

# Turner syndrome and pregnancy

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CHU Sainte-Justine  
*Le centre hospitalier  
universitaire mère-enfant*

*Pour l'amour des enfants*

Université   
de Montréal

# Conflict of interest

- None



# Objectives

- Proceed to a pre-conception evaluation of a woman with Turner syndrome contemplating pregnancy (assessment of vascular, renal and metabolic issues).
- Plan the appropriate maternal follow-up during pregnancy and participate the interdisciplinary discussion about the mode of delivery.



# Case

- 24 years old with Turner wants a baby
- She already has a donor
- Known with hypertension and bicuspid aortic valve
- BMI 32
- Meds: losartan 50 mg

She wants a baby now!



# Turner syndrome

- Complete or partial monosomy for the X chromosome
- Prevalence: 1 in 2,000 live-born girls
- Short stature and ovarian insufficiency
- Cardiovascular anomalies:
  - Hypertension
  - Bicuspid aortic valve: 15-30%
  - Coarctation of the aorta: 12-17%
  - Aortic dissection and rupture
- Diabetes, thyroid disease, structural renal anomalies, liver disease, celiac disease, osteoporosis....



# Evaluation

- Presence of hypertension
- TSH
- Fasting blood glucose, Hba<sub>1c</sub>
- Creatinine, liver enzymes
- Renal and liver imaging
- Both echocardiography and MRI imaging of aorta



# Mortality in Turner

- 3-fold increase in risk of premature death
- 1 in 40 dying of aortic dissection by the age of 85 years
- Median age at dissection or rupture: 35 yrs old
- Cardiac imaging every 5-10 yrs if initially normal and no risk factors: if anomalies repeat annually.



# Mortality, Morbidity in Pregnancy

- Catastrophic case reports of aortic dissection start appearing in 1990s
- Estimate of mortality rate: 2% in pregnancy
- High rate of hypertensive disorders and preterm delivery
- Patient with mosaic also considered at risk

Karnis MF et al. 2003

Chevalier et al. 2011





# Mortality in Turner syndrome

- Boissonnas et al 2009
  - One case of death in pregnancy: ASI was  $2.84\text{cm}/\text{m}^2$
- Carolyn Bondy in 2009:
  - Inadequate recommendations from the 2008 Practice Committee of the American Society for Reproductive Medicine
  - Women should not attempt pregnancy
    - If hypertension or congenital cardiac anomaly
    - If an aortic size index greater than  $2\text{ cm}/\text{m}^2$

*Boissonnas et al. Fertility and sterility. 2009*

*Bondy et al. Fertility and Sterility Vol. 91, No. 5, May 2009*

*Bondy et al. Circulation. 2007;116:1663*



# Aortic dissection in Turner syndrome

- In view of short stature: must relate aortic diameter to body surface area

Matura et al. 2007:

- Aortic diameter by MRI at the right pulmonary artery:
- Normal population:
- 95th percentile ASI (aortic size index):  $2 \text{ cm/m}^2$
- 24% of Turner exceeded that measure
- In 3 cases of dissection in the Turner group:  
The aortic size index was  $> 2.5 \text{ cm/m}^2$



# Is there a magic number ?

## 2010 French recommendation

- Pregnancy should be contraindicated if :
  - History of aortic repair
  - History of aortic dissection
  - Aortic dilatation  $> 25 \text{ mm/m}^2$  or  $> 35 \text{ mm}$
  - Aortic Coarctation
  - Treated uncontrolled hypertension.

On behalf of the joint practice committee of the French College of Obstetricians and Gynaecologists, the French Cardiologic Society, the French Chest and Cardiovascular Surgery Society, the French Society of Anaesthesia and Intensive Care, the French Endocrine Society, the French study group for oocyte donation, and the Biomedicine Agency.

Cabanes et al. 2010 Eur J Obst & Gyn and Repr Biol.



# Is there a magic number?

2012 Practice Committee of the American Society for  
Reproductive Medicine

- All Turner syndrome patients considered at risks for aortic dissection
- Risk is greater if
  - Bicuspid aortic valve
  - Coarctation of aorta
  - Hypertension
- Cardiac MRI revealing any significant abnormality and/or ASI  $>2$  cm/m<sup>2</sup> represents an absolute contraindication
- In addition, pregnancy-related changes to the aorta may increase the risk of aortic dissection, aortic rupture, and premature death in subsequent years



# In our patient

- MRI: aorta at 19 mm/m<sup>2</sup>
- Hypertension: amlolide stopped
  - Started on labetalol
- Glucose intolerance: diet
- Liver: steatosis
- No renal anomaly
- TSH: 5,8 synthroid adjusted



# In our patient

- More recent mortality rate in pregnancy: 0,8-1,25%
- Asaphen 81 mg when pregnancy confirmed
- Close BP monitoring
  - Consider metoprolol as  $\beta$ -blocker in all patient
  - Keep BP  $\leq$  135/85
- Glucose monitoring

Bondy et al. 2014



# What do we need to know



Weight, height, BSA

Cardiovascular : aortic root, BAV, CoAo.

Blood pressure

Endocrine functions: thyroid, blood glucose

Plasma lipid profile

Liver function tests

Kidney function tests

Location ?

Karyotype:

Monosomy vs mosaic

(45 X,O ; 45 X,O/  
46 XX)

Ovarian function:

Preserved ?

Failure ?

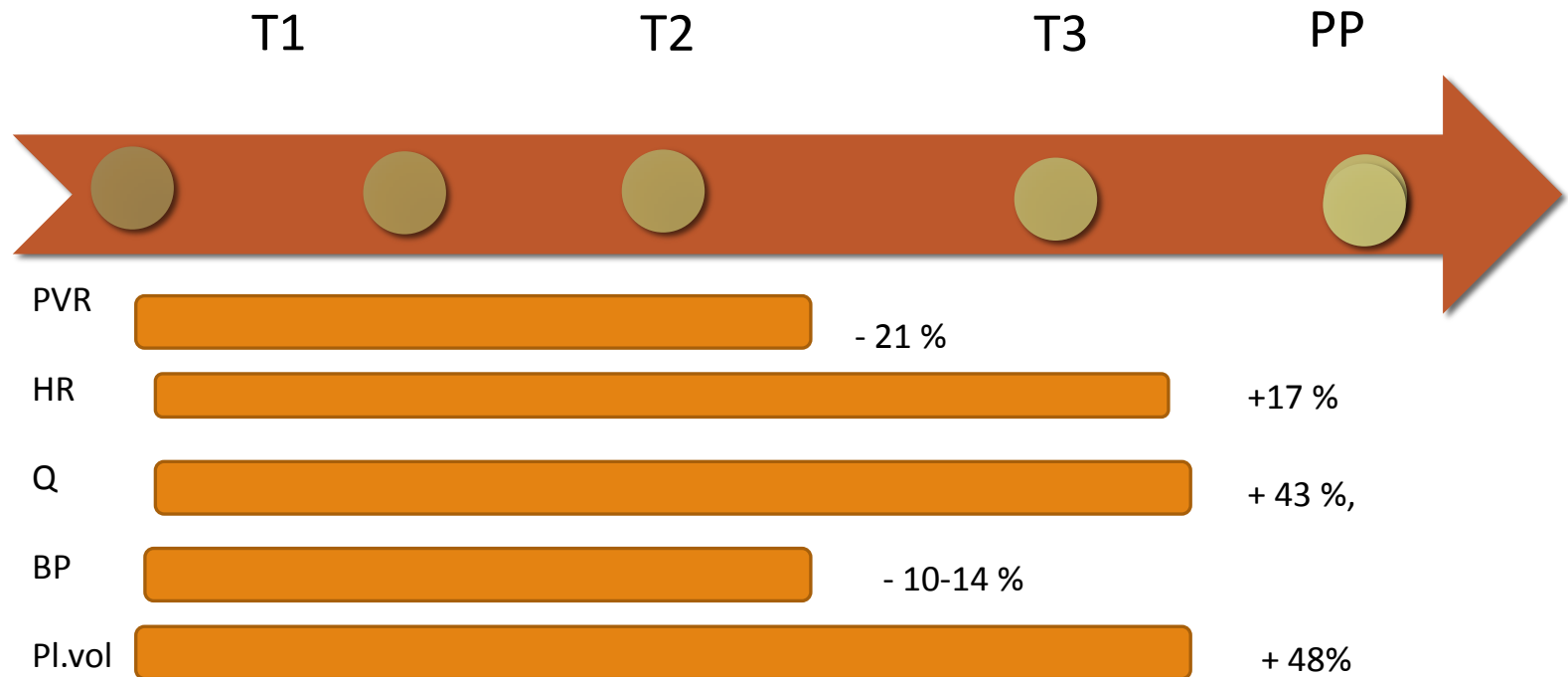
Pregnancy:

Spontaneous ?

ART: OD+IVF+ET ?

One embryo ?

# Pregnancy- cardiovascular changes





# PrePregnancy & Prenatal care

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**Prepregnancy** counseling: multidisciplinary team

Pelvic ultrasound: uterus size, kidneys location

Karyotype: genetic evaluation:                      Monosomy ?                      Mosaicism ?

Cardiac evaluation / blood pressure monitoring

Endocrine disorders: thyroid function, lipid profile, diabetes

## **Pregnancy :**

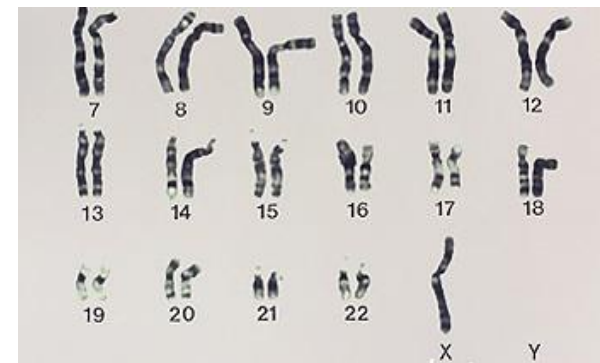
Prenatal genetic diagnosis: PGD, CVS, amniocentesis

Addition: Beta-blocker: metoprolol + ASA

Blood pressure monitoring, and signs of PE

Aortic root dimensions surveillance

Fetal growth



# Obstetric outcomes

	TS with spontaneous pregnancy (1-2%) N: 27 women. 52 pregnancies	TS with ART pregnancy
miscarriage	30%	
PIH or PE	6-13 %	15-28 %
SGA ≤ 10th perc.	0%	9-28 %
PTD	42%	8-38 %
C-section	47%	82%
Aortic root dissection	0%	1-2%
No complications	58 %	40%

1) Hadnott TN et al. Fertility & Sterility 2011;95:2251 2) Bernard V. et al. Human Reproduction 2016; 31: 782-88. 3) Chevalier N et al. J Clin Endocrinol Metab 2011; 96: E260-7. 4) Hagman A et al. Human Reproduction 2013;28:1598-609

# Obstetric outcomes

	Mosaic (French cohort) N: 27 women, 52 pregnancies.5.6%	Mosaic ( Nordic cohort) N: 50 women 50 pregnancies	Monosomy ( 45X,0)
Pregnancy	spontaneous	OD+IVF+ET	OD+IVF+ET
Miscarriage	30 %		
Delivery at term	58 %		
C-section	47 %	71-88 %	80 %
PIH	13 %	7-21 %	15 %
PE	6 %	7-32 %	15-20 %
Diabetes	3 %	7-15 %	6 %

# Delivery

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- Tertiary center
- If the aortic diameter remains unchanged and  $< 20 \text{ mm/m}^2$  (1) or  $< 25 \text{ mm/m}^2$  (2)
- Cesarean section (45-85%) - narrow pelvis
- Analgesia: epidural. Be careful: difficult intubation
  
- Vaginal delivery: epidural analgesia during labor, assisted delivery
- low forceps or vacuum.
- No Valsalva maneuver
- Close blood pressure monitoring

1: ASRM (2012) 2: Collège National des Gynécologues et Obstétriciens Français (2010). The French National Authority of Health 3) Canadian Cardiovascular Society position statement (2014)

# Delivery

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➤ **Acute dissection of the aortic root during pregnancy:**

- **< 25 weeks :** emergency aortic root surgery with ECC. Foetus in utero. Continuous fetal monitoring during cardiac surgery. Maternal and / or fetal death is high
- **≥ 25 weeks:** emergency c-section, immediately followed by aortic root surgery
- **if the aortic diameter becomes  $> 20 \text{ mm} / \text{m}^2$  ( 1) or  $\geq 25 \text{ mm}/\text{m}^2$  (2),  by 10%**
- Hospitalisation
- Betamethasone for fetal lung maturity
- Planned c-section

1: ASRM ( 2012) 2: Collège National des Gynécologues et Obstétriciens Français (2010). The French National Authority of Health 3) Canadian Cardiovascular Society position statement (2014)

# Multidisciplinary team

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## Our team:

Anesthesiologist- CHUSJ

Dr C. Crochetière / Dr S. Lesage

Cardiologist – MHI- CHUSJ

Dr F.P. Mongeon / Dr A. Dore / Dr J. Miro

Endocrinologist – CHUSJ

Dr C. Deal

Heart (aorta) surgeons – MHI – CHUSJ

Dr I. Al-Hamamsy / Dr N. Poirier

Internist - CHUSJ

Dr F. Morin / Dr E. Rey / Dr K. Lévesque / Dr M. Tardif

Maternal-Fetal Medicine – CHUSJ

Dr L. Leduc



Thank  
you !