Nandita S. Scott MD
Heart Disease and Pregnancy

FINANCIAL DISCLOSURE:
No relevant financial relationship exists
Introduction

- Heart disease is present in up to 4% of all pregnancies
- Data from the UK suggest that heart disease is the number one cause of indirect maternal death
- As maternal age advances, preexisting heart conditions more likely
- Increase in obesity and diabetes in population increase risk of CV complications during pregnancy
- Patients with congenital heart disease are surviving to reproductive age
- Childhood cancer survivors with cardiotoxic effects from therapy
- Limited prospective and RCT data
Objectives

- Understand the hemodynamic changes of pregnancy
- Review normal clinical and structural findings in pregnancy
- How to risk stratify a woman with cardiac disease
- Review specific cardiac conditions in pregnancy
- Review value of troponin and BNP in pregnancy
- Discuss importance of maternal placental syndromes
• This is how we started….

42 year old s/p VF arrest with ostial LAD occlusion treated with Xience to LAD - July 2011
Xience to RCA September 2011

December 2011 becomes pregnant
Please choose the best answer:

1. Dual antiplatelet therapy is safe during pregnancy and delivery
2. Dual antiplatelet therapy is safe for epidural catheter placement
3. There is an abundant amount of safety data on drug coated stents during pregnancy
4. None of the above
Our most concerning case....

- 32 year old originally from Somalia
- Saw cardiologist in 2009 – moderate rheumatic MS/AS/AI
- ‘Reminded her that pregnancy was contra-indicated’
- Did not return until 2012 – called OB to let them know she was 15 weeks pregnant
Increase in blood volume, red cell mass and HR

CO rises to 30-50% non pregnant levels
Rises even further with twin pregnancy
12% CO to uterus

Histological changes in aortic media
Catecholamine induced rise in HR/SV. Increase BP and CO. Tachycardia reduces diastole time. Relief of IVC compression causes increased preload.


POST
Autotransfusion
Blood loss
Loss of low resistance placenta
Mobilization of dependent edema
Symptoms

- Symptoms that often reflect cardiac disease in non-pregnant patients:
  - Fatigue, dyspnea, dizziness, palpitations, edema, and orthopnea all caused by weight gain, dilutional anemia, decreased venous return from caval compression.
  - Edema from increased total body sodium and reduced colloid osmotic pressure.

- Abnormal:
  - Dyspnea that limits activity
  - Progressive orthopnea/PND
  - Syncope with exertion
  - Palpitations
  - Chest pain
  - Hemoptysis
Normal physical examination

- Normal findings would otherwise be abnormal in non-pregnant females.
- Prominent X and Y descents, distinct A and V waves of JVP.
- Full systemic arterial pulses with brisk collapse.
- Hyperdynamic LV impulse.
- Palpation of the RV and pulmonary trunk.
- Loud S1, splitting of S1, loud S2.
- Flow murmurs.
- Diastolic murmurs may occur due to increased flow across MV and TV valves.
- Continuous murmur: venous hum over right supraclavicular fossa, mammary souffle.

Abnormal
- Pulse over 100, less than 60
- Cyanosis/clubbing
- Diastolic murmur
- Systolic murmur 3/6
- S3/S4
Prospective multicenter study of pregnancy outcomes in women with heart disease

(Siu et al. Circulation 2001)

562 consecutive women with heart disease
13 Canadian centers
617 pregnancies
1994-1999
derivation (60%) - validation (40%) model
74% congenital heart lesions
Major cardiac events in 80 (13%)

73 of these were either CHF or arrhythmia

4 patients had an embolic CVA

Dilated CMP, MVR w/suboptimal INR, MS, D-TGA s/p Mustard with low RVEF

3 patients died

Mustard, Dilated CM, severe pulmonary HTN
Table 4  Predictors of maternal cardiovascular events and risk score from the CARPREG study\textsuperscript{12}

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Risk Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior cardiac event (heart failure, transient ischaemic attack, stroke</td>
<td>CARPREG risk score: for each CARPREG predictor that is present a point is assigned. Risk estimation of cardiovascular maternal complications</td>
</tr>
<tr>
<td>before pregnancy or arrhythmia).</td>
<td>assigned. Risk estimation of cardiovascular maternal complications</td>
</tr>
<tr>
<td>Baseline NYHA functional class &gt;II or cyanosis.</td>
<td></td>
</tr>
<tr>
<td>Left heart obstruction (mitral valve area &lt;2 cm\textsuperscript{2}, aortic</td>
<td></td>
</tr>
<tr>
<td>valve area &lt;1.5 cm\textsuperscript{2}, peak LV outflow tract gradient &gt;30</td>
<td></td>
</tr>
<tr>
<td>mmHg by echocardiography).</td>
<td></td>
</tr>
<tr>
<td>Reduced systemic ventricular systolic function (ejection fraction &lt;40%)</td>
<td></td>
</tr>
</tbody>
</table>

Siu et al. Circulation 2001; 104: 515-521
Modified WHO Classification of Maternal cardiovascular risk

- WHO 1
  uncomplicated or mild: PS, PDA, MVP
  repaired simple lesions
  ectopic beats

- WHO 2
  unoperated ASD/VSD
  repaired Tetralogy of Fallot
  most arrhythmias

- WHO 2-3
  mild LV impairment
  HCM
  heart transplant
  Marfans without aortic dilatation
  valvular disease not in WHO 4
Modified WHO Classification of Maternal cardiovascular risk

- WHO 3
  - mechanical valve
  - systemic RV
  - post Fontan
  - cyanotic heart disease
  - other complex congenital heart disease
  - aortic dilatation above 40 mm in Marfans
  - aortic dilatation above 45 mm in BAV
Modified WHO Classification of Maternal Cardiovascular Risk

• WHO 4

  Pulmonary artery hypertension
  LV EF less than 30%
  NYHA 3-4
  Previous PPCM with residual impairment
  Severe MS
  Severe symptomatic AS
  Marfan with root over 45 mm
  BAV with root over 50 mm
  Severe coarctation

• PREGNANCY IS CONTRAINDICATED
Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology

Jolien W. Roos-Hesselink1*, Titia P.E. Ruys1, Jörg I. Stein2, Ulf Thilén3, Gary D. Webb4, Koichiro Niwa5, Harald Kaemmerer6, Helmut Baumgartner7, Werner Budts8, Aldo P. Maggioni9, Luigi Tavazzi10, Nasser Taha11, Mark R. Johnson12, and Roger Hall13, on behalf of the ROPAC Investigators

- Created in 2007
- Goal: improve understanding of consequences of heart disease during pregnancy

Now over 2500 patients worldwide

MGH is now a member of this registry
Correlation with WHO category

<table>
<thead>
<tr>
<th></th>
<th>WHO 1 (n = 241)</th>
<th>WHO 2 (n = 514)</th>
<th>WHO 3 (n = 504)</th>
<th>WHO 4 (n = 53)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal mortality (%)</td>
<td>241</td>
<td>514</td>
<td>504</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Maternal hospital admission (%)</td>
<td>0.4</td>
<td>0.6</td>
<td>1.5</td>
<td>4.0</td>
<td>0.035</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure (%)</td>
<td>13</td>
<td>18</td>
<td>36</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Supraventricular arrhythmias (%)</td>
<td>1.2</td>
<td>5.6</td>
<td>19</td>
<td>57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventricular arrhythmias (%)</td>
<td>0.4</td>
<td>1.4</td>
<td>1.4</td>
<td>3.8</td>
<td>0.13</td>
</tr>
<tr>
<td>Obstetrics complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy-induced hypertension (%)</td>
<td>2.1</td>
<td>2.9</td>
<td>3.4</td>
<td>3.8</td>
<td>0.32</td>
</tr>
<tr>
<td>(pre-)Eclampsia (%)</td>
<td>27</td>
<td>37</td>
<td>49</td>
<td>60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Caesarean section (%)</td>
<td>0.0</td>
<td>1.2</td>
<td>5.2</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-partum haemorrhage (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foetal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apgar score &lt;7 (%)</td>
<td>4.1</td>
<td>10</td>
<td>11</td>
<td>17</td>
<td>0.001</td>
</tr>
<tr>
<td>Preterm birth &lt;37 weeks (%)</td>
<td>8.7</td>
<td>15</td>
<td>17</td>
<td>30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Foetal death (%)</td>
<td>0.4</td>
<td>0.6</td>
<td>2.8</td>
<td>5.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Neonatal death (%)</td>
<td>1.2</td>
<td>0.4</td>
<td>0.4</td>
<td>0.0</td>
<td>0.24</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>3109</td>
<td>3074</td>
<td>2925</td>
<td>2735</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pregnancy duration (weeks)</td>
<td>39</td>
<td>38</td>
<td>38</td>
<td>37</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Contraceptive Counseling

- Consideration of pregnancy risk
- Available contraception, risks, benefits and failure rates
- Consequences of unplanned pregnancy
- Patient’s preference

- ACC/AHA guidelines ‘it is the duty of the cardiologist to provide advice regarding informed decision on contraception’
Contraceptive choices

Most comprehensive guidance comes from British Working Group

WHO 1 – no restriction on use of combined contraceptives
WHO 2 – benefits outweigh risks of the use of combined
WHO 3 - risk of combined OC outweighs benefits
WHO 4 – highest risk group for combined OCP

IUD is probably safest in women with cyanotic CHD and pulmonary vascular disease
Risk of vagal reactions at time of implant
Aortic Disease

- Hormonal changes lead to histologic changes in aorta increasing the susceptibility to dissection
  - fragmentation of reticular fibers
  - diminished acid mucopolysaccharides
  - loss of normal corrugation of elastic fibers

- Circulating elastase breaks up elastic lamellae and weakens media
- Relaxin detectable in serum causes reduced collagen synthesis

- Hemodynamically uterine compression can increase outflow resistance of lower arterial tree

- Pregnancy high risk period for all patients with aortic pathology

- Dissection occurs most often in the last trimester or early postpartum
Guideline Recommendations for Marfans

• 2011 ESC – if ascending aorta over 45 mm, treat surgically pre pregnancy

• 2009 Canadian Guidelines recommend surgery before pregnancy if over 45 mm

• 2010 American Thoracic Aortic Guidelines recommend surgery if over 40 mm
69 women with 199 pregnancies followed, 29 controls
86% live births
Mean aortic root diameter was 36.1 mm +/- 4.4 mm
27% started with root over 40 mm
Increased by 3 mm during pregnancy
2 carotid dissections
One patient with root 49, rapid increase in AR
No aortic dissections
**Table 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pregnant (n = 69)</th>
<th>Nulliparous (n = 29)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective surgery</td>
<td>13.0% (9)</td>
<td>6.5% (2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Adverse outcome</td>
<td>23.0% (16)</td>
<td>0% (0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Values are % (n).
### Table 3

Factors Associated With Long-Term Adverse Cardiovascular Outcome in Women With a Prior Pregnancy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic size</td>
<td>1.3</td>
<td>1.11–1.61</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>1.5</td>
<td>1.15–1.97</td>
</tr>
<tr>
<td>Prospective care</td>
<td>0.1</td>
<td>0.05–0.39</td>
</tr>
<tr>
<td>Medications</td>
<td>0.3</td>
<td>0.14–0.92</td>
</tr>
<tr>
<td>Aorta &gt;4 cm</td>
<td>3.8</td>
<td>1.11–13.3</td>
</tr>
</tbody>
</table>
Marfans and Pregnancy

Little data on roots over 45 mm – advised against pregnancy
Under 40 mm root lower risk

Bottom line: aorta will increase during pregnancy
will not return to normal
increase risk of long term adverse outcomes
low risk of dissection if less than 45 mm

BAV – 50% have dilatation of ascending aorta
Risks of pregnancy not been well studied
Consider surgery preconception if root over 50 mm
BAV and Marfans and aortic disease

- Echo every 4-12 weeks throughout pregnancy and 6 months post partum
- Beta blockers

- C section should be considered when aortic diameter over 45 mm in Marfans
- Vaginal delivery if less than 40 mm

- If prior dissection should be advised against pregnancy
Call from OB:
35 year old, preterm labor 30 weeks

Has emergent C section and immediately post partum, start coughing

Pulmonary edema and positive troponins, bedside echo with anteroapical wall motion
Acute Myocardial Infarction Associated with Pregnancy – Roth et al. JACC 2008

Literature review of 95 cases between 1995-2005

Majority of patients were over 30

1 in 16, 129 deliveries nationwide

High incidence of known risk factors

11% maternal mortality rate

9% fetal death

40% stenosis, 8% thrombus, 27% dissection, 2% spasm, 13% normal
• Retrospective cohort of 87 patients
• Mean age 42.6, 82% women
• 18% postpartum, mean age 33, mean 38 days postpartum
• Detect fibromuscular dysplasia in other territories
• Median follow-up 47 months, 17% recurrence all female
• 10 year mortality 7.7% and MACE 47%
CPR during pregnancy

- Relieve IVC compression – occurs around 20 weeks
- Deliver with 5 minutes – need to consider viability
- Anoxia occurs earlier due to reduced FRC
- Consider Magnesium toxicity
- Chest compressions, hand placement more cephalad
Troponins

- Troponin levels have also been studied during pregnancy and are generally felt to remain in the normal range, but may rise to the upper limit of normal.
- They are higher in those with hypertensive disorders of pregnancy, particularly pre-eclampsia.
Brain Natriuretic Peptide

- Conflicting results but generally felt that:
  
  despite increase in volume load during pregnancy, values at upper limits of normal

- Higher than normal in preeclampsia

- Toronto Pregnancy and Heart Disease Research Program studied BNP in pregnant women with heart disease
Prospectively enrolled 66 women with heart disease and 12 healthy controls

BNP at 14 +/-5 weeks antenatal

Repeat BNP third trimester and > 6 weeks postpartum
B-Type Natriuretic Peptide in Pregnant Women With Heart Disease

Adverse maternal events in 13%
Peak BNP over 100 in all, predated Event in 88%

100% negative predictive value
100% sensitivity
70% specificity

In women with CARPREG 0
No events if BNP < 100
8% if BNP over 100

In women with CARPREG 1
No events if BNP < 100
60% if over 100
Prosthetic Valves
Valve Selection Pre Conception

- Bioprosthetic: risk of structural valve deterioration may be accelerated by pregnancy
- Mortality for redo higher
- Newer bioprosthetic valves are lower profile with improved hemodynamics
- Very little information available
- Mechanical: need for lifelong anticoagulation
Warfarin Embryopathy

- Flattened nasal bridge
- Bone deformities
- CNS abnormalities
- Bleeding
- Spontaneous abortion

- Low IQ
- Optic atrophy
Anticoagulation During Pregnancy for Mechanical Valves

- Increased risk of thrombosis due to hypercoagulable state of pregnancy

- Unfractionated heparin and LMWH do not cross placenta

- In a large review, the risk of valve thrombosis was
  - 3.9% with warfarin throughout pregnancy
  - 9.2% with UFH in first trimester then warfarin
  - 33% with UFH throughout pregnancy
Anticoagulation during pregnancy for mechanical valves

• Safest option for valve is warfarin throughout pregnancy

• Lower risk of warfarin embryopathy if dose less than 5 mg
Anticoagulation options for mechanical valves

Chest 9th edition antithrombotic guidelines

One of the following recommended:

• BID LMWH throughout pregnancy (max peak anti Xa levels)
• BID UFH throughout pregnancy, PTT > 2 X normal
• UFH/LMWH until 13th week, then warfarin, resume UFH/LMWH close to delivery

High risk for thrombosis: warfarin throughout, replacement with UFH/LMWH close to delivery

MGH Obstetricians DO NOT use warfarin during pregnancy
Case

- 35 year old, G1P0 presents 38 weeks pregnant with shortness of breath, edema and orthopnea
- Physical exam supports congestive heart failure
- Echo demonstrates: reduced LV EF at 32%
Please choose the best answer:

1. She should be started on beta blockade, ace inhibitor, lasix and referred for immediate C section
2. She should be diuresed with furosemide, then discharged home to await spontaneous labor
3. She should be diuresed with furosemide, labor should be induced with plans for vaginal delivery if remains stable
4. She should receive an IABP to support blood hemodynamics for C section
Peripartum Cardiomyopathy

- Idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction towards the end of pregnancy or months following
- Diagnosis of exclusion

- 1:3000-4000 pregnancies
- 1:300 Haiti
- In US 1:2229, higher in African-Americans lowest in Hispanics (1:9861)

- Incidence rising in US
Peripartum Cardiomyopathy

- Predisposing factors: multiparity, multiple childbirths, family history, ethnicity, smoking, diabetes, hypertension, preeclampsia, malnutrition, advanced age, teenage pregnancy

- Suspected to be the consequence of oxidative stress leading to proteolytic cleavage of prolactin which causes apoptosis
Peripartum Cardiomyopathy

- Heart failure can develop rapidly
- Prognosis better than dilated cardiomyopathy
- Significant proportion normalizing/improving LV EF over 6 months
- 50% spontaneous recovery - lower in African Americans
- Predictors of recovery: LV EDD less than 50 mm
  LV EF over 30%
  low BNP, troponin

diagnosis after delivery
Peripartum Cardiomyopathy – Management

- If mother unstable – urgent delivery
- Anticoagulation for low LV EF
- Usual medical therapy for CHF except: avoid ACE/ARB during pregnancy, ACE OK if breastfeeding
- Diuretics judiciously

- Plan vaginal delivery
- Consider NO breastfeeding

- Await 6 months if possible to decide on ICD/transplant
Peripartum Cardiomyopathy – Novel therapies

- Immune globulin – 6 patient study

- Pentoxifylline – prevents apoptosis – 30 patient study, LV EF 52% vs. 27%, no other studies, safety unknown during pregnancy

- Bromocriptine – prolactin blocker – 20 patient study – LV EF 31% vs. 9%, lower mortality in treatment group
  Bromocriptine also suppresses milk reduction and risk of acute MI
Peripartum Cardiomyopathy – subsequent pregnancies

Stress echo preconception to evaluate contractile reserve

Figure 6: Incidence of Maternal Complications Associated With Subsequent Pregnancy in Women With PPCM

Red bars represent women with recovered left ventricular (LV) function before subsequent pregnancy; green bars represent women with persistent LV dysfunction. HF = heart failure; LVEF = left ventricular ejection fraction. Data derived from Elkayam et al. (76).
Which of the following conditions increases a woman’s risk of cardiovascular disease

1. in vitro fertilization
2. prolonged labor
3. multiple gestation pregnancy
4. preeclampsia
5. cervical incompetence
Maternal Placental Syndromes

- Hypertensive disorders of pregnancy
- Placental abruption and infarction

- Doubles the risk of cardiovascular disease over lifetime - first described in 1927

- If preterm and severe preeclampsia – risk is highest
HAD MPS Study – Ray et al. Heart 2012

• Retrospective cohort in 1,130,764 women in Ontario
  » 6.7% had MPS (75,242)
  » 42% gestational hypertension
  » 35% preeclampsia
  » 15% placental abruption
  » 12% placental infarction
  » 3.6% combination of above

• Median duration of follow-up 7.8 years
• 61% relative increase in risk of CHF/arrhythmias
Women with gestational diabetes, preeclampsia or pregnancy induced hypertension puts a woman ‘at risk’ for CVD

Perhaps unmask early or pre-existing endothelial dysfunction

Failed Stress test of Pregnancy
Arrhythmias

- Most palpitations in pregnancy are benign
- Premature beats and sustained tachyarrhythmia become more frequent or manifest for first time in pregnancy
- Studies on use of antiarrhythmics during pregnancy are limited
- Individualized decision re: risk of continuing antiarrhythmics vs. stopping
- Postpone ablation to second trimester as high radiation
- Presence of ICD does not contraindicate future pregnancy
Arrhythmias during Pregnancy

Arrhythmogenesis

Atrial/ventricular stretch
- Ion channels activated
- Membrane depolarization
- Slowed conduction
- Shortened refractoriness

Hyperdynamic state

Higher resting heart rate
- Late potentials
- VPBs
- ↓ HR variability

↑ adrenergic responsiveness
- Estrogen ↑ myocardial α receptors → enhanced automaticity, triggered activity

Slide borrowed from L. Feinberg MD
Pregnancy Drug Class

- Category A: controlled studies in women show no risk, possibility of fetal harm remote
- Category B: animal studies have shown no risk, no controlled studies in women
- Category C: animal studies have shown adverse effects, no studies in women, or no studies in animals/women
- Category D: evidence of human fetal risk, but risk may be acceptable for some
- Category X: contra-indicated
# Cardiac Medications during Pregnancy

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Classification (Vaughan Williams for AA drugs)</th>
<th>FDA category</th>
<th>Placenta permeable</th>
<th>Transfer to breast milk (fetal dose)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abciximab</td>
<td>Monoclonal antibody with antithrombotic effects</td>
<td>C</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Inadequate human studies; should be given only if the potential benefit outweighs the potential risk to the fetus.</td>
</tr>
<tr>
<td>Acenocoumarol*a</td>
<td>Vitamin K antagonist</td>
<td>D</td>
<td>Yes</td>
<td>Yes (no adverse effects reported)</td>
<td>Embryopathy (mainly first trimester), bleeding (see further discussion in Section 5 for use during pregnancy).</td>
</tr>
<tr>
<td>Acetylsalicylic acid (low dose)</td>
<td>Antiplatelet drug</td>
<td>B</td>
<td>Yes</td>
<td>Well-tolerated</td>
<td>No teratogenic effects known (large datasets).</td>
</tr>
<tr>
<td>Adenosine*b</td>
<td>Antiarrhythmic</td>
<td>C</td>
<td>No</td>
<td>No</td>
<td>No fetal adverse effects reported (limited human data).</td>
</tr>
<tr>
<td>Aliskiren</td>
<td>Renin inhibitor</td>
<td>D</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown (limited experience).</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Antiarrhythmic (Class III)</td>
<td>D</td>
<td>Yes</td>
<td>Yes</td>
<td>Thyroid insufficiency (9%), hyperthyroidism, goitre, bradyarrhythmia, growth retardation, premature birth.</td>
</tr>
<tr>
<td>Ampicillin, amoxicillin, cephalosporins, erythromycin, mezlocillin, penicillin</td>
<td>Antibiotics</td>
<td>B</td>
<td>Yes</td>
<td>Yes</td>
<td>No fetal adverse effects reported.</td>
</tr>
</tbody>
</table>

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*a: Dibucaine (high dose) is used in atrial fibrillation control.

*b: Intravenous (IV) is preferred.
<table>
<thead>
<tr>
<th>Drugs</th>
<th>Classification (Vaughan Williams for AA drugs)</th>
<th>FDA category</th>
<th>Placenta permeable</th>
<th>Transfer to breast milk (fetal dose)</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem, rifampicin, telithromycin, vancomycin</td>
<td>Antibiotics</td>
<td>C</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Risk cannot be excluded (limited human data).</td>
</tr>
<tr>
<td>Aminoglycosides, quinolones, tetracyclines</td>
<td>Antibiotics</td>
<td>D</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Risk to the fetus exists (reserved for vital indications).</td>
</tr>
<tr>
<td>Atenolol</td>
<td>β-blocker (class II)</td>
<td>D</td>
<td>Yes</td>
<td>Yes</td>
<td>Hypospadias (first trimester); birth defects, low birth weight, bradycardia and hypoglycaemia in fetus (second and third trimester).</td>
</tr>
<tr>
<td>Benazepril</td>
<td>ACE inhibitor</td>
<td>D</td>
<td>Yes</td>
<td>Yes* (maximum 1.6%)</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>β-blocker (class II)</td>
<td>C</td>
<td>Yes</td>
<td>Yes</td>
<td>Bradycardia and hypoglycaemia in fetus.</td>
</tr>
<tr>
<td>Candesartan</td>
<td>Angiotensin II receptor blocker</td>
<td>D</td>
<td>Unknown</td>
<td>Unknown; not recommended</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Captopril</td>
<td>ACE inhibitor</td>
<td>D</td>
<td>Yes</td>
<td>Yes* (maximum 1.6%)</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>Antiplatelet drug</td>
<td>C</td>
<td>Unknown</td>
<td>Unknown</td>
<td>No information during pregnancy available.</td>
</tr>
<tr>
<td>Colestipol, clofibrate, cholestyramine</td>
<td>Lipid-lowering drugs</td>
<td>E</td>
<td>Unknown</td>
<td>Yes- lowering fat-soluble vitamins</td>
<td>May impair absorption of fat-soluble vitamins, e.g. vitamin K → cerebral bleeding (neonatal).</td>
</tr>
<tr>
<td>Danaparoid</td>
<td>Anticoagulant</td>
<td>B</td>
<td>No</td>
<td>No</td>
<td>No side effects (limited human data).</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Cardiac glycoside</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Serum levels unreliable, safe.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Calcium channel blocker (class IV)</td>
<td>C</td>
<td>No</td>
<td>Yes*</td>
<td>Possible teratogenic effects.</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Antiarrhythmic (class IA)</td>
<td>C</td>
<td>Yes</td>
<td>Yes* (maximum 1.6%)</td>
<td>Uterus contraction.</td>
</tr>
<tr>
<td>Enalapril</td>
<td>ACE inhibitor</td>
<td>D</td>
<td>Yes</td>
<td>Yes* (maximum 1.6%)</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>Aldosterone antagonist</td>
<td>-</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown (limited experience).</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>Lipid-lowering drug</td>
<td>C</td>
<td>Yes</td>
<td>Yes</td>
<td>No adequate human data.</td>
</tr>
<tr>
<td>Flecainide</td>
<td>Antiarrhythmic (class IC)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Unknown (limited experience).</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Anticoagulant</td>
<td>-</td>
<td>Yes (maximum 10%)</td>
<td>No</td>
<td>New drug. (limited experience).</td>
</tr>
<tr>
<td>Furosemide</td>
<td>Diuretic</td>
<td>C</td>
<td>Yes</td>
<td>Well tolerated; milk production can be reduced</td>
<td>Oligohydramnion.</td>
</tr>
<tr>
<td>Gemfibrozil</td>
<td>Lipid-lowering drug</td>
<td>C</td>
<td>Yes</td>
<td>Unknown</td>
<td>No adequate human data.</td>
</tr>
<tr>
<td>Gliclazide</td>
<td>Nitrater</td>
<td>B</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Bradycardia, tocolytic.</td>
</tr>
<tr>
<td>Heparin (low molecular weight)</td>
<td>Anticoagulant</td>
<td>B</td>
<td>No</td>
<td>No</td>
<td>Long-term application; seldom osteoporosis and markedly less thrombocytopenia than UF heparin.</td>
</tr>
<tr>
<td>Drug</td>
<td>Category</td>
<td>Letter</td>
<td>Can Be Used in Pregnancy</td>
<td>Contraindicated in Pregnancy</td>
<td>Maternal Side Effects</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>---------------------------------</td>
<td>--------</td>
<td>--------------------------</td>
<td>------------------------------</td>
<td>------------------------------------------------------------</td>
</tr>
<tr>
<td>Heparin unfractionated</td>
<td>Anticoagulant</td>
<td>B</td>
<td>No</td>
<td>No</td>
<td>Long-term application: osteoporosis and thrombocytopenia.</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Vasodilator</td>
<td>C</td>
<td>Yes</td>
<td>Yes (maximum 1%)</td>
<td>Maternal side effect: lupus-like symptoms; fetal tachyarrhythmias (maternal use).</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>Diuretic</td>
<td>B</td>
<td>Yes; milk production can be reduced</td>
<td></td>
<td>Oligohydramnion.</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>Angiotensin II receptor blocker</td>
<td>D</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Isosorbide dinitrate</td>
<td>Nitrates</td>
<td>B</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Bradycardia.</td>
</tr>
<tr>
<td>Lercanidine</td>
<td>Calcium channel blocker</td>
<td>C</td>
<td>Yes</td>
<td>Unknown</td>
<td>Potential synergism with magnesium sulfate may induce hypotension.</td>
</tr>
<tr>
<td>Labetalol</td>
<td>α₁-β-blocker</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Intrauterine growth retardation (second and third trimester), neonatal bradycardia and hypotension (used near term).</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>Antiarrhythmic (class IB)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Fetal bradycardia, acidosis, central nervous system toxicity.</td>
</tr>
<tr>
<td>Methyldopa</td>
<td>Central α-agonist</td>
<td>B</td>
<td>Yes</td>
<td>Yes*</td>
<td>Mild neonatal hypotension.</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>β-blocker (class II)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Bradycardia and hypoglycaemia in fetus.</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Antiarrhythmic (class IV)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Fetal bradycardia.</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>Calcium channel blocker</td>
<td>C</td>
<td>Yes (maximum 1.8%)</td>
<td></td>
<td>Tocolytic; s.i. application and potential synergism with magnesium sulfate may induce hypotension (mother) and fetal hypoxia.</td>
</tr>
<tr>
<td>Phenprocoumon</td>
<td>Vitamin K antagonist</td>
<td>D</td>
<td>Yes</td>
<td>Yes (maximum 10%), well tolerated as inactive metabolite</td>
<td>Coumarin-embryopathy, bleeding (see further discussion in Section 5 for use during pregnancy).</td>
</tr>
<tr>
<td>Procainamide</td>
<td>Antiarrhythmic (class IA)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Unknown (limited experience).</td>
</tr>
<tr>
<td>Propafenone</td>
<td>Antiarrhythmic (class IC)</td>
<td>C</td>
<td>Yes</td>
<td>Unknown</td>
<td>Unknown (limited experience).</td>
</tr>
<tr>
<td>Propranolol</td>
<td>β-blocker (class II)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Bradycardia and hypoglycaemia in fetus.</td>
</tr>
<tr>
<td>Quinidine</td>
<td>Antiarrhythmic (class IA)</td>
<td>C</td>
<td>Yes</td>
<td>Yes*</td>
<td>Thrombopenia, premature birth, VIIIth nerve toxicity.</td>
</tr>
<tr>
<td>Ramipril</td>
<td>ACE inhibitor</td>
<td>D</td>
<td>Yes</td>
<td>Yes (maximum 1.6%)</td>
<td>Renal or tubular dysplasia, oligohydramnion, growth retardation, ossification disorders of skull, lung hypoplasia, contractures, large joints, anaemia, intrauterine fetal death.</td>
</tr>
<tr>
<td>Sotalol</td>
<td>Antiarrhythmic (class III)</td>
<td>B</td>
<td>Yes</td>
<td>Yes*</td>
<td>Bradycardia and hypoglycaemia in fetus (limited experience).</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>Aldosterone antagonist</td>
<td>D</td>
<td>Yes</td>
<td>Yes (maximum 1.2%); milk production can be reduced</td>
<td>Antiandrogenic effects, oral clefts (first trimester).</td>
</tr>
<tr>
<td>Statins</td>
<td>Lipid-lowering drugs</td>
<td>X</td>
<td>Yes</td>
<td>Unknown</td>
<td>Congenital anomalies.</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>Antiplatelet</td>
<td>C</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown (limited experience).</td>
</tr>
</tbody>
</table>
What happened to our patients?

- 42 year old s/p VF arrest with ostial LAD occlusion treated with Xience to LAD - July 2011
  Xience to RCA September 2011

- 32 year old with multivalvular rheumatic heart disease

- 35 year old with peripartum cardiomyopathy
Conclusions

• Rising incidence of heart disease during pregnancy

• Counseling and management of patients with heart disease should begin before conception

• All diseases are not created equal so evaluation of maternal risk is key

• Limited data on most conditions

• Moderate or high risk patients require close collaboration between OB, anesthesia and cardiology