythmias. Caffeine and nicotine may, in some cases, cause premature ventricular contractions, which, over time, may develop into more serious arrhythmias. Cocaine and amphetamines also accelerate the heart rate, in some cases leading to ventricular fibrillation and sudden death. Supplements or some herbal remedies may increase the risk of arrhythmias. For instance, Ephedra, the herbal supplement once promoted as a diet aid and energy booster, increases the risk of arrhythmia. In 2004 the FDA pulled it from the shelves for that very reason.

- *Avoiding unnecessary stress*, such as anger, anxiety or fear, and finding ways to manage or control stressful situations that cannot be avoided.
- *Avoiding stimulant medications*

Many drugs may cause arrhythmias. Over-the-counter cough and cold medicines may speed up the heart. And approximately 50 FDA-approved medications have the potential to prolong the QT interval—the measure of time it takes for the electrical system in the ventricles to recharge after each heartbeat—and thus cause the acquired form of long QT syndrome (LQTS), in which the heart's mechanical or pumping function is normal but its recharging system is slow or ineffective. Those medications include certain antibiotics, antidepressants, antifungal, antihistamines, psychotropic medications, oral hypoglycemic (medications for diabetes), anesthetic agents, and even drugs used to treat heart disease like lipid-lowing drugs and diuretics. Patients with inherited LQTS should always ask physicians and pharmacists if a prescribed drug has the potential to aggravate the condition. Women have a longer QT interval on the electrocardiogram compared to men, despite higher heart rates.

Tocolitics may induce arrhythmias. Corrected QT and Tpeak-Tend intervals were unchanged from pre-operative values after induction of spinal anaesthesia in women undergoing caesarian section, but increased significantly after oxytocin injection. The risk-benefit balance of oxytocin bolus during caesarean delivery should be discussed with women with a history of long QT syndrome. (Guillon, 2010). Women with a long QT syndrome are more susceptible to ventricular arrythmias during pregnancy, labour, delivery and postpartum (Drake, 2007; Seth, 2007).

- *Having regular physical exams* and promptly reporting any unusual symptoms to a physician. The Centers for Disease Control and Prevention suggests that families with a history of arrhythmias or sudden cardiac arrest consider screening younger family members.
- *Seeking treatment for underlying health problems* that may contribute to arrhythmias and heart disease.

Any of the following conditions can increase the likelihood of developing arrhythmias: coronary artery disease, congenital heart disease, heart failure, stroke, atherosclerosis, heart valve damage, high blood pressure, high cholesterol, diabetes, obesity, thyroid disease, advancing age

## 5.2 Monitoring and treating existing heart disorders

Effectively treating any existing heart disorder is the best way to prevent it from becoming more severe. This can be done by:

- Having regular check ups
- Understanding how various conditions increase the risk of arrhythmias.

- Learning about heart disorders, tests, and treatment options, and discussing them with caregivers.
- Finding out if the heart's electrical system and its ability to pump blood efficiently have been affected by heart muscle damage from a heart attack or another cause.
- Learning the importance of an ejection fraction (EF). EF is a measure of the proportion, or fraction, of blood the heart pumps out with each beat. An abnormally low EF is the single most important factor in predicting the risk of Sudden Cardiac Arrest (SCA).
- Following treatment plans.
- Reporting any new symptoms or changes in existing symptoms to physicians as soon as possible.

## 5.3 Treatment

When the treatment plan is conceived, the physician has to consider factors like: the severity of the arrhythmia, the severity of patient's symptoms, if the patient has other health problems/medications that the patient takes, patient's age, overall health, and personal and family medical history of the patient.

Arrhythmia treatments may include one or more of the following:

1. Medicine to prevent and control arrhythmias and to treat related conditions such as high blood pressure, coronary artery disease and heart failure
2. Anticoagulant medication to reduce the risk of blood clots and stroke
3. A pacemaker that uses batteries to help the heart to beat more regularly
4. Cardiac defibrillation and implanted cardioverter defibrillators (ICDs)
5. Cardiac ablation; cryoablation (the defective cells are detected with the help of computerized mapping techniques and destroyed with a cold probe).
6. Surgery
7. Cardioversion
8. Other therapies.

In association with the effect on the human body, heart medication is categorized into two groups: "rate control" medicines, are used to slow the heart rate to less than 100 beats per minute or "rhythm control" medications (antiarrhythmic/cardioversion drugs) used in order to restore your heart's normal sinus rhythm. The aforementioned drugs are being used less, with more care and often in conjunction with implantable cardioverter defibrillators (ICDs) or cardiac ablation.

Many of the prescription medications reviewed here are also used to treat other kinds of heart-related conditions, including heart failure, high blood pressure, and angina (chest pain).

## 5.3.1 Rate control heart medication

Rate control heart medicine may include beta or calcium channel blockers. The first group of medication reduces the heart rate and cardiac output by lowering the blood pressure by blocking adrenalin. The most used beta blockers are: Acebutolol, Atenolol, Betaxolol, Bisoprolol/hydrochlorothiazide, Carteolol, Esmolol, Metoprolol, Nadolol, Penbutolol, Pindolol, Propranolol and Timolol. Calcium channel blockers, also called "calcium antagonists", work by interrupting the movement of calcium into heart and blood vessel tissue, slowing the heart rate. They are used in other disorders like: angina and arrhythmias. Examples of calcium channel blockers: Amlodipine, Diltiazem, Felodipine, Isradipine, Nicardipine, Nifedipine, Nimodipine, Nisoldipine and Verapamil.

### 5.3.2 Rhythm control heart medications

Rhythm control medication includes sodium channel blockers, beta blockers, class III antiarrhythmics that slow the electrical conductivity of the heart to improve rhythm problems. This type of medication can be administrated intravenously in emergency situations and orally in long term situations: Amiodarone, Bepridil Hydrochloride, Disopyramide, Dofetilide, Flecainide, Ibutilide, Lidocaine, Procainamide, Propafenone, Propranolol, Quinidine, Sotalol and Tocainide.

### 5.3.3 Drug administration

All medications have potential side effects and risks. Antiarrhythmic drugs must be taken daily and indefinitely. There are also side effects that are hard to manage. These side effects may include proarrhythmia, which means drug-related arrhythmia. When medication proves unsuccessful, the American College of Cardiology and the American Heart Association suggest catheter (cardiac) ablation or surgical ablation as a safe and effective treatment option.

The greatest risk is however drug-induced congenital malformation, that is most prone to occur during fetal organogenesis, a process which is completed by the end of the first trimester. Thereafter, the risk is mainly of impaired growth and functional development, or direct toxicity to fetal tissues. Drugs given shortly before term or during labour may have adverse effects on labour or the neonate after delivery. Most antiarrhythmic drugs are categorized by the US Food and Drug Administration (FDA) as category C during pregnancy which signifies that: risk (to the fetus) cannot be ruled out. Adequate well-controlled human studies are lacking, and animal studies have shown a risk to the fetus or are lacking as well. There is a chance of fetal harm if the drug is administered during pregnancy; but the potential benefits may outweigh the risks (Blomstrom-Lundqvist, 2003).

Drug treatment is not required for a benign tachycardia that is well tolerated. A low dose should be used initially with titration according to response, and this must be accompanied by regular monitoring. The selection of an appropriate drug depends on knowledge of the arrhythmia mechanisms, and only drugs with a safe track record in pregnancy should be used. The most common drugs are: Adenosine, Digoxine, and Beta Blockers.

Research showed that Adenosine is useful for the emergency management of SVT and broad QRS complex tachycardias, and has been used safely in pregnant women (Blomstrom-Lundqvist, 2003). It is administered as a bolus dose and it has a very short duration of action of no more than 5–10 s. The role of this medication is to depress sinus and AV nodal function causing transient bradycardia and AV block in the mother, but it has no detectable effect on the fetal cardiac rhythm. Adenosine is contraindicated in patients with brittle asthma, in whom it may cause bronchospasm, and in those taking dipyridamole because of the risk of prolonged asystole.

There is a long history of digoxin use during pregnancy and it is considered to be safe (Blomstrom-Lundqvist, 2003). It crosses the placenta, but is not teratogenic. It is cleared by the kidney, although renal excretion is inhibited by concomitant use of amiodarone. It is mainly used for the control of ventricular rate in patients with persistent atrial fibrillation, but may also be effective in some cases of focal atrial tachycardia.

Propranolol is the beta blocker with the longest track record and is considered safe in pregnancy (Blomstrom-Lundqvist, 2003). Beta blockers are not teratogenic, but beta1-selective blockers, such as atenolol or metoprolol, may be preferred because they may interfere less with beta2-receptor-mediated uterine relaxation. However, beta1-selective agents achieve less complete cardiac beta blockade because there are functional beta2-

receptors on cardiac myocytes, and these may, therefore, be less effective anti-arrhythmic agents. There have been reports linking beta blockers to fetal bradycardia, hypotonia, hypoglycemia and intrauterine growth retardation.

Sotalol is a combined beta blocker and class III anti-arrhythmic drug. It does cross the placenta and is excreted renally. It has achieved class B classification with the FDA and its use in pregnant patients has been reported with no adverse outcome (Blomstrom-Lundqvist, 2003).

Flecainide has been used frequently during pregnancy and is a reasonable choice for patients with a structurally normal heart (Blomstrom-Lundqvist, 2003). It should probably be avoided in those with myocardial disease, and in particular patients with ventricular tachycardia or vulnerability to myocardial ischemia.

The conflict between the interests of the mother and the well-being of the fetus is thrown into sharp relief with Amiodarone. Amiodarone is a very effective anti-arrhythmic drug to treat and prevent life-threatening ventricular arrhythmias in patients with ventricular disease. Amiodarone crosses the placenta and achieves fetal concentrations of around 10% of maternal serum values (Ovadia, 1994). Maternal amiodarone use may cause a goiter, which in turn compromises the upper airway in the neonate. Amiodarone is prone to cause, neonatal hypothyroidism, and fetal growth retardation. For these reasons, amiodarone should be used only when the mother's life is significantly threatened and no other agent will do (Chow, 1998).

There are no reports of teratogenicity, but verapamil does cross the placenta and may have fetal cardiovascular effects (Klein, 1984). Intravenous verapamil is a useful alternative to adenosine for emergency termination of SVT, and oral verapamil may be used in patients to prevent SVT recurrence when beta blockers are contraindicated or not tolerated (Klein, 1984).

Anticoagulant medications help to prevent new clots appearance in the blood or existing clots from getting larger. They are often prescribed for patients with atrial fibrillation to help reduce stroke risk. Aspirin also is often recommended for these patients in addition to or instead of prescription anticoagulants.

The pacemaker is a small device that's surgically placed under the skin at the collarbone; wires lead from it to the atrium and ventricle(s). The pacemaker sends small electric signals through the wires to control the speed of the heartbeat. Most pacemakers contain a sensor that activates the device only when the heartbeat is abnormal.

An ICD (Implantable Cardioverter Defibrillator) provides automatic electrical therapy on a chronic basis for patients suffering from recurrent tachycardias. (When an episode of fast, irregular heartbeat begins, the device delivers a shock to end the tachycardia, preventing the heart from going into ventricular fibrillation, which is frequently fatal). The device is connected to leads positioned inside or on the surface of the heart. These leads sense cardiac rhythm, provide necessary electrical shocks when necessary, and at times - pace the heart as needed. Various leads are connected to a pulse generator implanted in a pouch beneath the skin of the chest or abdomen. Newer devices are smaller, with simpler lead systems and can be installed through blood vessels.

Women with an implanted cardioverter defibrillator (ICD) may undergo pregnancy successfully with a good reported outcome. Potentially threatening arrhythmias are promptly detected and automatically terminated by an ICD by, either a series of rapid pacing impulses delivered via an endocardial right ventricular pacing lead, or delivery of a synchronized shock between a coil electrode in the right ventricular cavity and a second

electrode formed by the ICD box, which is located in the pre-pectoral position on the left. Prompt detection and termination of an arrhythmia by an ICD minimize the hemodynamic disturbance and thereby limit the risk of harm to the fetus. ICDs are configured to concentrate the maximal electrical field strength to the mother's ventricular myocardium, and the electrical energy to which the fetus is exposed is minimal. Delivered energies (2–40 J) are about a tenth of those used for external DC cardioversion. Research found Cardioversion safe for the entire pregnancy state therefore, it can be used, if necessary (Blomstrom, 2003). Also, there is not additional risk (excepting patients with underlying heart condition) to develop ICD complications, during pregnancy (Natale, 1997).

Ablation is a nonsurgical technique that neutralizes parts of the abnormal electrical pathway (tissue) that is causing the arrhythmia. The technique utilizes a variety of imaging and monitoring systems that navigate flexible wires (catheters) to the heart through an artery or vein, locate the abnormal electrical activity (where ablation is needed), and evaluate their progress.

Once in the heart, one or more catheters are used to pinpoint the source of the abnormal electrical signals. When the source of the arrhythmia is located, the catheter delivers bursts of high-energy waves that eliminate the abnormal areas.

There are two techniques of ablation: radiofrequency ablation and transcatheter technique. In this first technique, a catheter with an electrode at its tip is guided to the damaged portion of heart muscle and mild, painless radiofrequency energy is transmitted to the site of the pathway, killing a few cells (about 1/5 of an inch). Consequently, these cells stop conducting the extra impulses that caused the rapid heartbeats. This non-surgical procedure is used to treat patients suffering from atrial fibrillation, atrial flutter, atrial tachycardia and supraventricular tachycardia. The second technique, however, electrocauterization is performed at a targeted spot in the heart. This technique is generally used to treat supraventricular tachycardia.

Most patients who receive this treatment experience a long-term reduction in the number of episodes of arrhythmia and the severity of symptoms, or a permanent return to normal heart rhythm.

Sometimes, surgery is used to treat arrhythmia. Often this is done when surgery is already being performed for another reason, such as repair of a heart valve. One type of surgery for atrial fibrillation is called "maze" surgery. In this operation, the surgeon makes small cuts or burns in the atria, which prevent the spread of disorganized electrical signals. Ventricular resection implies the removal of a part of the heart's muscle, where the arrhythmia originates.

Coronary artery bypass surgery may be needed for arrhythmias caused by coronary artery disease. The operation improves blood supply to the heart muscle.

Cardioversion treatment can be chemical (implemented through fast-acting drugs) or electric (implemented through a direct current using paddles over the chest) and is used to restore the heart's normal rhythm. DC cardioversion may be used to terminate sustained tachycardias. It should be carried out with general anesthesia, or deep sedation with midazolam or diazepam. Traditionally, the cardioversion electrodes are placed at the right sternal edge and cardiac apex, but for atrial fibrillation, it may be more effective to use an anterior–posterior configuration. Firm downward pressure on the sternal paddle reduces the electrode separation and increases the intensity of the electrical field, thus maximizing the chance of success. A waveform that reverses polarity during delivery (biphasic waveform) achieves cardioversion at energy thresholds that are half those

required when a monophasic waveform is used. For all tachyarrhythmias, except ventricular fibrillation, the shock should be synchronized to the R wave, to minimize the risk of inducing ventricular fibrillation. Patients with atrial flutter or fibrillation are particularly vulnerable to systemic thromboembolism after restoration of sinus rhythm. DC cardioversion should not be carried out on patients who have been in atrial fibrillation for longer than 24 hours unless the arrhythmia results in serious cardiovascular compromise, or the patient has been fully anticoagulated since the onset of arrhythmia, or the absence of thrombus in the left atrium has been verified by transesophageal echocardiography. Anticoagulation should be continued for a minimum of 4 weeks after DC cardioversion. DC cardioversion seems to be quite safe in all stages of pregnancy because the intensity of the electrical field to which the fetus is exposed is low. Nevertheless, the fetus should be carefully monitored throughout the procedure. In the later stages of pregnancy, full general anesthesia and intubation are used, considering the increased risk of gastric aspiration.

Vagal maneuvers are another arrhythmia treatment. These are simple exercises that sometimes can stop or slow down certain types of supraventricular arrhythmias. They stop the arrhythmia by affecting the vagus nerve, which controls the heart rate. Some vagal maneuvers include:

- Gagging
- Holding breath and bearing down (Valsalva maneuver)
- Immersing the face in ice-cold water
- Coughing
- Putting the fingers on the own eyelids and pressing down gently.

## 6. Management of specific arrhythmias during pregnancy, labour and delivery

Dynamic changes in maternal physiology, as well as concern for the fetal well-being, are factors that complicate the treatment of arrhythmia. Premature atrial and ventricular contractions associated with a structurally normal heart are considered to be benign. However, in order to prevent them, exacerbating factors (dehydration, caffeine, sleep deprivation) should be avoided. Also, nonpharmacologic vagal maneuvers are recommended in atrial tachycardias. In the aforementioned case, drug therapy is indicated as long as the patient present refractory symptoms. In order to prevent recurrence, digoxin and beta-blockers are recommended. If the patient does not respond to these, flecainide and propafenone should be taken into consideration. Cardioversion or intravenous adenosine is indicated in acute management. Arrhythmias in association with the Wolf-Parkinson-White syndrome should be treated with Prosainamide, during pregnancy.

Records demonstrating the safety usage of digoxin and beta-blockers have determined the specialists to use these drugs in diseases like atrial flutter and fibrillation. In these cases, there are some who appeal to a rate or rhythm control strategy, similar to the nonpregnant state.

The management of ventricular arrhythmias is closely associated to the underlying heart condition; for instance patients suffering from idiopathic ventricular tachycardia (VT), but whith a structurally normal heart will receive, as first line therapy, beta-blockers, with IC agents or sotalol as second-line agents.

In pregnancy, congenital heart diseases have a complex prognosis. In most cases, long QT or hypertrophic cardiomyopathy are associated with ventricular arrhythmias. Sustained VT

can develop into peripartum cardiomyopathy or vasospastic coronary artery disease. In each case daily evaluation is compulsory. If VT is unstable hemodynamically, emergent cardioversion is recommended. Well tolerated VT is treated with lidocaine, however if VT is sustained or recurrent, procainamide, flacainide, propafenone, sotalol or amiodarone are required.

Conservatory management is the best option for asymptomatic bradycardia. In pregnancy, pacemakers' insertions are tolerated.

During labour as well as delivery, hemodynamic changes occur, due to pain, anxiety. These hemodynamic changes increase the risk of arrhythmia.

Holter monitorization of the pregnancies with arrhythmias showed a high incidence of ventricular and/or atrial extrasystoles, with no consequences on the future mother or on the child. They will gradually disappear in post-partum.

## 7. Conclusion

Pregnancy increases cardiac output, heart rate and prevalence of dysrrhythmias in normal healthy women. The factors that can promote arrhythmias during pregnancy are: the direct electrophysiological effects of the hormones, the increased sympathetic tone and sensitivity, hemodynamic changes, electrolyte imbalances, atrial stretch, increased end-diastolic volumes and underlying heart diseases.

The most important problem in patients diagnosed with cardiac arrhythmia in pregnancy is the early detection, a multidisciplinary monitorization and an adequate therapy. The purpose is to decrease the cardiovascular complications in pregnancy and to have a good pregnancy outcome.

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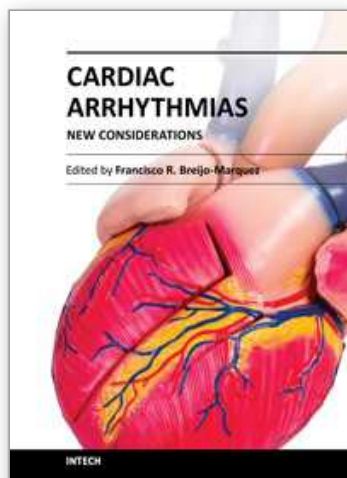
**Cardiac Arrhythmias - New Considerations**

Edited by Prof. Francisco R. Breijo-Marquez

The most intimate mechanisms of cardiac arrhythmias are still quite unknown to scientists. Genetic studies on ionic alterations, the electrocardiographic features of cardiac rhythm and an arsenal of diagnostic tests have done more in the last five years than in all the history of cardiology. Similarly, therapy to prevent or cure such diseases is growing rapidly day by day. In this book the reader will be able to see with brighter light some of these intimate mechanisms of production, as well as cutting-edge therapies to date. Genetic studies, electrophysiological and electrocardiographyc features, ion channel alterations, heart diseases still unknown , and even the relationship between the psychic sphere and the heart have been exposed in this book. It deserves to be read!

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