Doctor, can I have a baby?

Pre-pregnancy cardiac consultation.

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Risks of Pregnancy

- Hemodynamic burden
- Vascular changes – histologic, reactivity
- Coagulation – hypercoagulability, use of anti-coagulants
- Fluid and electrolyte balance
- Anemia, endocrine-metabolic changes
- Risks to fetus

Etiology of cardiac disease

- Congenital heart disease
- Rheumatic heart disease
- Cardiomyopathy (dilated, hypertrophic, post-partum, metabolic, post adriamycin)
- Ischemic heart disease
- Arrhythmia and conduction disease
- Pulmonary hypertension – PAH, thrombo-embolic, other (non-congenital)

Severity of cardiac disease

- Minor problem – no clinical consequences – consultation mainly regarding risk to fetus, risk of endocarditis
- Moderate problem – pregnancy poses a definite risk but is feasible with all precautions taken and best medical care
- Major problem – major risk to mother and fetus despite optimal management – immediate and long term risk
- Possiblity of reducing risk by pre-pregnancy intervention.

Hemodynamic changes in pregnancy

- Cardiac output increases by 30-50%
- Heart rate increases by 20%
- Plasma volume increases by 40-50%
- Pulse pressure increases
- Systemic and pulmonary vascular resistance decrease
- Venous pressure unchanged (but peripheral increases due to compression by uterus)

Hemodynamic changes during labor

- Changes are more pronounced when gravida is supine compared to lateral decubitus position
- Oxygen consumption increases X3
- Cardiac output increases 15-25%
- Reflex bradycardia
- Blood loss - 0.5 – 1 liter

Respiratory changes in pregnancy

- Increase in minute ventilation (tidal volume)
- Decrease in residual volume
- Increased arterial pO2
- Decreased arterial pCO2
- Compensated respiratory alkalosis

Non hemodynamic changes of pregnancy

- Hematologic – plasma volume increases 40-50%, red cell mass increases 20-30%
- Hypercoagulability – hormone induced, during late pregnancy
- Vascular – fragmentation of reticular fibers, decrease acid mucopolysacharides, loss of normal corrugation of elastic fibers, hypertrophy- hyperplasia of smooth muscle

Atrial septal defects and pregnancy

- Usually not a problem, even with large shunts
- Many patients are first diagnosed after multiple uneventful and successful pregnancies.
- Risk of atrial flutter-fibrillation, risk of paradoxical emboli (leg care)
- Treatment has become much simpler with device closure (for II ASD)

PDA, VSD and pregnancy

- If small- no dilatation of left heart chambers - SBE prophylaxis only
- If clinically important – better treat before pregnancy, although risk of pregnancy is small – mainly atrial arrhythmia
- If patient is already pregnant, treatment with vasodilators may be justified

Pulmonary valve stenosis

- When mild – not a problem
- When moderate or severe – can cause fatigue, chest discomfort
- Treatment of valve is easy and successful long-term. Preferably done beforehand
- Patient needs volume to sustain cardiac output. Avoid diuretics for edema
- Long term effect not known – myocardial restriction?

Aortic coarctation

- Can be treated percutaneously beforehand
- Toxemia less frequent than in other forms of hypertension
- Increased risk of rupture and dissection, especially in conjunction with bicuspid aortic valve
- Rupture of berry aneurysm
- Heart failure - rare
- Risk of multiple pregnancies on aortic wall long term are not known, even after repair

Aortic valve and sub-aortic stenosis

- Bicuspid – SBE, dissection
- Aortic and sub-aortic stenosis – if moderate or severe – may become symptomatic.
- Literature not reliable but risk is probably similar to surgical risk. Better operate.
- Marked increase of gradient - frightening
- Regurgitation – well tolerated due to increase of HR and decrease of PVR. Vasodilators indicated
- High risk of endocarditis

Surgical considerations in women of childbearing potential

- Ross operation for aortic valve disease
- Bio-prosthetic valves
- Balloon aortic valvoplasty not a good option above age 25 years.
- Dacron patch aortoplasty increases the risk of pregnancy – dehiscence

Fallot's tetralogy and pulmonary atresia

- Simple Fallot's should be operated. Mild TOF become more cyanosed. Pink Fallot's may have pulmonary congestion, LV failure. Abrupt shifts of resistance during delivery may be dangerous
- Unoperable (complex) pulmonary atresia should be evaluated individually – risk to fetus becomes a major problem with O2 sat. below 85% at rest.
- Operated TOF – residual VSD, PS or more commonly severe pulmonary regurgitation. Difficult decision – no curative surgery. Judge by functional class

Ebstein's anomaly

- Increased incidence of arrhythmia in WPW
- Volume overload of the ventricle due to tricuspid regurgitation
- Risk of cyanosis, paradoxical embolism – increase of right heart filling pressure + patent foramen ovale
- Increased risk to congenital anomalies in the fetus

Patients with systemic right ventricle

- Congenitally corrected transposition, transposition after Mustard/Senning
- Right ventricle unadjusted for systemic circulation.
- Tricuspid valve incompetence, baffle leaks, baffle stenosis, bradycardia-heart block
- Correct the treatable problems
- Treat with vaso-dilators (prophylactic)
- Long term?

Complex congenital heart disease

- Rare natural survivors, some palliated with Glenn or Fontan
- Individualize risk according to: functional capacity, degree of O2 saturation, pulmonary pressure, myocardial function and arrhythmia.
- Physiology like TOF or Eisenmenger.
- In Fontan – risk of thromboembolism, arrhytmia, paradoxical embolism, myocardial dysfunction, protein losing enteropathy

Marfan Syndrome

- Risk of aortic dilatation and dissection during pregnancy – even when baseline dimensions are normal
- Unacceptable risk when pre-conception aorta is >4.0 cm and in patients with malignant family history
- Use of beta blockers and close monitoring of the aorta during gestation
- Ehlers-Danlos type IV and Loeys-Dietz syndrome even more dangerous

Mitral stenosis

- Intervention beforehand
- High dose beta-blockers

Cardiomyopathies

- Adriamycin - pre-pregnancy functional class and myocardial function are predictive of pregnancy outcome and long term myocardial function
- Post partum cardiomyopathy – if full recovery – pregnancy possible but recurrence may happen
- Exercise echocardiogram

Heart block and arrhythmia

- Congenitally corrected transposition, post Mustard/Senning, idiopathic
- Implantation of pace-maker according to functional state. Treadmill testing
- Problems with anti-arrhythmic drugs: amiodarone – iodine – fetal goiter
- SVT -beta blockers preferable to verapamil
- Long QT – increased incidence of events, mainly post-partum

Eisenmenger syndrome

- Most dangerous period – around gestation and puerperium. Reported death – 40-70%. No evidence of improvement with new drugs.
- Abrupt changes in systemic and pulmonary vascular resistance cannot be compensated. Decrease in resistance results in deepening cyanosis. Increase causes abrupt fall in cardiac output and fatal syncope. (severe pain, bearing down)
- Pulmonary vessels respond with vasoconstriction worsening the already poor pulmonary flow, starting a vicious cycle

Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996

- Eisenmenger s. – 73 pts
- iPAH – 30 pts
- oPH – 25 pts

- Eisenmenger s.

1. Three died during pregnancy
2. Twenty three died within 30 days of delivery, while 14 of them died between 2-nd and 7-th days of delivery

J of Am Coll Cardiol 1998

New Era?

- New (advanced) PAH therapies
- Improvement in management of high risk pregnancies
- Earlier recognition of the underlying disease
- Improved understanding of cardiopulmonary pathophysiology
- Better obstetric/ anesthetic management
- Introduction of multidisciplinary approach

Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension?

Review

E. Bedard, K. Dimopoulos, M. Gatzoulis
European Heart Journal 2009; 30 : 256- 265

Results

- In total 73 parturients with PAH
- Three subgroups:
  - iPAH, CHD – PAH, oPH
- Overall median age -29 (21-39) years
- NYHA FC III- IV
  - 61% of parturients (Classified 44/ 73pts)

Management

	iPAH (n=29)	CHD-PAH (n=29)	oPH (n=15)
Hospital admission, wks of pregnancy	28 (12-37)	32 (17-40)	28 (23-35)
Delivery, wks of pregnancy	34 (25-39)	34 (26-40)	32 (26-36)
Mode of delivery			
-Vaginal	8 (30%) *	8 (28%)	1 (7%) **
- Cesarean section	19 (70%)	21 (72%)	13 (93%)
Monitoring – peripartum			
- R. artery &/or CVP	9 (31%)	11 (38%)	5 (33%)
- Swan – Ganz catheter	22 (76%)	9 (31%)	9 (60%)
Anesthesia			
- Regional	18 (67%) *	17 (59%)	4 (28%) **
- General	8 (29%)	9 (31%)	6 (43%)
- Not reported	1 (4%)	3 (10%)	4 (29%)

* 2 pts died before delivery; ** one pt died before delivery

Management. Therapy

	iPAH (n=29)	CHD -PAH (n=29)	oPH (n= 15)
Antithrombotic			
- During pregnancy	15 (52%)	7 (24%)	7 (47%)
- Post- partum (PP)	11 (41%)	9 (31%)	5 (36%)
Advanced therapy ^	**21 (72%)**	**15 (52%)**	**7 (47%)**
- Nitric oxide	7 (24%)	7 (24%)	5 (33%)
- Prostacyclin analogues	18 (62%)	9 (31%)	3 (20%)
- Bosentan *	1 (3%)	1 (3%)	0 (0%)
- Sildenafil *	1 (3%)	4 (14%)	0 (0%)
-- None	8 (28%)	14 (48%)	8 (53%)
- CCB	9 (31%)	6 (21%)	4 (27%)

* Given post-partum; ^ During pregnancy, labour or delivery

Outcomes

	iPAH (n= 29)	**CHD –PAH (n= 29)**	**oPH (n= 15)**
Follow-up, days PP	310 (± 229)	243 (± 147)	255 (± 196)
Maternal death	**5 (17%) ^**	**8 (28%) ^^**	**5 (33%)**
- During pregnancy	2 (7%)	0 (0%)	1 (7%)
- Wks of pregnancy	12 & 28	-	23
- PP (≤ 90 days)	3 (10%)	8 (28%)	4 (26%)
- Days PP	**14 (7-90)**	**6 (0-24)**	**15 (1-21)**
Other complications *			
- Pulmonary hypertensive crisis	3 (10%)	2 (7%)	0 (0%)
- Pulmonary Emboli	0 (0%)	4 (14%)	3 (20%)
- RV failure/ c. collapse	9 (31%)	9 (31%)	4 (27%)
- Bleeding, Hg fall + transfusion	3 (10%)	11 (38%)	4 (27%)

* Including pts who did not die; ^ 1 late maternal death – 19 mo post delivery;
^^ 1 late maternal death – 14 mo post delivery

Outcomes

	iPAH (n= 29)	CHD – PAH (n= 29)	oPH (n= 15)
Premature delivery *	23 (85%) ^	25 (86%)	14 (100%) ^^
Neonatal or fetal death	3 (10%) ^^^	2 (7%) ***	2 (13%)*^
Intrauterine growth retardation	1 (3%)	7 (24%)	5 (33%)

* Delivery that occurs before 37 completed weeks of gestation

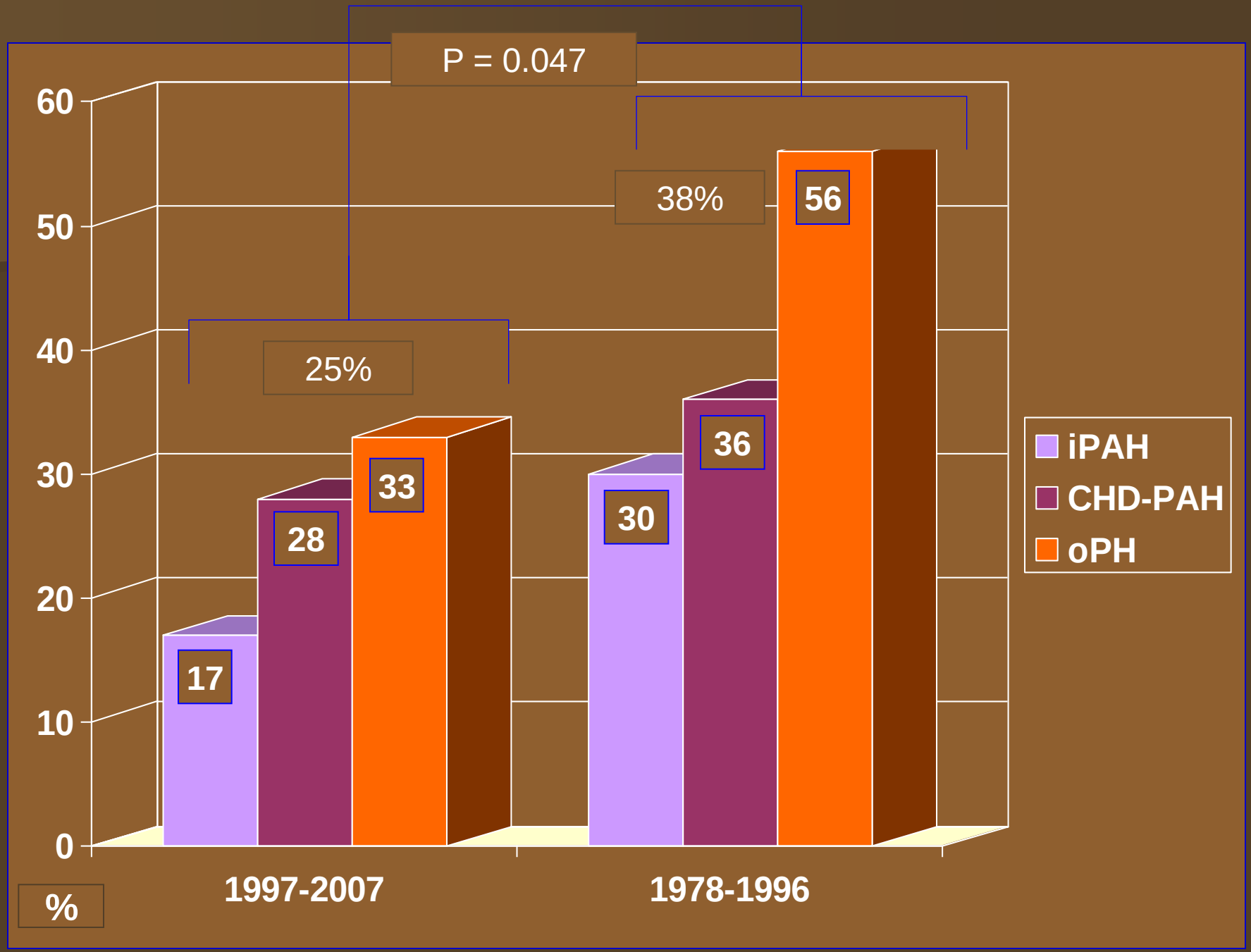
^ 2 pts died before delivery; ^^ one pt died before delivery

^^^ 2 secondary to maternal death; 1 a twin, died in utero at 17 weeks of gestation

*** 1 stillbirth at 36 wks; 1 premature delivery at 30 wks (died 26 days- sepsis)

*^ 1 fetal death d/t maternal death (23 wks); 1 premature delivery (32 wks), died in early neonatal period

Maternal mortality & predictors of outcome


P = 0.047
38%
25%
60
50
40
30
20
10
0
%
17
28
33
30
36
56
1997-2007
1978-1996
iPAH
CHD-PAH
oPH

Maternal death & predictors of outcome

- NS differences in mortality were seen between the 3 subgroups over the last decade ($p = 0.41$)
- Pts receiving general anesthesia were 4 times more likely to die, compared with pts receiving regional anesthesia (OR 4.37, 95% CI 1.28- 16.5, $p = 0.02$)
- Primigravidae were at higher mortality risk compared with those with previous pregnancies (OR 3.70, 95% CI 1.15-12.5, $p = 0.03$)
- No other clinical variables, including advanced PAH therapies related to maternal mortality

Study limitations

- Possible publication bias towards cases with a favorable outcome, resulting in artificially lower mortality
- Number of late death could be underestimated (short term follow – up)
- Highly heterogeneous population of pts with PAH
- Relatively small number of pregnant women

Pregnancy outcome in patients with pulmonary arterial hypertension receiving prostacyclin therapy.

Bendayan D ,**Hod M** ,**Oron G** ,**Sagie A** ,**Eidelman L** ,**Shitrit D** ,**Kramer MR**.
Pulmonary Institute, the Perinatal Division and WHO Collaborating Center for Perinatal Care, Department of Obstetrics and Gynecology, Beilinson Campus, Petah Tiqva, and Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.

BACKGROUND: Pregnancy is contraindicated in cases of pulmonary hypertension, a highly morbid disease affecting young women of childbearing age.
CASES: We describe the pregnancies of 3 patients with pulmonary arterial hypertension (idiopathic, Eisenmenger syndrome, and related to systemic lupus erythematosus). They received epoprostenol and low-molecular-weight heparin throughout pregnancy.
The patient with Eisenmenger syndrome started epoprostenol in gestational week 16. Cesarean delivery under general anesthesia was performed at 28-33 weeks of gestation; early delivery was necessary in the patient with Eisenmenger syndrome because of fetal growth restriction. All deliveries were uneventful, and birth weights were 1,700, 1,500, and 795 g.
There were no postpartum complications.
CONCLUSION: Pregnancy in women with pulmonary hypertension should still be considered high risk for both mother and child, but stable patients on epoprostenol may successfully complete pregnancy.

Conclusion

- Maternal mortality in parturients with PAH remains prohibitively high (lower rates of death during the last decade)
- Early advice on the risk of pregnancy and methods of contraception is of paramount importance
- Women with PAH who become pregnant should followed by a multidisciplinary team, and advanced PAH therapies should be given consideration in a timely fashion

Guidelines

- Canadian Consensus Conference. Recommendations for the Management of Adults with Congenital Heart Disease, 2001
- Management of Grown – Up CHD (ESC), 2003
- Expert consensus document on management of cardiovascular diseases during pregnancy (ESC), 2003
- Guidelines on diagnosis and treatment of PAH, 2004 (ESC)
- ACC/ AHA Guidelines for the Management of Adults with Congenital heart Disease, 2008

ACC/ AHA ACHD Guidelines, 2008

- Women with severe CHD – PAH, especially with Eisenmenger physiology should be counseled about the absolute avoidance of pregnancy in view of the high risk of maternal death (1B)
- Women with CHD – PAH who become pregnant should undergo the earliest possible pregnancy termination after counseling (1C)
- Surgical sterilization carries some operative risk for women with CHD - PAH, but is a safer option than pregnancy(1C)

Pre-pregnancy evaluation

- Stress-echo – useful in evaluation of FC and hemodynamic/myocardial response to stress
- Holter monitoring
- Cardiac catheterization in complex cases
- Nuclear perfusion studies (IHD)
- MRI CT-angio (aneurysm, accurate measurements of aorta, pulm. artery)

Pregnancy and Prosthetic Heart Valves

Complications of Prosthetic Heart Valves

- annual rate of complications in appropriately managed, non-pregnant patients = 3%
- thromboembolism
- structural failure
- bleeding due to anticoagulation
- infection

Factors that increase thromboembolic risk include:

- A mechanical prosthesis versus a bioprosthetic valve or homograft
- History of a prior thromboembolic event
- Atrial fibrillation
- Prosthesis in the mitral position
- Multiple prosthetic valves

Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature.

Chan WS; Anand S; Ginsberg JS (Women's college hospital, Toronto)
Arch Intern Med 2000;160:191-6.

- comparison of three regimens: oral anitcoagulants throughout, replacement with heparin wks 6-12, heparin throughout (LMW heparin not included)
- 976 women, 1234 pregnancies, 1966-1997, 7% bileaflet
- warfarin - embryopathy 6.4% (CI 4.6-8.9%)
- heparin replacement 6-12 wks - eliminates embryopathy
- spontaneous abortion, stillbirths, and neonatal deaths - similar between the two regimens
- maternal mortality was 2.9% (CI 1.9%-4.2%)
- OA=lowest risk of valve thrombosis 3.9% (CI 2.9-5.9%)
- heparin replacement 6-12 9.2% (CI 5.9%-13.9%)
- major bleeding - 2.5% (80% around delivery)

Prosthetic valve thrombosis in pregnancy

- Prosthetic valve thrombosis in pregnancy. A single-center study of 12 cases
  Sahnoun-Trabelsi I; Jimenez M; Choussat A; Roudaut R
  Arch Mal Coeur Vaiss 2004;97:305-10.
- 10 women, 12 episodes.
- 8 mitral, 4 aortic
- 1 cage-ball, 3 tilting disk, 8 bileaflet
- treatment: surgery 4, thrombolysis 7, heparin 2 (one with heparin converted to surgery)
- 3 deaths (30%) - all with mitral prostheses
- thrombolysis - 1 major bleeding requiring drainage, no ebmolization
- 1 fetal loss post surgery in a survivor

structural failure

- bio-prosthetic valves: calcification and stenosis or degeneration and regurgitation
- xenograft valves - 30-35% in 10-15 years
- homograft valves - 10-20% in 10-15 years
- pregnancy does not accelerate valve degeneration according to more recent and better conducted studies
- Young age is an important predictor of early structural degeneration

Long-term survival and valve-related complications in young women with cardiac valve replacements.

North RA; Sadler L; Stewart AW; McCowan LM; Kerr AR; White HD

Circulation 1999;99:2669-76.

Department of Obstetrics and Gynaecology, University of Auckland, New Zealand.

women 12 to 35 years old, valve replacements between 1972 and 1992. Follow-up was available in 93%. The 232 women were followed up for 1499 patient-years. Ten-year survival of women with mechanical (n=178), bioprosthetic (n=73), and homograft (n=72) valves was 70%, 84% and 96% P=0.002. Thromboembolic events - 45% mechanical valves within 5 years, compared with 13% with bioprosthetic valves. Valve loss at 10 years - bioprosthetic valves 82% mechanical 29% homograft 28%. Mechanical valves may be associated with reduced patient survival in young women. Thromboembolic complications, often with long-term sequelae, were common with mechanical valves. Pregnancy did not increase structural deterioration or reduce survival of bioprosthetic valves.

warfarin

- lowest rate of maternal complications
- congenital fetal malformations when used between weeks 6-12 gestation
- specific embryopathy affecting cartilage and bone.
- fetal CNS abnormalities have been associated with warfarin therapy at any stage of pregnancy
- estimated incidence of 5 to 7 percent
- correlate with the dose - two papers from the same institution, small numbers

Risk of warfarin during pregnancy with mechanical valve prostheses.

Cotrufo M; De Feo M; De Santo LS; Romano G; Della Corte A; Renzulli A; Gallo C

Obstet Gynecol 2002;99:35-40.

Department of Cardio-Thoracic and Respiratory Sciences, V. Monaldi Hospital, Naples, Italy

OBJECTIVE: To assess the determinants of pregnancy outcome in patients with mechanical valve prostheses anticoagulated with warfarin. METHODS: Between January 1987 and January 2000, 52 patients with mechanical valve prostheses who had 71 pregnancies were anticoagulated with warfarin for the entire duration of pregnancy. Warfarin was withdrawn 48 hours before and 24 hours after a scheduled cesarean delivery carried out by the end of the 37th gestational week. The targeted international normalized ratio ranged between 2.25 and 4.0, depending on the prosthetic model. Exact univariate and multivariable analyses were performed to assess which among the following variables predicted poor pregnancy outcome: patient age, prosthetic model, site of implantation, average international normalized ratio, and average daily dose of warfarin. RESULTS: Pregnancy loss occurred in 23 of 71 of pregnancies, stillbirth in five of 71, embryopathy in four of 71 (two aborted fetuses and two full-term infants). There were no maternal deaths or thromboembolic or hemorrhagic complications. Warfarin daily dosage over 5 mg per day was a significant predictor of poor pregnancy outcome ($P < .001$). CONCLUSION: The risk for pregnancy complications in patients treated with sodium warfarin is higher when the mean daily dose exceeds 5 mg.

A previous paper from the same group (JACC 1999) had two valve thromboses

unfractionated heparin

- not teratogenic
- very few reports on heparin throughout pregnancy - risk of osteoporosis (reversible to some extent post partum)
- most replace warfarin during wks 6-12
- older reports - old generation valves and inadequate dosing (very difficult to maintain
- adequate dosing - aptt > x2 baseline levels reduces valve thrombosis but not embolism

low molecular weight heparin

- potential benefits - less impact on bone density, less bleeding and thrombopenia, more predictable therapeutic levels
- but - FDA 2002: enoxaparin not recommended for thromboprophylaxis in pregnant women with prosthetic heart valves.
- endorsed by american college of obgyn
- but - american college chest physicians 2004: LMWH is a treatment option
- recommended dose enoxaparin - 1 mg/kg x2, anti Xa peak 4-6 hours post injection 1-1.2 u/ml

Enoxaparin treatment in women with mechanical heart valves during pregnancy.

- OBJECTIVE: This prospective audit reports pregnancy outcomes, anticoagulation complications, and anti-Xa levels in women with mechanical heart valves who were treated with therapeutic enoxaparin plus aspirin during pregnancy. STUDY DESIGN: Between 1997 and 1999, 11 women with mechanical heart valves were treated with enoxaparin, 1 mg/kg twice daily, and aspirin, 100 to 150 mg daily during 14 pregnancies. Predose and 4-hour postdose anti-Xa levels were monitored monthly. RESULTS: There were 9 live births, 3 miscarriages, and 2 terminations. In 48 months of enoxaparin treatment, one woman who had a documented valve thrombosis when she presented at 8 weeks' gestation also had a valve thrombosis at 20 weeks' gestation. There were no enoxaparin-related hemorrhagic complications. Mean (SD) anti-Xa levels were 0.46 (0.12) U/mL predose and 0.89 (0.22) U/mL 4 hours postdose. CONCLUSION: Successful pregnancy outcome may be achieved with therapeutic subcutaneous enoxaparin, but its efficacy at preventing valve thrombosis remains uncertain. Further data are required before use of enoxaparin during pregnancy in women with mechanical heart valves can be recommended.

Low molecular weight heparin for the prophylaxis of thromboembolism in women with prosthetic mechanical heart valves during pregnancy.

Oran B; Lee-Parritz A; Ansell J

Thromb Haemost 2004 Oct;92(4):747-51.

Department of Medicine, Boston University Medical Center

review the risks of maternal and fetal complications with mechanical heart valves treated with LMWH during pregnancy.

MEDLINE and EMBASE (1989 to 2004) abstract proceedings, and reference lists of selected articles.

Among 81 pregnancies in 75 women, the proportion of valve thrombosis was 8.64% (7/81; 95% CI, 2.52%-14.76%). The frequency of overall thromboembolic complication (TEC) was 12.35% (10/81; 95% CI, 5.19%-19.51%). Nine of ten patients with TEC received a fixed dose of LMWH and two of these received a fixed low dose of LMWH. Among 51 pregnancies whose anti-factor Xa levels were monitored, only one patient was reported to have a thromboembolic complication. The frequency of live births with LMWH was 87.65% (95%CI, 80.49%-94.81%). In pregnant women with mechanical heart valves, LMWH appears to be a suitable option to a vitamin K antagonist. The use of LMWH warrants monitoring and appropriate dose adjustments to maintain a 4-6 hr post-injection anti-factor Xa level at a minimum of 1.0 U/ml to decrease the incidence of TEC.

supplemental aspirin

compare the effectiveness and safety of adding antiplatelet therapy to standard oral anticoagulation among patients with prosthetic heart valves.

Cochrane Central Register of Controlled Trials etc.

Eleven studies involving 2,428 subjects met the inclusion criteria. Year of publication ranged from 1971 to 2000. Compared with anticoagulation alone, the addition of an antiplatelet agent reduced the risk of thromboembolic events - odds ratio 0.39 (95% confidence interval 0.28 to 0.56; p<0.00001)) and total mortality - odds ratio 0.55 (95% confidence interval 0.40 to 0.77; p=0.0003)). Aspirin and dipyridamole reduced these events similarly. The risk of major bleeding was increased when antiplatelet agents were added to oral anticoagulants odds ratio 1.66 (95% confidence interval 1.18 to 2.34; p=0.003)).

dipyridamole or low-dose aspirin, to oral anticoagulation decreases the risk of systemic embolism or death among patients with prosthetic heart valves. The risk of major bleeding is increased with antiplatelet therapy. These results apply to patients with mechanical prosthetic valves or those with biological valves and indicators of high risk such as atrial fibrillation or prior thromboembolic events. The effectiveness and safety of low dose aspirin (100 mg daily) appears to be similar to higher dose aspirin and dipyridamole.

ACC/AHA guidelines — The 2006 ACC/AHA guidelines emphasize the following points
Anticoagulation during pregnancy in women with mechanical prosthetic valves must ensure continuous, monitored, therapeutic anticoagulation.
Pregnancy tests should be monitored in women who are attempting pregnancy while are on long term warfarin to ensure prompt adjustment of anticoagulation therapy if needed.
Women who elect to stop warfarin between weeks 6 and 12 of gestation, to decrease the risk of fetal defects, should receive continuous IV, or dose adjusted SQ UFH or LMWH.
The choice of anticoagulant up to week 36 of gestation includes warfarin, continuous IV UFH, dose adjusted SQ UFH, or dose adjusted SQ LMWH, after discussion with the patient of the fetal and maternal risks of each option. Dose adjustment is recommended as follows:

- LMWH twice daily to maintain an anti-Xa level between 0.7 and 1.2 U/ml 4 hours after administration.
- UFH to achieve an aPTT at least twice control.
- Warfarin to achieve an INR goal of 3.0 (range 2.5 to 3.5).
- Low dose aspirin (75 to 100 mg daily in the second and third trimester) is reasonable in addition to anticoagulation with warfarin or heparin.

Warfarin should be discontinued and continuous IV UFH given starting two to three weeks before planned delivery. After delivery, UFH is resumed four to six hours after delivery and warfarin is restarted, in the absence of significant bleeding.
The AHA guidelines emphasize that SQ heparin dosing (UFH or LMWH) requires dose adjustment based on frequent monitoring of the level of anticoagulation.

The 2008 Eighth American College of Chest Physicians (ACCP) guidelines

- Aggressive adjusted-dose LMWH therapy throughout pregnancy (eg, enoxaparin initiated at a dose of 1 mg/kg subcutaneously every 12 hours). It is suggested that the dose be adjusted to achieve a four hour post-injection anti-Xa heparin level at the manufacturer's peak anti-Xa level (approximately 1.0 U/mL).
- Aggressive adjusted-dose UFH throughout pregnancy. Heparin is administered subcutaneously every 12 hours in doses adjusted to keep the mid-interval aPTT at least twice the control, or an anti-Xa heparin level of 0.35 to 0.70 U/mL.
- UFH or LMWH therapy (using the above regimens) until the 13th week, a change to warfarin until close to delivery, and then restart UFH or LMWH therapy until delivery. Warfarin should not be given close to term in order to minimize the possibility of serious bleeding caused by the trauma of delivery to the anticoagulated fetus.
- In women judged to be at very high risk of thromboembolism in whom concerns exist about the efficacy and safety of UFH or LMWH as dosed above (eg, older generation prosthesis in the mitral position or history of thromboembolism), vitamin K antagonists are suggested throughout pregnancy with replacement by UFH or LMWH (as above) close to delivery, after a thorough discussion with the patient of the potential risks and benefits of this approach.

Urgent delivery
patient on LMWH or UFH

- discontinuation of therapy and a delay of four to six hours without protamine
- Vaginal delivery is preferred unless there are obstetric indications for cesarean delivery
- emergent delivery - protamine (will only partially reverse the anticoagulant effect of LMWH).

urgent delivery
patient on oral anticoagulants

- Because the fetus is also anticoagulated, cesarean delivery is preferred to reduce risks of fetal trauma and hemorrhage.
- If time allows, delay and/or administration of small doses of vitamin K to a target INR of 2.0 should permit safe cesarean delivery.
- If emergent delivery is necessary, fresh frozen plasma should be administered prior to cesarean delivery in sufficient amount to reach a target INR of 2.0
- Depending upon timing and dose, the administration of vitamin K to the mother prior to delivery can also reverse the effect of OACs in the fetus and therefore reduce the risk of fetal hemorrhage. If the mother was not fully reversed at the time of delivery, the newborn may be given FFP and vitamin K.

Postpartum

- In the absence of significant bleeding, anticoagulation should be resumed shortly after delivery.
- UFH or LMWH should be resumed four to six hours after delivery.
- OACs can be resumed the same day.
- Heparin can be discontinued once the INR is in the therapeutic range, although standard anticoagulation guidelines suggest continuing heparin until the INR has been therapeutic for 24 to 48 hours.

preparation for delivery

- Oral anticoagulants should be switched to LMWH or UFH, usually no later than 36 weeks.
- Women treated with LMWH should be switched to IV UFH at least 36 hours prior to the induction of labor or cesarean delivery.
- UFH should be discontinued four to six hours prior to anticipated delivery, and should be restarted four to six hours after delivery if there are no bleeding complications

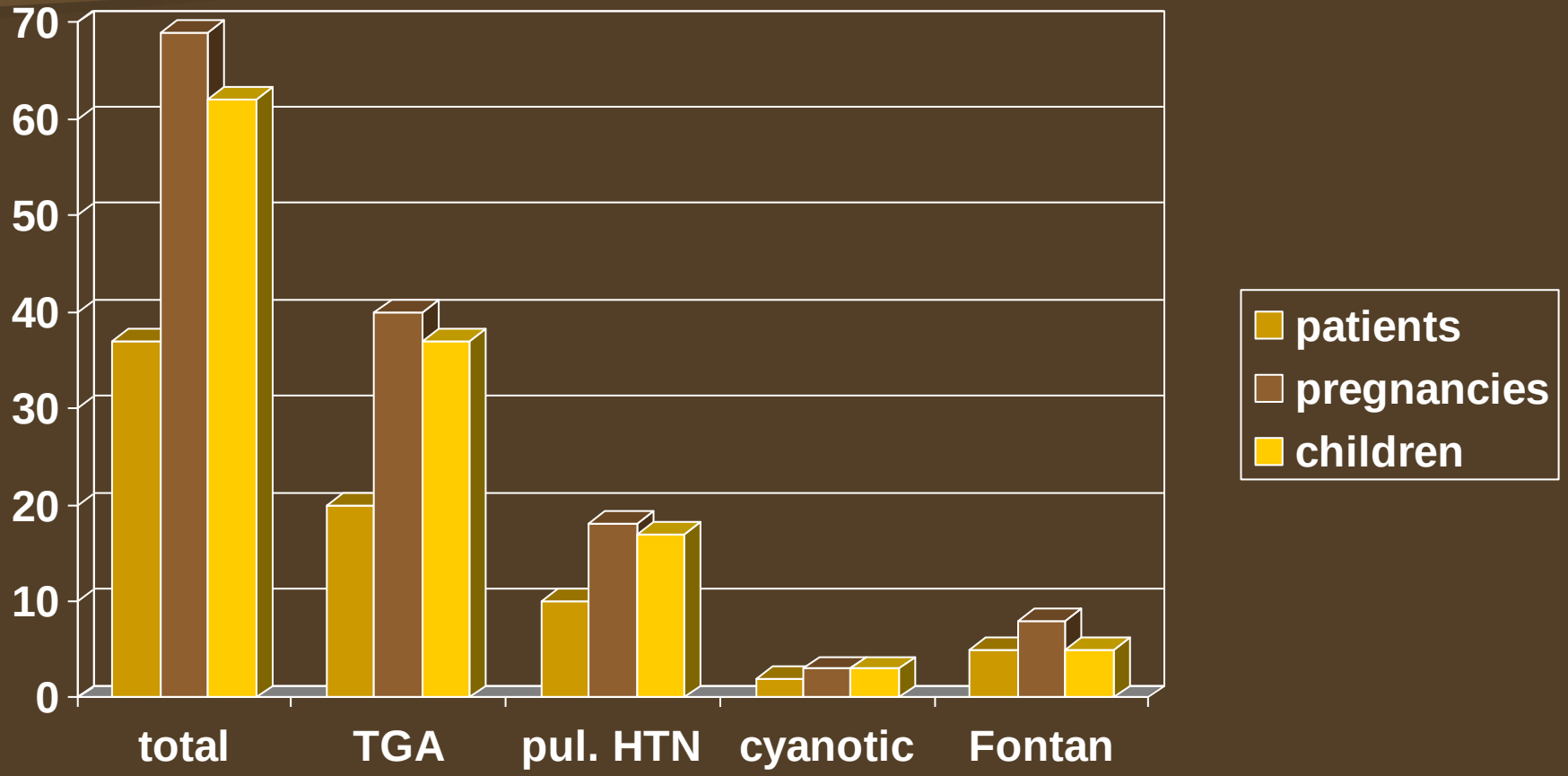
Pregnancy in Complex Congenital Heart Disease

The Rabin Medical Center experience

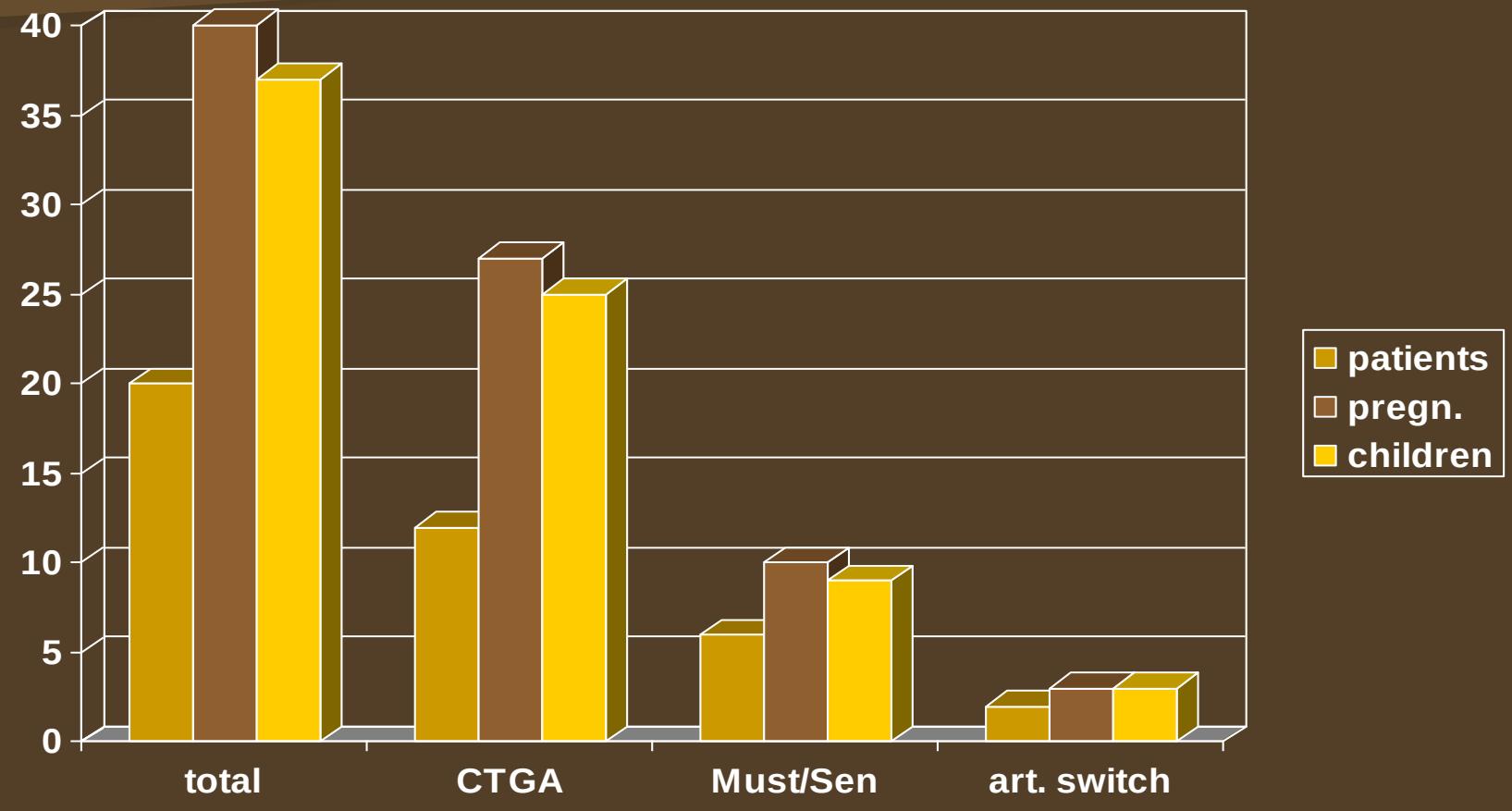
Introduction

- One of the main concerns pertaining to female patients with congenital heart disease, is their ability to sustain a successful pregnancy and delivery without major risk to mother or fetus
- This issue is particularly important in patients with complex congenital malformations, either operated or natural survivors.
- To date, little has been published on this subject.

37 patients, total - 69 pregnancies, 62 children



transposition complex



congenitally corrected transpositon

- 12 patients, 27 pregnancies, 25 children
- Uncomplicated pregnancies:
- 2 previous surgery
- One with VSD had banding then debanding + VSD closure, perm. PM - 3 uneventful preg. & deliv. by 25 years of age. No medication because husband is not aware of heart condition!
- One with VSD closure + perm. PM. Known to have severe systemic tricuspid regurgitation for the last 10 years. Avoided medical trt. and FU. 3 uneventful preg. & deliv. by 28 y. Recent successful TVR - mechanical, age 34 y.

CTGA - uncomplicated pregnancies - continued

- 7 pts. without associated lesions, including 2 sisters, had a total of 13 children. One is well at 68 y, one on medication for RV dysfunction at 57 y, one died at 64 y in CHF after TVR + PM, and two were diagnosed only at 49 and 70 years of age. The latter died at 80 y.
- 1 pt. with mod. sub PS and small VSD had 3 children, first child at 16 y, and is well at 40y.

CTGA - complicated pregnancies

- One pt. with SBE X 3, severe sub PS and a large II ASD had one IVF pregnancy. During pregnancy increased severity of mitral regurgitation (from mild to moderate), otherwise well. Later she had device ASD closure. Now well at 39 years.
- One 20 y.o. pt.with mod. TR on medication became pregnant with worsening TR + RV dysfunction despite renewal of medication on 2nd trimester, had termination of preg. at 22 wks. gestation and awaits TVR

Atrial switch - Mustard/Senning

- 6 pts, 10 pregnancies, 9 children
- 2 pts. had xenograft replacement of the TV due to severe tricuspid regurgitation before pregnancy. One remained with mild RV dysfunction.
- 3 pts. received vasodilators during preg.
- 2 pts. had mildy symptomatic bradycardia
- There was no worsening TR or RV function.
- One pt. had fetocide at 38 wks. gestation for severe intracranial hemorrhage. 2nd preg. & deliv. OK

TGA post arterial switch - Jatene

- 2 patients, 3 children
- one born in 1979 who has a dilated LV, aortic regurgitation, small residual VSD, small PDA and is non-compliant with medication and follow up, had 2 uneventful preg. & deliv. She had a permanent pacemaker implanted 3 years ago.
- one born in 1988 had one uneventful preg. & delivery

Pulmonary hypertension -1

- 10 patients, 18 pregnancies, 17 children
- 8 Eisenmenger syndrome - 3 PDA, 2 VSD, 1 ASD, 1 AVSD, 1 TGA post palliative Mustard.
- 2 repaired VSD - one at age 1.6 years, one at 11 years
- 4 of the Eisenmenger pts. - 2 PDA, 1 ASD, 1 AVSD, had 9 successful preg. & deliv. long before the full blown syndrome was diagnosed.

Pulmonary hypertension - 2

- 4 pts. with full blown Eisenmenger syndrome when pregnant had the following outcome:

1. Pt. with a PDA had already two children when first seen at the GUCH unit. She was severely symptomatic and died in France at age 22 y (around 1995).
2. Pt. with VSD had a CS delivery at 34 wks. gestation, and died several days later despite trt. with inhaled iloprost and NO, age 21 years (1999). Child OK

Pulmonary hypertension - 3

3. Pt. with VSD trt. with Flolan during preg. and CS delivery at 28 wk. She remains well at 39 y. Child OK
4. Pt. with TGA/pal. Must. was treated with Flolan and sildenafil, CS at 34 wks. died after one week (2008). Child OK
- One pt. with VSD repaired at age 11 y, had 3 pregnancies (1982, 1983, 1988) resulting in 2 live births. She had significant deterioration and has been on inhal. iloprost for the last 9 yrs. Now 50 y.o

Pulmonary hypertension - 4

- Pt. with repaired VSD was on Flolan and cialis and had CS at 34 wks. Preg. resulted in worsening RV function and severe tricuspid regurgitation.
- Outcome of 4 pts. with late Eisenmenger syndrome; pt. with ASD is 62 y.o. severe CHF on s.c. remodulin, pt. with PDA is 59 and stable, pt. with PDA died at 57 y, and pt. with AVSD was on sc remodulin, had heart lung tx. and died one year later at 59 y.

Cyanotic heart disease

- 2 pts, 3 successful preg. & deliv
- One pt. with complex pulmonary atresia (TOF with MAPCAs), O2 sat. at rest 87%, had two uneventful pregnancies (1998, 2000). Both children had mild IUGR but otherwise well. Mother now 33 y.o. and well
- One pt. with unoperated TOF had one child. She became increasingly cyanosed many years later, had surgery at 52 years with many complications but is well now at 58 y.

Fontan - 1

- 5 ptients, 8 pregnancies, 5 children
- 3 tricuspid atresia, 2 DILV
- 1 mod. Fontan (Bjork), 2 lateral tunnel, 1 extracardiac
- One pt. had 2 IVF preg: one spont. abortion at 18 wks gest. One termination at 22 wks due to hypoplastic left heart
- One patient had mild PLE before pregnancy, but developed severe PLE with cachexia and end stage renal failure post delivery (1994), despite favorable hemodynamics. Has been on chronic hemodyalisis for the last few years

Fontan - 2

- Pt. with DILV, lateral tunnel and mild LV dysfunction before pregnancy, received vasodilators for 6 months, LV normalized, and she had an uneventful preg. & deliv. on vasodilators
- Pt. with TA, ex.card. Fontan and reoperation for sub-AS, received vasodilators, and had CS at 34 wks because of periph. edema & mild symptoms (2008)
- Pt. with TA had normal 1st. preg, prematurity on 2 nd. and spont. abortion on 3rd.

Summary

- Pregnancy can be successful and safe in pts. with transposition complex and a systemic right ventricle and in unoperated cyanotic anomalies.
- Pregnancy in Eisenmenger syndrome and repaired congenital shunt lesions remains dangerous and contraindicated.
- Pts with Fontan physiology may complete successful pregnancies but impact on long term outcome is not known.

Pregnancy outcome in women with heart disease undergoing induction of labour.

Oron G, Hirsch R, Ben-Haroush A, Hod M, Gilboa Y, Davidi O, Bar J.
BJOG. 2004;111:669-75.

OBJECTIVE: To examine the safety and outcome of induction of labour in women with heart disease. DESIGN: Prospective single-centre comparative study. SETTING: Major university-based medical centre. POPULATION/SAMPLE: One hundred and twenty-one pregnant women with heart disease. METHODS: The sample included all women with acquired or congenital heart disease who attended our High-Risk Pregnancy Outpatient Clinic from 1995 to 2001. The files were reviewed for baseline data, cardiac and obstetric history, course of pregnancy and induction of labour and outcome of pregnancy. Findings were compared between women who underwent induction of labour and those who did not. Forty-seven healthy women in whom labour was induced for obstetric reasons served as controls. MAIN OUTCOME MEASURES: Pregnancy outcome. RESULTS: Of the 121 women with heart disease, 47 (39%) underwent induction of labour. There was no difference in the caesarean delivery rate after induction of labour between the women with heart disease (21%) and the healthy controls (19%). Although the women with heart disease had a higher rate of maternal and neonatal complications than controls (17%vs 2%, P= 0.015), within the study group, there was no difference in complication rate between the patients who did and did not undergo induction of labour. CONCLUSION: Induction of labour is a relatively safe procedure in women with cardiac disease. It is not associated with a higher rate of caesarean delivery than in healthy women undergoing induction of labour for obstetric indications, or with more maternal and neonatal complications than in women with a milder form of cardiac disease and spontaneous labour.

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STATE-OF-THE-ART PAPER

Outcome of Pregnancy in Women With Congenital Heart Disease

A Literature Review

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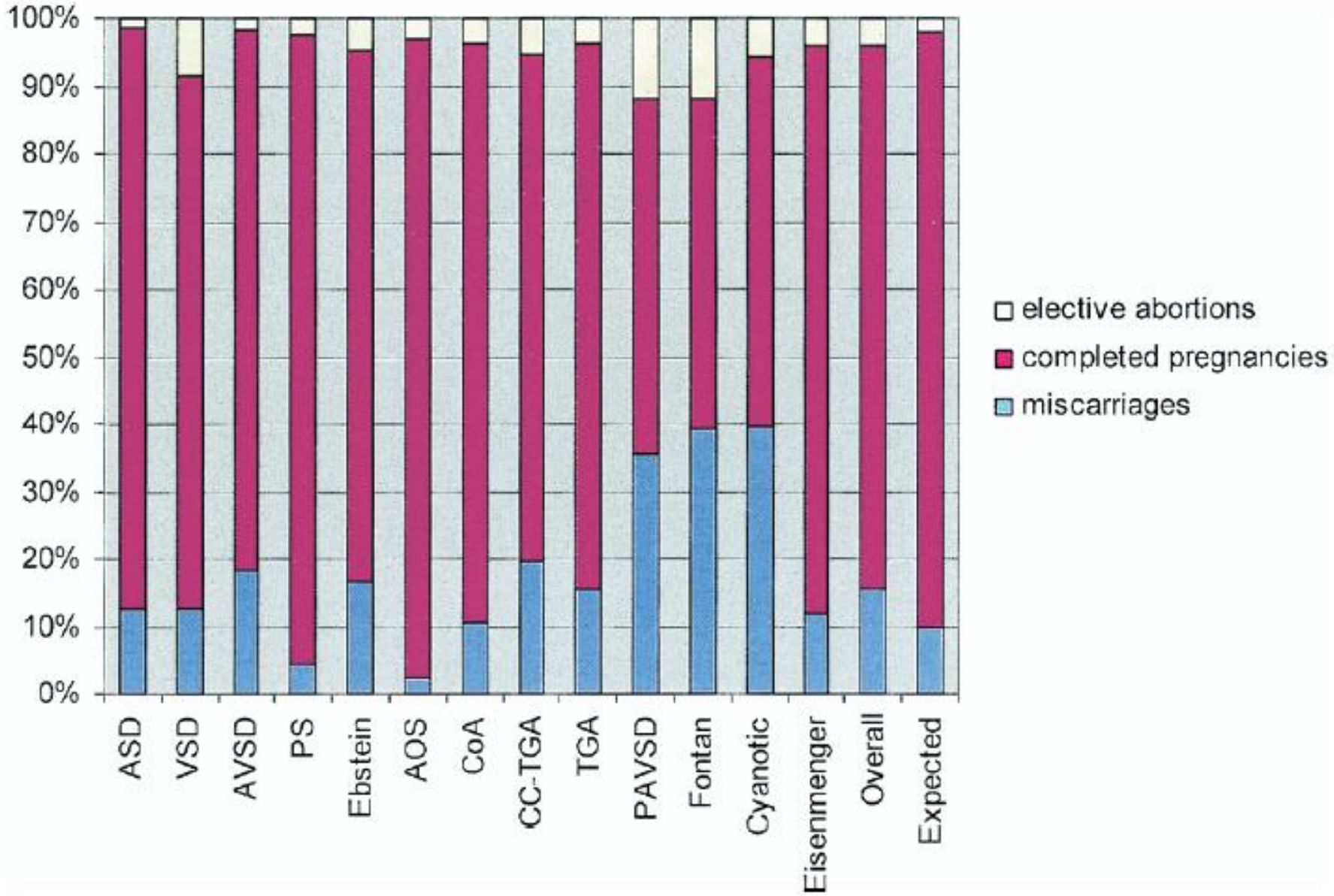
Groningen, Rotterdam, Amsterdam, Nijmegen, and Leiden, the Netherlands; and Leuven, Belgium

A search of peer-reviewed literature was conducted to identify reports that provide data on complications associated with pregnancy in women with structural congenital heart disease (CHD). This review describes the outcome of 2,491 pregnancies, including 377 miscarriages (15%) and 114 elective abortions (5%). Important cardiac complications were seen in 11% of the pregnancies. Obstetric complications do not appear to be more prevalent. In complex CHD, premature delivery rates are high, and more children are small for gestational age. The offspring mortality was high throughout the spectrum and was related to the relatively high rate of premature delivery and recurrence of CHD. (J Am Coll Cardiol 2007;49:2303–11) © 2007 by the American College of Cardiology Foundation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CoA
CC-TGA
TGA
PAVSD
Fontan
Cyanotic
Eisenmenger
Overall
Expected
elective abortions
completed pregnancies
miscarriages