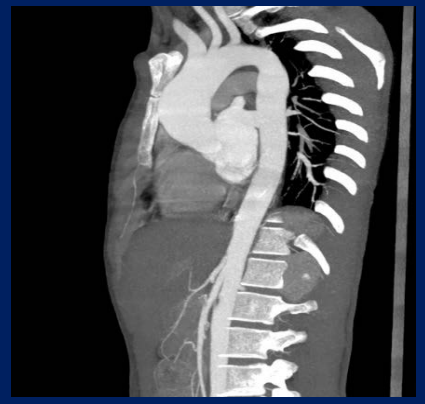
Considerations in Pregnancy for Women with Marfan & Loeys-Dietz Syndrome



Melissa L. Russo, M.D.

Marfan Pregnancy Webinar

April 22, 2020

THE MARFAN FOUNDATION

Know the signs. Fight for victory.

Women & Infants

New England's premier hospital for women and newborns

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Alpert Medical School

Goals of Today's Talk

- Discuss pregnancy's effects on a connective tissue disorder and the risks associated with pregnancy
- Learn things to consider if you are wanting to get pregnant
- Acquire tools and resources to assist you in having safe and healthy pregnancy

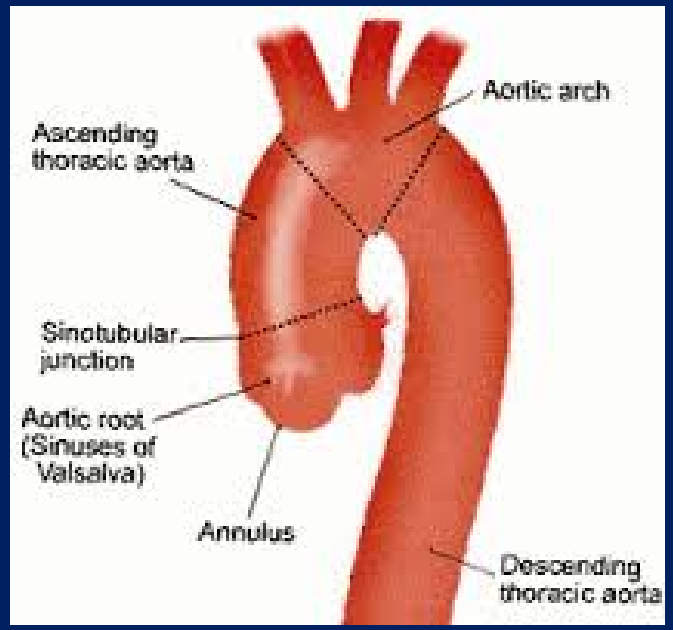
Connective Tissues Disorder

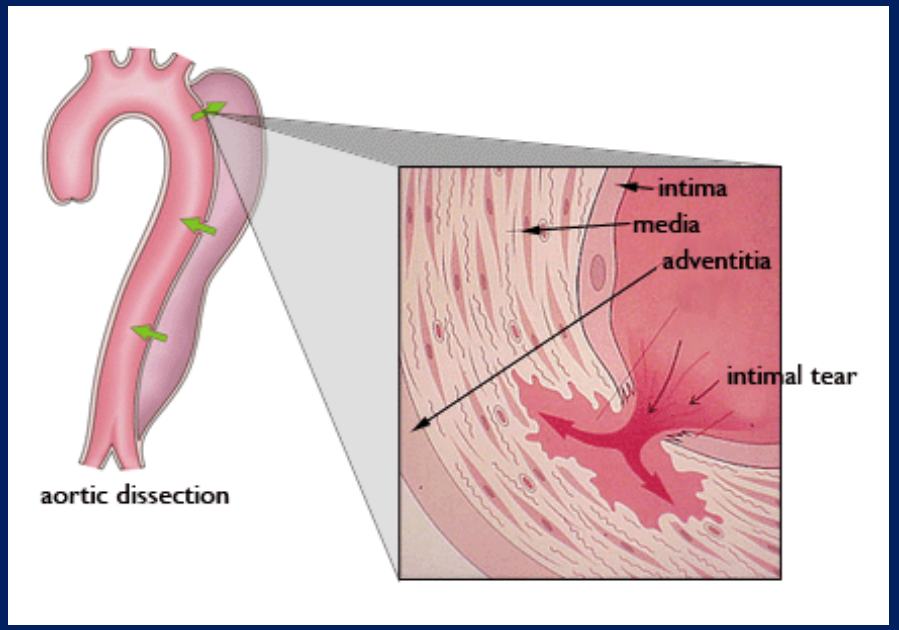
A **connective tissue disorder** involves ligaments, bones, blood vessels.

- Connective tissues - extensive extracellular matrix –framework- collagen & elastin
- Connective Tissue = Heart, eyes, blood vessels, skeleton

The aorta is the main artery from the heart that carries blood to entire body.

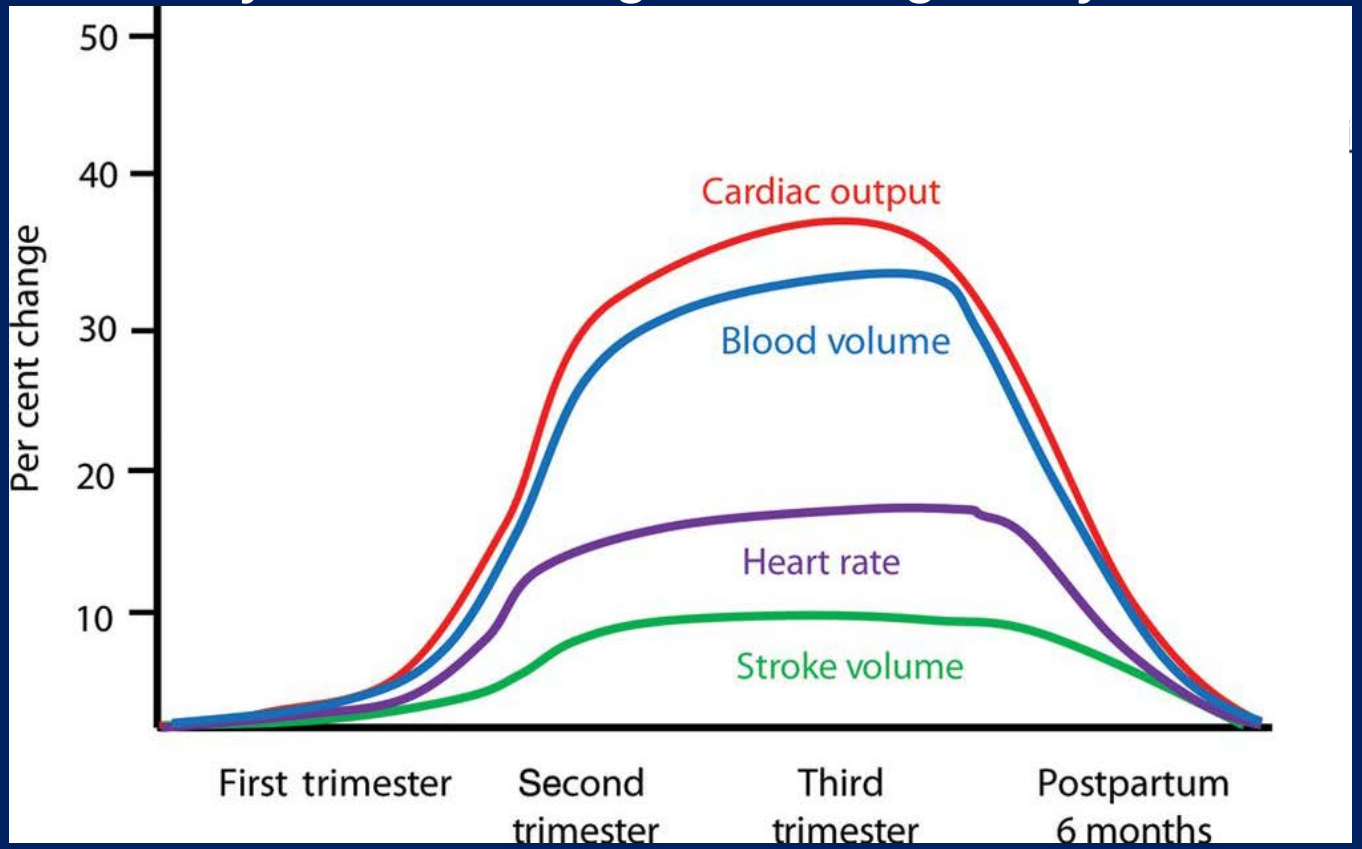
- CTDs –Aneurysm "dilation" at Aortic Root
- Dissection- Tear in intima layer and creates false lumen and bleeds into false lumen





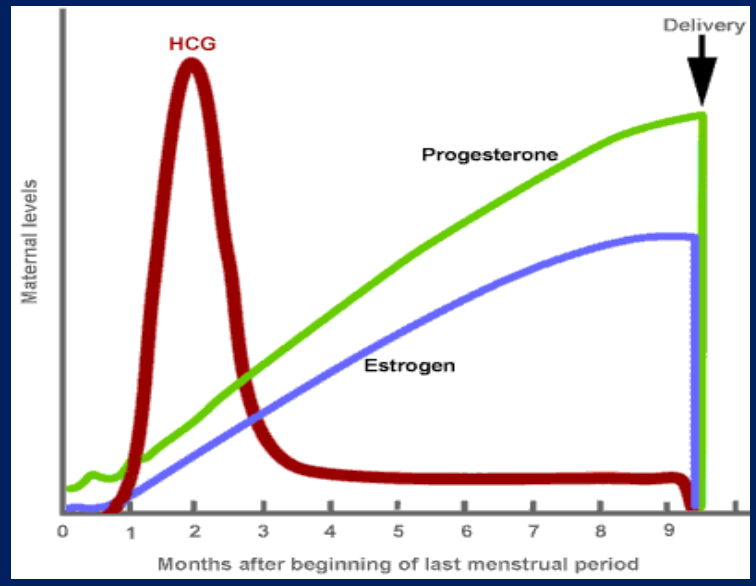
Normal Cardiovascular Changes in Pregnancy:

Hemodynamic Changes in Pregnancy



ESC Guidelines on Cardiovascular Diseases during Pregnancy 2016

Hormonal Changes in Pregnancy



Nolte et al. J Vascular Surgery 1995

Histology Large Arteries

- Loss of reticulin
- Decreased Mucopolysaccharide
- Loss of corrugation fibers

Timing and Risk Factors for Aortic Dissection in Pregnancy

Overall rate of aortic dissection in pregnancy/postpartum period 5-6%*

- Majority of aortic complications occur in the 3rd trimester or postpartum period

Aortic Root Size significantly affects risk of dissection

≥4cm risk of dissection 10%

<4cm risk of dissection 1%

Other risk factors:

- Rapid aortic root growth
- HTN disorders/preeclampsia

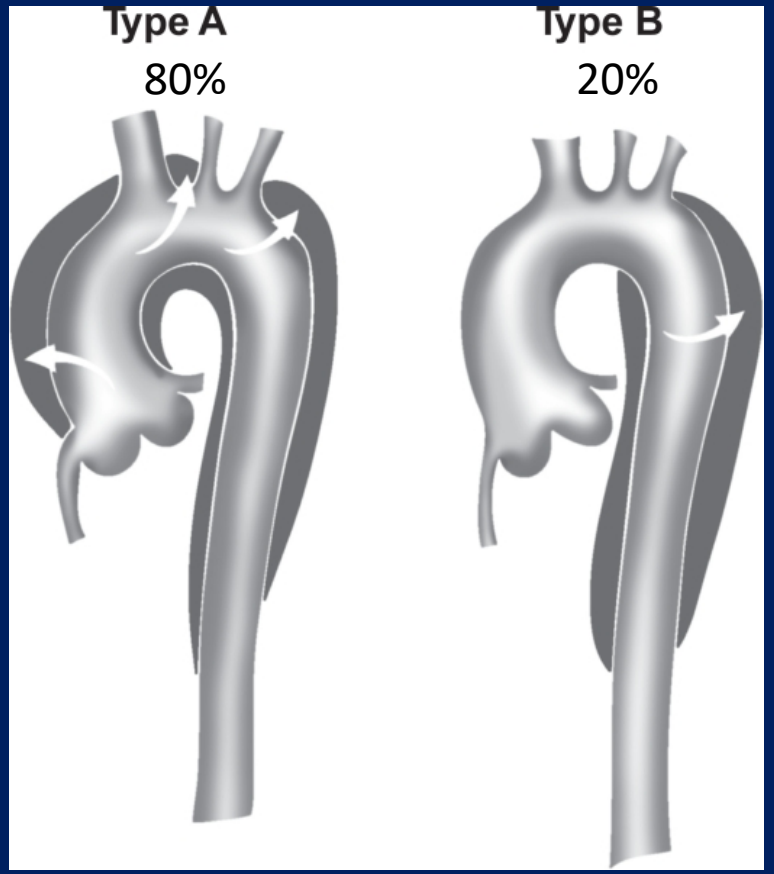
Rossiter et al. 1995, Lipscomb et al. 1997, Lind et al. 2001, Pacini et al. 2009, Curry et al. 2014; Pyeritz et al. 1981, Goland et al. 2009; Loeys et al. 2006

Aortic Dissection in Pregnancy

A rare but significant event if it occurs….

- 3rd most frequent cause of maternal death from cardiovascular disease
- High mortality for mother and fetus (15 and 30%)
- Delays in diagnosis and treatment can be difference between life or death
  - Mortality rate for untreated proximal aortic dissection increases 1-3% per hour following presentation

Aortic Dissection Type in Pregnancy



Zhu et al. 2017

Knight et al 2015; Immer et al 2003; Jovic et al 2014

Connective Tissues Disorder

Signs of aortic dissection:

Chest pain, Back Pain, Dyspnea, Stroke sx, Syncope, focal neurological signs

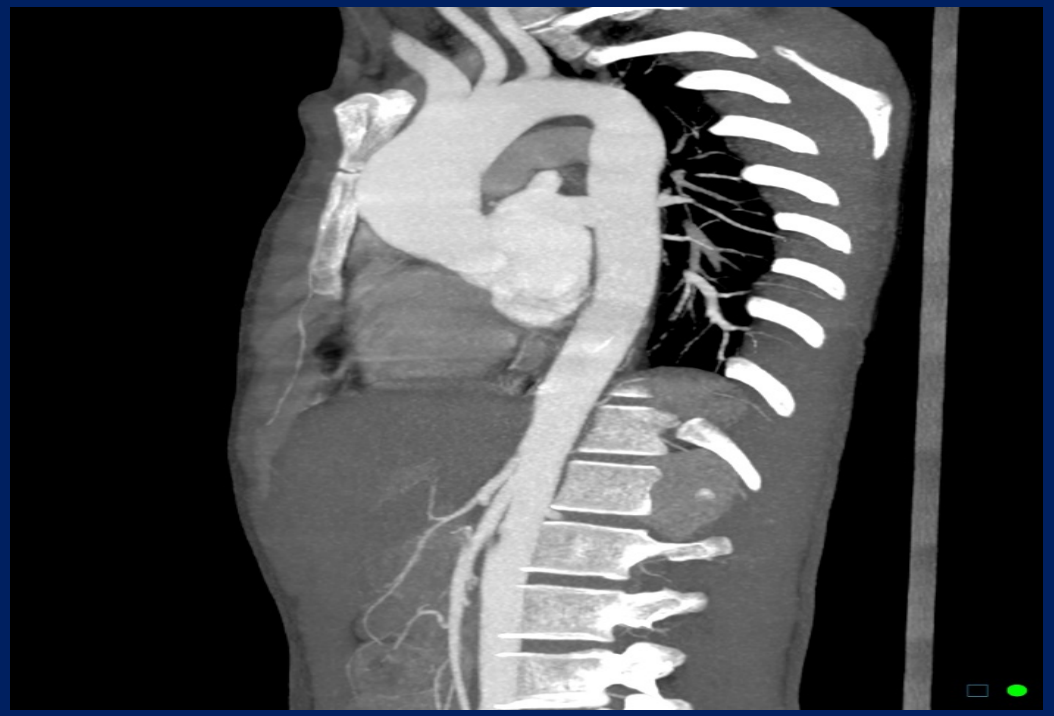


Table 4 – Symptoms and physical findings in aortic dissection.

Pulse deficit
Systolic blood pressure limb differential >20 mmHg
Focal neurological deficits
Aortic regurgitation
Pericardial tamponade
EKG—ST-segment elevation
Syncope

Risk Factors for Long-Term Adverse Outcomes After Pregnancy

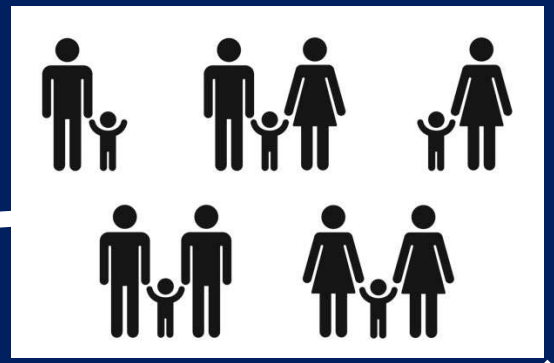
Risk Factors	Protective Factors
Aorta >4 cm	Prospective care
Rate of aortic root change	Medications
Initial aortic root size	
Number of pregnancies	

Table 2
Risk factors for long-term outcome after pregnancy in women with Marfan syndrome. Modified from Donnelly et al.[23]

Associated factors with long-term adverse outcome:	Odds ratios
Aortic size	1.3 (1.11–1.61)
Number of pregnancies	1.5 (1.15–1.97)
Prospective care	0.1 (0.05–0.39)
Medication	0.3 (0.14–0.92)
Aorta > 4 cm	3.8 (1.11–13.3)
Independent correlates	
Initial aortic size	1.8 (1.07–3.07)
Rate of aortic change (log)	7.4 (1.32–41.22)

The Decision to Become a Parent

Pregnancy



Plant Parent

Pet Parent

In Vitro Fertilization

Surrogacy

Adoption

Considerations in Pregnancy for Women with Marfan or Loeys-Dietz syndrome

1. Plan Ahead
2. Assemble your Team
3. To Test or Not to Test…….
4. Protect aorta- meds/imaging
5. Delivery decisions- how, when where
6. Is breast the best?

PREGNACY MANAGEMENT GUIDELINES

Women with Marfan or Loeys-Dietz syndrome

- Preconception counseling
- Antepartum care
- Anesthesia considerations
- Delivery recommendations
- Postpartum surveillance

AMERICAN COLLEGE of CARDIOLOGY

American Heart Association®

Expert Opinion

PLAN AHEAD - Pre-conception Counseling

- Titration off of Angiotensin-Receptor Blocker (ARB) onto Beta-Blocker
- Imaging Studies- CV imaging (CTA vs MRA) and Spinal Imaging
- Genetic counseling of heritability risk and genetic testing options
- Counseling about risks of pregnancy- Meet with Maternal-Fetal Medicine Specialist
  - Cardiovascular risks, obstetric risks and potential effect on long term health
- Discussion of Contraceptive Options:




- *Discuss prophylactic Aortic Root Replacement (ARR) before pregnancy (4-4.5 cm)

Consideration of Prophylactic Aortic Root Replacement

- Discussion about prophylactic aortic root replacement 4-4.5 cm
  - ONLY for Marfan, Loeys-Dietz syndrome and BAV

- Mitigates future type A dissection
  - Potential risk for type B dissection beyond the graft
  - Surveillance in pregnancy- imaging of entire aorta- beyond echocardiograms

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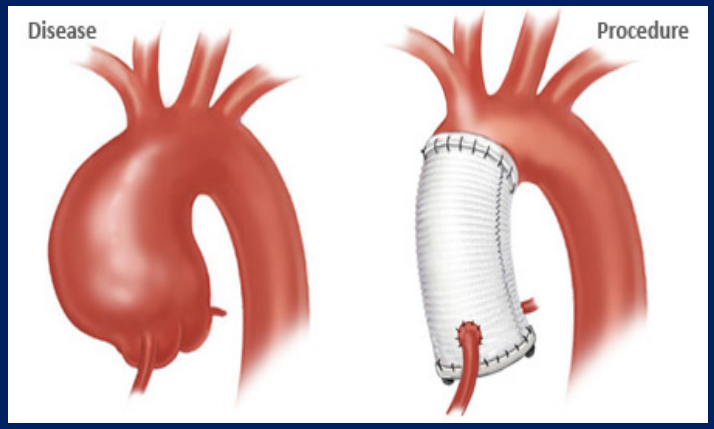


Marfan and Loeys-Dietz Syndrome

Risks to Discuss in Relation to Pregnancy

	Marfan	Loeys Dietz	vEDS
CARDIAC	• Aortic root growth • Aortic dissection • Arrhythmias	• Aortic root growth • Aortic dissection	• Arterial dissection • Maternal mortality 6-50%
OBSTETRIC	• PTB/ PPROM • Fetal growth restriction • Postpartum Hemorrhage • VTE (Blood clot) • Spontaneous pneumothorax	• PTB/ PPROM • Fetal growth restriction • Uterine rupture*	• PTB/ PPROM • Uterine rupture • Hollow organ rupture (bowel, liver, spleen)

Assemble Your Team

Multi-Disciplinary Approach

- Team includes:
  - Maternal-Fetal Medicine, Cardiology
  - CV surgery, Anesthesia , NICU,
  - Nursing leaders and nurses from all specialties

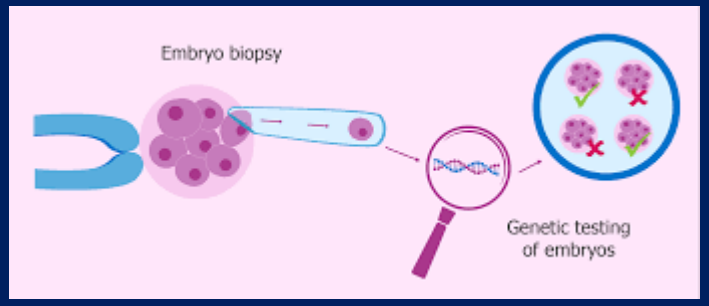
- Delivery at hospital with Cardiothoracic Surgery
- Education, Contingency Plans & Simulation

To Test or Not to Test:

Genetic Testing Options in Pregnancy

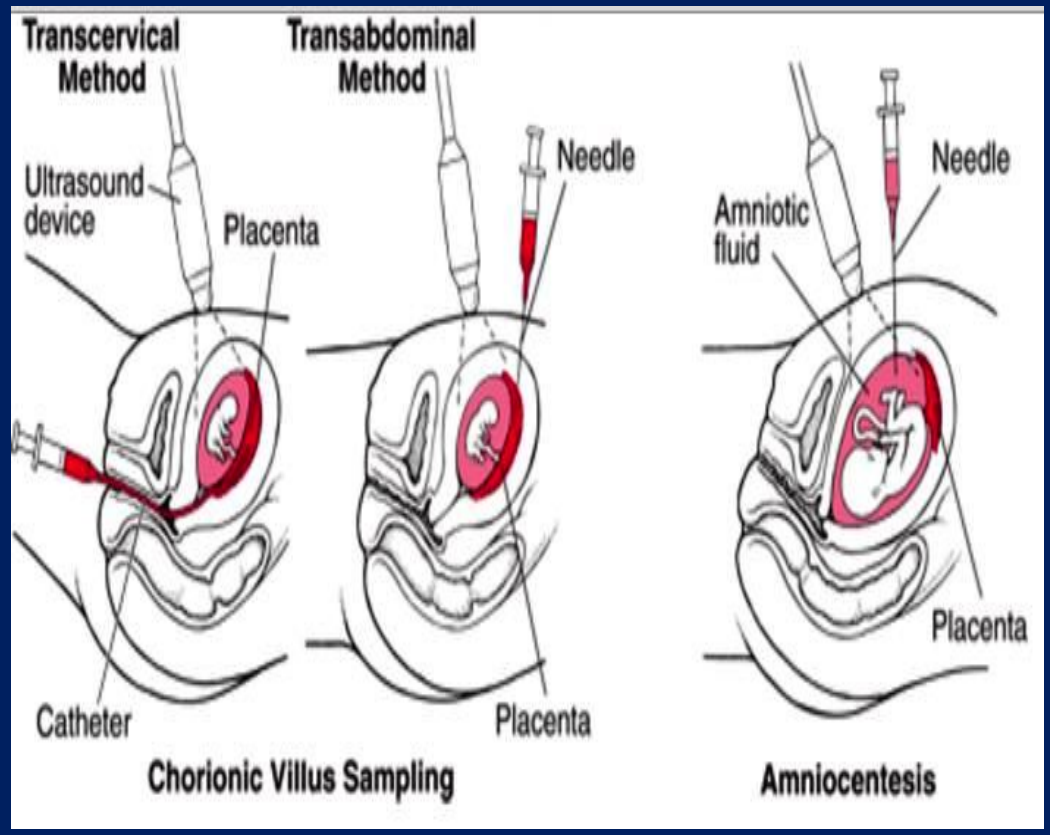
Before Pregnancy

Preimplantation Genetic Diagnosis (PGD)



During Pregnancy

CVS or Amniocentesis



After Pregnancy

Test child after delivery

Protection of Aorta and Risks to the Fetus

Antepartum Care during Pregnancy

Aorta and Vascular Management & Surveillance

- Beta-blockade during pregnancy –metoprolol preferred
- Maternal echocardiogram
  Frequency depends on severity (q trimester to q 4-8 weeks)
- Assessment of entire vascular tree (MRA)

Fetal Surveillance

- Level II ultrasound
- Growth ultrasounds q 4 weeks
- +/- Fetal echocardiogram

Prenatal Ultrasound Findings in Aortopathy Syndromes

Marfan	Loeys-Dietz	vEDS
No fetal findings *Neonatal Marfan	• Aortic /Pulm dilation • Other CHD • Clefts • Club feet	• Club feet • Amniotic band syndrome-limb abnormalities

Anesthesia Considerations

- Spinal imaging- scoliosis, dural ectasia, cervical spine stability (LDS)

Marfan	Loeys-Dietz	vEDS
• Scoliosis • Dural ectasia	• Scoliosis • Dural ectasia • Vascular anomalies • Cervical spine instability	• Vascular anomalies

- Regional vs General Anesthesia
- Dural ectasia

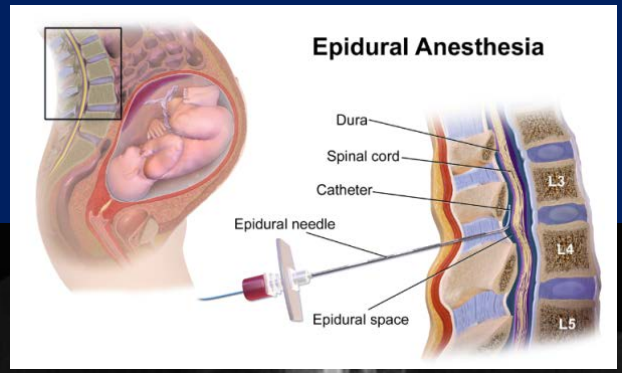
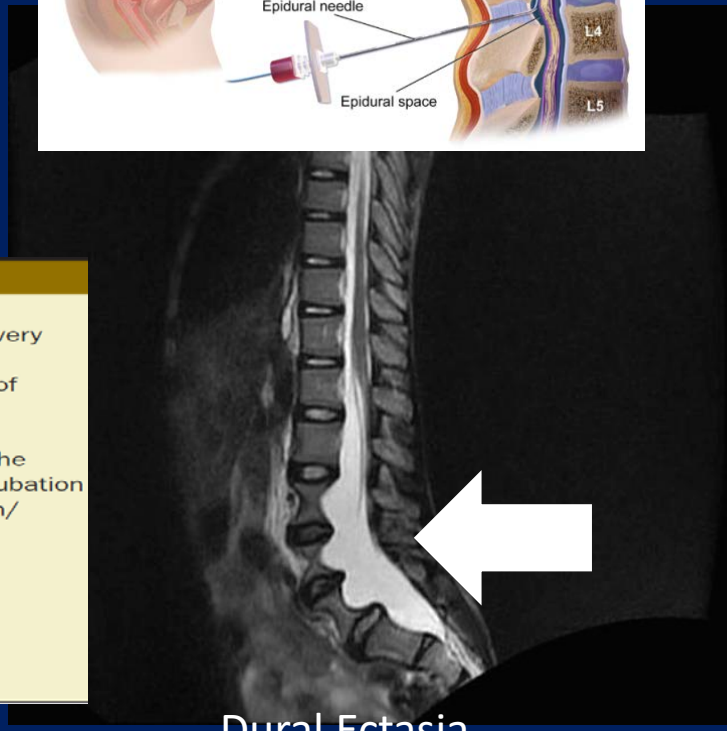


Table 1. Factors Considered When Choosing EA Versus GETA

	EA	GETA
Speed of onset	Slow, controlled—our plan for elective cesarean delivery only	Fast—our plan for emergent cesarean delivery
Inadequate surgical anesthesia	Possible, but safe EA for cesarean delivery in LDS had been reported.[12] Spinal ruled out due to possibility of sequestration of local anesthetic within dural ectasias.[13]	Possible but monitoring available for level of anesthesia
Trauma to c-spine	Negligible risk unless intubation required	Possible risk if c-spine instability exists
Aspiration	Negligible risk since patient is awake. Neuraxial is preferred anesthetic for nonemergent cesarean deliveries.	At risk, especially with pregnancy altering the airway, and requiring rapid sequence intubation
Hemodynamic instability	Possible—controlled or mitigated by incrementally establishing surgical level block	Possible—controlled with smooth induction/ intubation
Dural puncture with vascular complications	Possible—theoretic risk of decreased intracranial pressure with CSF leakage secondary to intrathecal insertion may increase arterial transmural pressure facilitating rupture of vascular malformation[14]	No risk
Uterine atony	Not enhanced by EA	Possible with volatile anesthetics
Experience of childbirth	Possible—this patient declined any sedative medication	Not possible

Kapoor R, Mann DG, Mossad EB. AA Case Reports. 2017



Dural Ectasia

Delivery Recommendations- How, When and Where

	Marfan and Loeys-Dietz

Mode of Delivery	Vaginal vs Cesarean
	• Ao Root
	• Institution
	
	• Vaginal Considerations
	  • Ao root <4-4.5cm
	  • Regional Anes
	  • Operative Delivery

Timing of Delivery	Plan at 39 weeks *36-39 weeks No consensus

How…..Vaginal vs C-section

- Depends on institution, aortic root size
- Vaginal– Forcep or vacuum –decreases time/effort pushing (Vaginal <4-4.5cm)
- Cesarean delivery- >4.5 cm, rapid growth

When…. 37- 39 weeks

Where….Hospital w/ Cardiovascular Surgery

- Tertiary care center
- Cardiologist, CV surgeon

Postpartum Recommendations

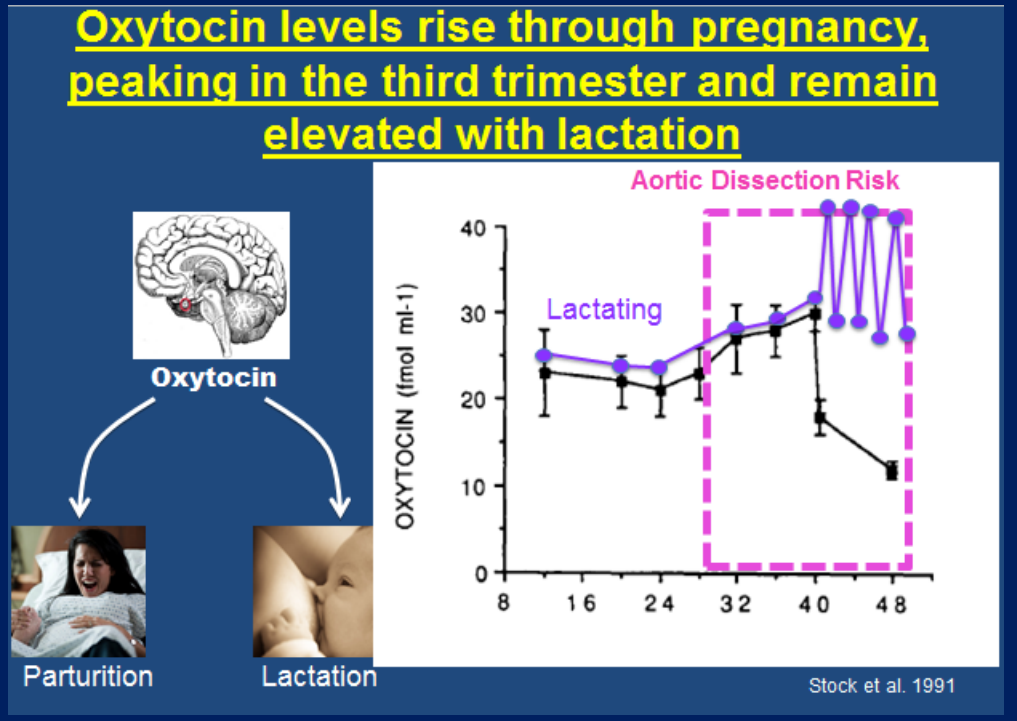
Is the Breast Best????

Postpartum Management

- Inpatient observation for 48-72 hrs
- Imaging prior to discharge- echocardiogram vs CTA/MRA
- Echocardiogram at 3-6 months PP

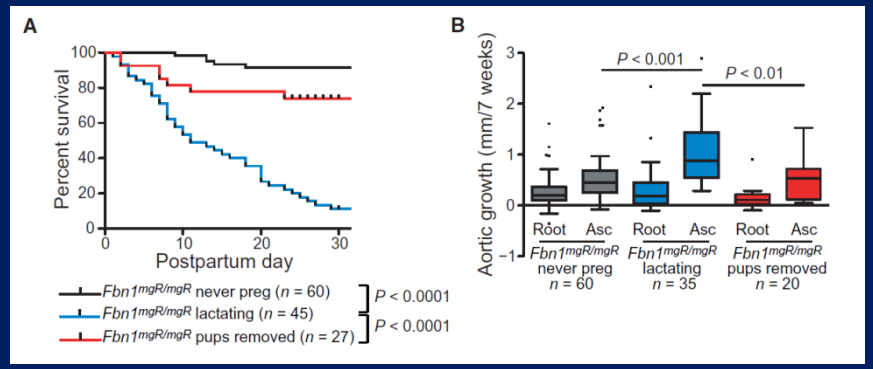
Breast Feeding- the Potential Risks

- Mouse model demonstrates potential detrimental effects of oxytocin



Oxytocin antagonism prevents pregnancy-associated aortic dissection in a mouse model of Marfan syndrome

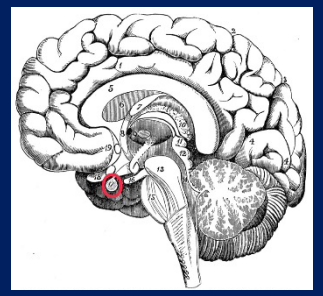
Jennifer Pardo Habashi[1]*, Elena Gallo MacFarlane[2]*, Rustam Bagirzadeh[2], Caitlin Bowen[2], Nicholas Huso[2], Yichun Chen[2], Djahida Bedja[3], Tyler J. Creamer[4], Graham Rykiel[2], Maurice Manning[5], David Huso[3†], Harry C. Dietz[2,6‡]



Marfan Mouse Model
15% normal fibrillin

Are there similar effects in humans???

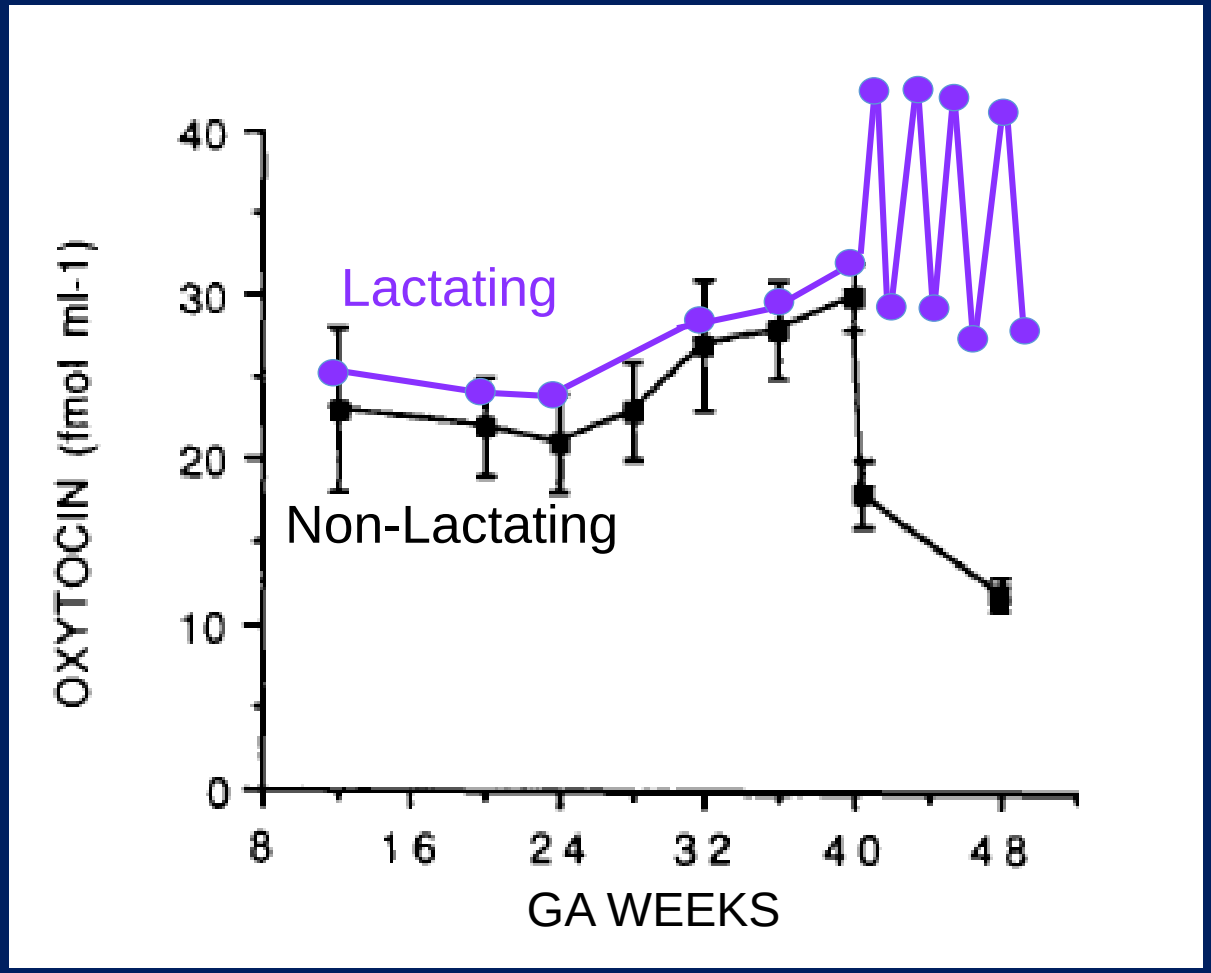
Oxytocin levels rise through pregnancy, peaking in the third trimester and remain elevated with lactation



Oxytocin

Parturition

Lactation



Stock et al. 1991

Summary Points about Pregnancy

- Women with CTD can have successful pregnancies with close management

- Whether to pursue a pregnancy is an individualized decision

- The optimal delivery method (vaginal vs C-section) and whether breast feeding is detrimental is not yet known

- Current and Future Research:
  - To better understand the mechanisms of how pregnancy effects the cardiovascular system
  - To be able to better predict who will develop cardiovascular and obstetrical complications in pregnancy

Summary Points about Pregnancy

- Plan Ahead
  - See your obstetrician before you decide to get pregnant
  - Birth control plan – to prevent unplanned pregnancy

- Assemble your Team
  - MFM, Cardiology, CV surgery, anesthesia, nursing specialists, genetics counselors, intensive care specialists

- Get care through the Pregnancy
  - Protect aorta with meds and surveillance
  - Protect aorta with good anesthesia and safe delivery plan
  - Protect aorta with close post-delivery surveillance