

# Successful Pregnancy and Delivery Following Two Heart Transplantations

Emily M Williams, MD<sup>1</sup>, Tara Banaszek Daming, MD<sup>1</sup>, Anna Grodzinsky, MD<sup>1,3</sup>, Karen Florio, DO<sup>1,2</sup>, Laura Schmidt, MD<sup>1,3</sup>, Darcy White, RN<sup>2</sup>, Becky Gray, RN<sup>2</sup>, Valerie Rader, MD<sup>1,3</sup>, John Lee, MD<sup>1,3</sup>, Anthony Magalski, MD<sup>1,3</sup>, John Spertus, MD<sup>1,3</sup>

<sup>1</sup>University of Missouri - Kansas City

<sup>2</sup>Saint Luke's Hospital

<sup>3</sup>Saint Luke's Cardiovascular Consultants



# Presentation Goals

- History of transplant and pregnancy
- Complications of transplant and pregnancy
- Post transplant obstetric management
- Case presentation
- Conclusions
- Questions



# Transplant and Pregnancy

- 1958: First child born to kidney transplant recipient
- 2006: Over 14,000 births among transplant recipients worldwide<sup>1</sup>
- 1988: First child born to heart transplant recipient
- 2017: At least 406 pregnancies in 301 cardiothoracic transplant recipients reported<sup>2</sup>
  - 183 heart, 42 heart-lung, 76 lung transplants

<sup>1</sup>McKay DB, Josephson MA. Pregnancy in Recipients of Solid Organs -- Effects on Mother and Child. *N Engl J Med.* 2006Mar23;354:1281–93.

<sup>2</sup>D'Souza RD, Acuna S, Zaffar N, Bhagra C, Ross H, Silversides C. Pregnancy outcomes of cardiothoracic transplant recipients: a systematic review and meta-analysis. *American Journal of Obstetrics and Gynecology.* 2017Jan;S440–S440.


# Transplant and Pregnancy

- Complications related to transplant
  - Spontaneous abortion 15-20%<sup>3</sup>
  - Preterm birth 39.8%<sup>2</sup>
  - Preeclampsia 16.3%<sup>2</sup>
  - Maternal mortality 2.5%<sup>2</sup>
- Complications related to pregnancy
  - Allograft rejection 8.5%<sup>2</sup>
    - Hyperemesis gravidarum<sup>3</sup>
    - Fetal immunogenicity<sup>3</sup>
  - Increased risk of thromboembolic events<sup>3</sup>

<sup>3</sup>Abdalla M, Mancini D. Management of Pregnancy in the Post-Cardiac Transplant Patient. Semin Perinatol. 2014Aug;38(5):318–25.



# Obstetric Care - Systematic Approach

- Baseline and serial echocardiography
    - Hemodynamic changes of pregnancy increase workload of graft
    - Complications are decreased with normal graft function<sup>3</sup>
  - Anti-rejection medications
    - Transition to non-teratogenic drugs
    - Regular serum testing and medication titration
  - Corticosteroids
    - Increased risks of low birth weight, preterm labor, fetal adrenal insufficiency<sup>3</sup>
  - Antenatal testing
  - Blood pressure monitoring
- 

# Patient History - Antepartum Course

37yo G2P1001 presented to care at five weeks gestation as self referral

- Planned pregnancy, complicated by:
  - History of two heart transplantations
    - 1997: presumed viral dilated cardiomyopathy
    - 2006: cardiac allograft vasculopathy
  - Tacrolimus-induced diabetes mellitus
  - Hypertension
  - Herpes simplex
- Medications:
  - Tacrolimus                      Diltiazem
  - Prednisone                      Aspirin
  - Insulin                              Acyclovir



# Patient History - Antepartum Course

## Transplant/Cardiology:

- Serial echocardiograms
- Tacrolimus monitoring

## Endocrine/perinatology:

- Blood glucose monitoring
- Insulin titration



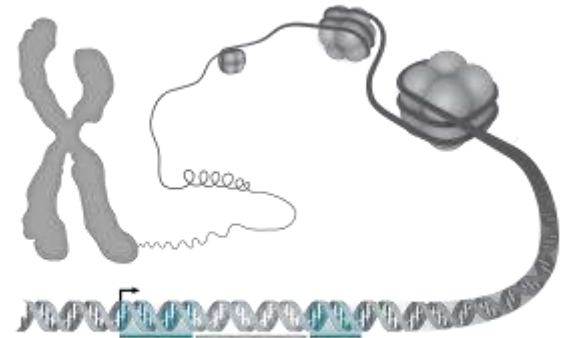
## Perinatology:

- Anatomy/growth ultrasound
- Fetal echocardiography
- Antenatal testing
- Preeclampsia monitoring
- Delivery



# Patient History - Postpartum Course

- Six weeks postpartum: intrauterine device placed
- Seven months postpartum: routine post transplant monitoring
  - Normal echocardiogram, electrocardiogram and coronary angiogram
- Postpartum genetic testing for hereditary cardiomyopathies (previously declined)
  - Lamin A/C (LMNA)
  - Desmoplakin (DSP)
  - Both daughters carry LMNA; second child carries DSP as well.

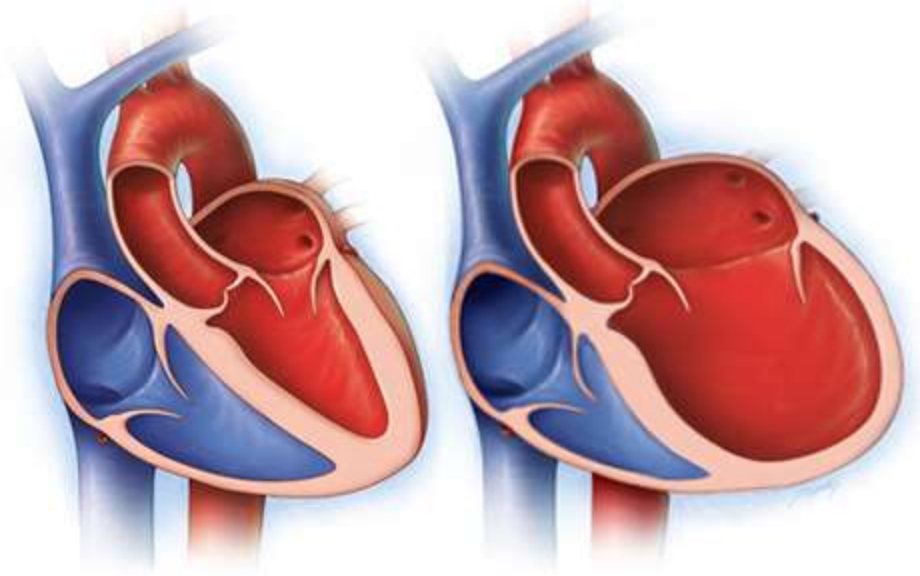




# LMNA Related Dilated Cardiomyopathy

- Classifications:
  - Malignant arrhythmia
  - Dilated cardiomyopathy
- Presents in early adulthood
  - Arrhythmia
  - Heart failure
  - Embolus from LV mural thrombus
  - Sudden cardiac death

- Therapy is based on phenotype



# Summary

- Increasing number of pregnancies affected by transplant
- Increased risks for post transplant patients in pregnancy
- Systematic, multidisciplinary approach is necessary
- Successful outcomes possible with this approach
- Genetics offers choices in reproductive planning

# Conclusion

- Successful pregnancy outcomes following a second heart transplantation can be achieved by employing a multidisciplinary approach
- Saint Luke's Hospital - Heart Disease in Pregnancy Program
  - Coordinated care for heart patients at all stages of pregnancy
    - See poster (#218) for further information on Center of Excellence
- Future directions
  - Establishing a prospective registry
    - Safety and efficacy of immunosuppressive agents
    - Effects of pregnancy on graft function
    - Effects of transplant on fertility
    - Optimization of contraception



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# Questions?





# LMNA Related Dilated Cardiomyopathy

- Involved in lamin production
- Chromosome 1
- Autosomal dominant,
  - Unknown rate of de novo mutation
- Variable expression/penetrance, unpredictable pattern of:
  - Onset
  - Severity
  - Disease course
- Positive genetic testing should prompt screening for DCM
  - Surveillance exams q1-2y and with symptoms
  - History, exam, EKG, ECHO
- Women of childbearing age desiring pregnancy may be offered:
  - Genetic counseling
  - Preimplantation genetics
  - Prenatal diagnosis

# Post Cardiac Transplant Contraception

- Permanent sterilization
  - Transabdominal tubal occlusion
    - 18.5/1000 over 10 years
      - Clips: 36.5/1000
      - Partial salpingectomy: 7.5/1000
      - Unipolar cautery: 7.5/1000
  - Vasectomy
    - 7.4/1000
- Reversible Contraception
  - Intrauterine devices
    - Low antirejection interaction
    - Immunosuppression may reduce efficacy<sup>1</sup>
  - Oral contraceptive pills
    - CYP-450 - requires monitoring
    - Avoid in severe hypertension, active liver disease, estrogen sensitive cancers, high risk for thromboembolic disease<sup>5</sup>
  - Depo provera
    - Osteoporosis<sup>5</sup>
  - Condoms
    - Adjunct method<sup>5</sup>

<sup>4</sup>Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of pregnancy after tubal sterilization: Findings from the US Collaborative Review of Sterilization. American Journal of Obstetrics and Gynecology. 1996Apr;174(4):1161-70

<sup>5</sup>Costanzo MR, Dipchand A, Starling R, Anderson A, Chan M, Desai S, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. The Journal of Heart and Lung Transplantation. 2010Aug;29(8):914-56.



# Heart Disease in Pregnancy Program

## Program statistics

- Since inception (2014), 403 women with cardiac problems served:
  - 140 full term deliveries
  - 85 cesarean deliveries
  - 82 vaginal deliveries
  - 12 operative vaginal deliveries
  - 20 deliveries in intensive care setting
  - 44 neonatal intensive care admissions
  - 2 patients requiring cardiothoracic surgery services
  - 1 maternal death

## Critical components:

- availability of a tertiary care center
- specialized personnel
- ancillary services
- designated program coordinator
- robust and clear communication
- an organizational culture that supports innovation and collaboration