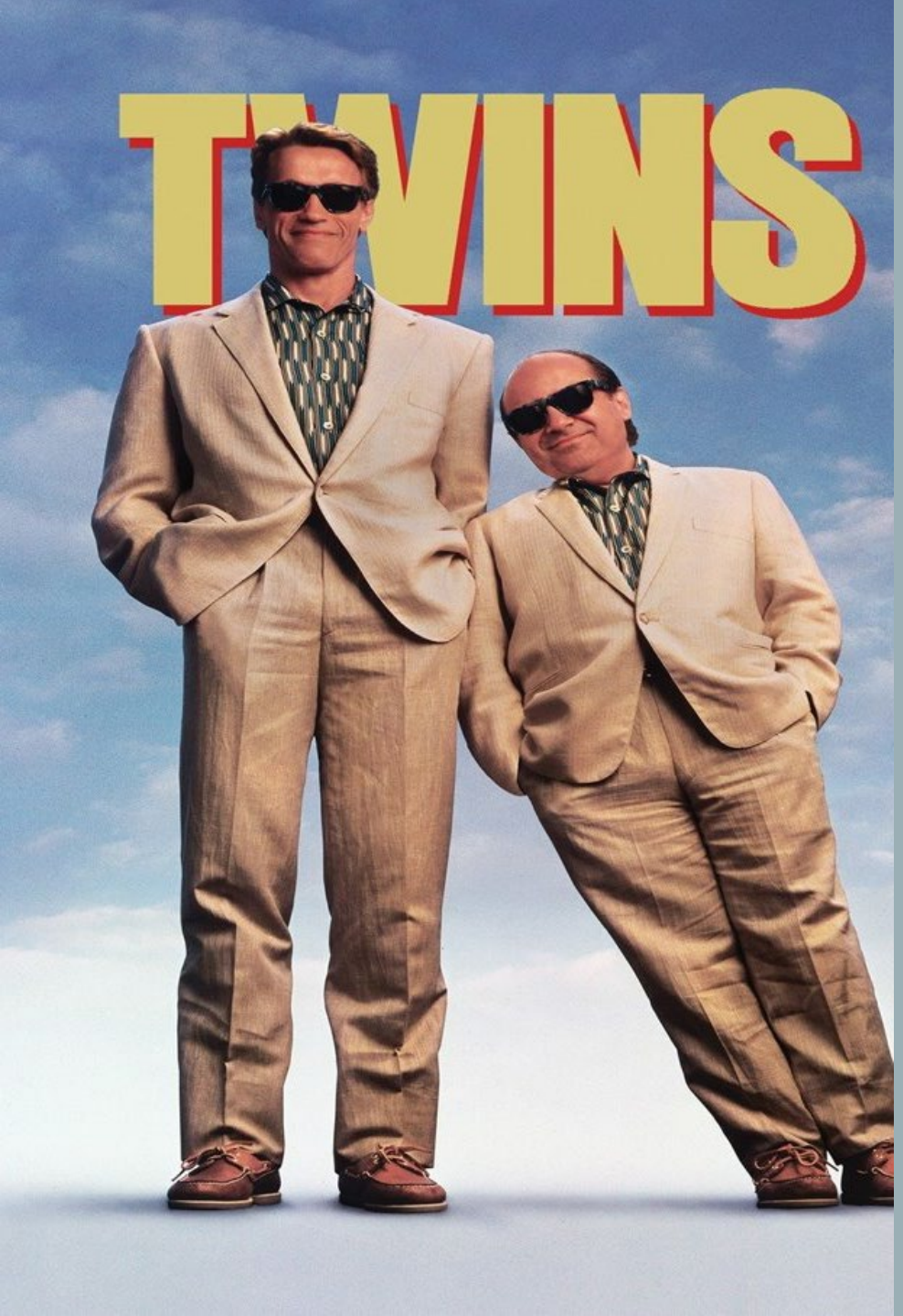

TWIN TO TWIN TRANSFUSION SYNDROME

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Financial
Disclosures

LEARNING OBJECTIVES

- Describe how ultrasound is utilized to determine different types of twins based on number of placentas (chorionicity) and the number of membranes observed (amnionicity)
  - Explain why this is important to know
- List important ultrasound findings that help to distinguish between the different categories of twins.
- Recite ultrasound findings that are consistent with a diagnosis of Twin to Twin Transfusion Syndrome (TTTS)
- Contrast the types of interventions that can be performed to prolong a pregnancy complicated by TTTS.
  - Describe complications associated with these interventions
- Explain the rationale for monitoring fetal vascular Doppler patterns in monochorionic pregnancies

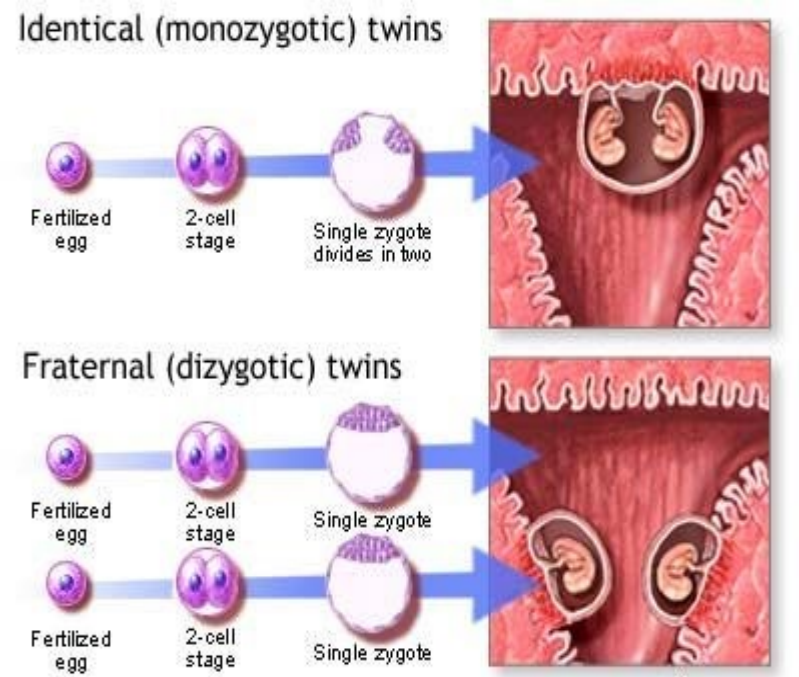
CASE PRESENTATION

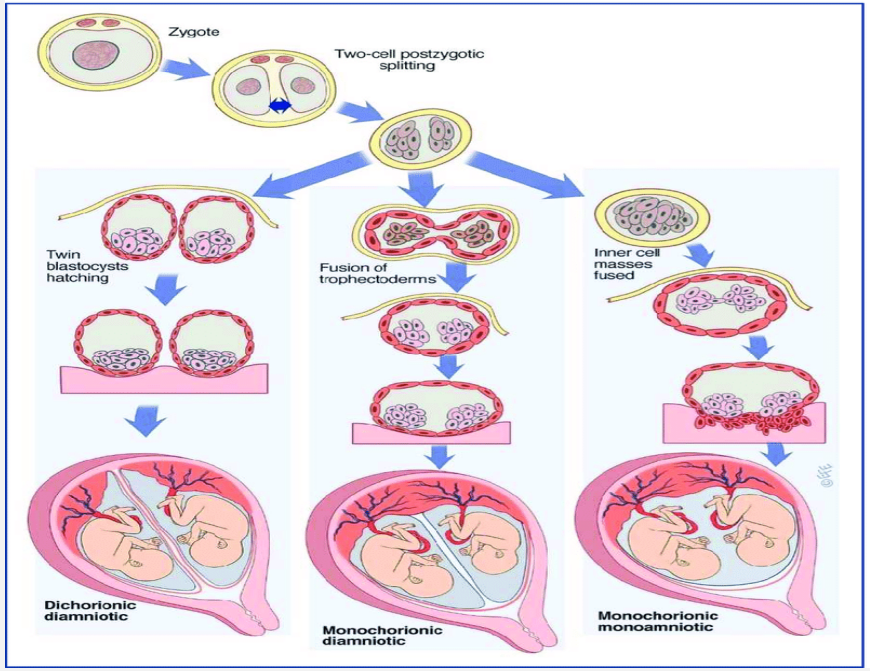
- 32 y/o G4P1021 with a twin pregnancy at 22 weeks 5 days
- Referred from an outside facility due to concerns for ruptured membranes of one of the twins
- Diagnosed with a monochorionic diamniotic twin pregnancy complicated by Twin-to-Twin Transfusion Syndrome (TTTS)

INCIDENCE AND CONTRIBUTING FACTORS

- Twin births account for approximately 3 percent of live births and 97 percent of multiple births in the United States
- Artificial Reproductive Technology: In the U.S. twin births increased from 1/53 infants in 1980 to 1/29 infants in 2014 (1/3rd of dizygotic twins are a result of ART)
- Maternal Age: increase in FSH with age and increased use of ART
- Race/Region: naturally conceived dizygotic twins accounted for 1.3/1000births in Japan, 8/1000 births in United States and Europe, and 50/1000 births in Nigeria
- Family Hx: maternal family hx. Paternal hx does not affect maternal partner's risk for having twins but genes can be passed to his daughters
- Weight and Height: obese and taller women have an increased risk (superovulation?)

TWINNING

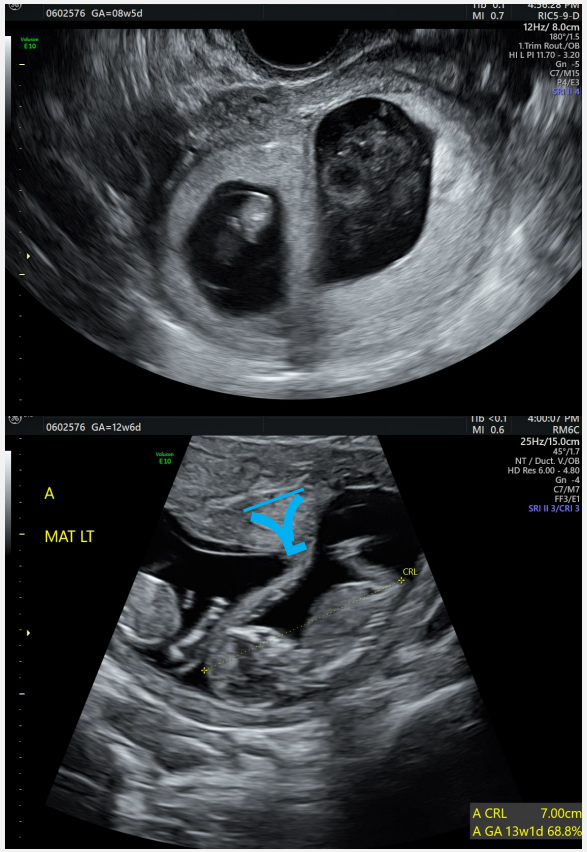




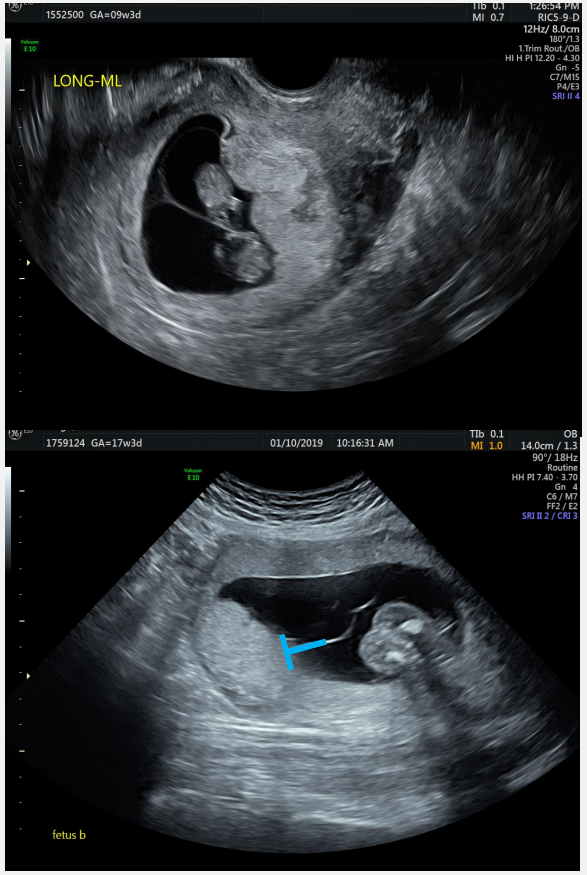
1-3 days 3-8 days 8-13 days

Amnionicity and Chorionicity Dependent on when the zygote splits

CHORIONICITY DETERMINATION WITH ULTRASOUND



- Lambda/twin peak sign or two placentas (Dichorionic)
- "T" sign (monochorionic)
- Genders
- Yolk sacs have been linked to determining number of amnions but is not reliable
- Best to assess between 8-16W GA

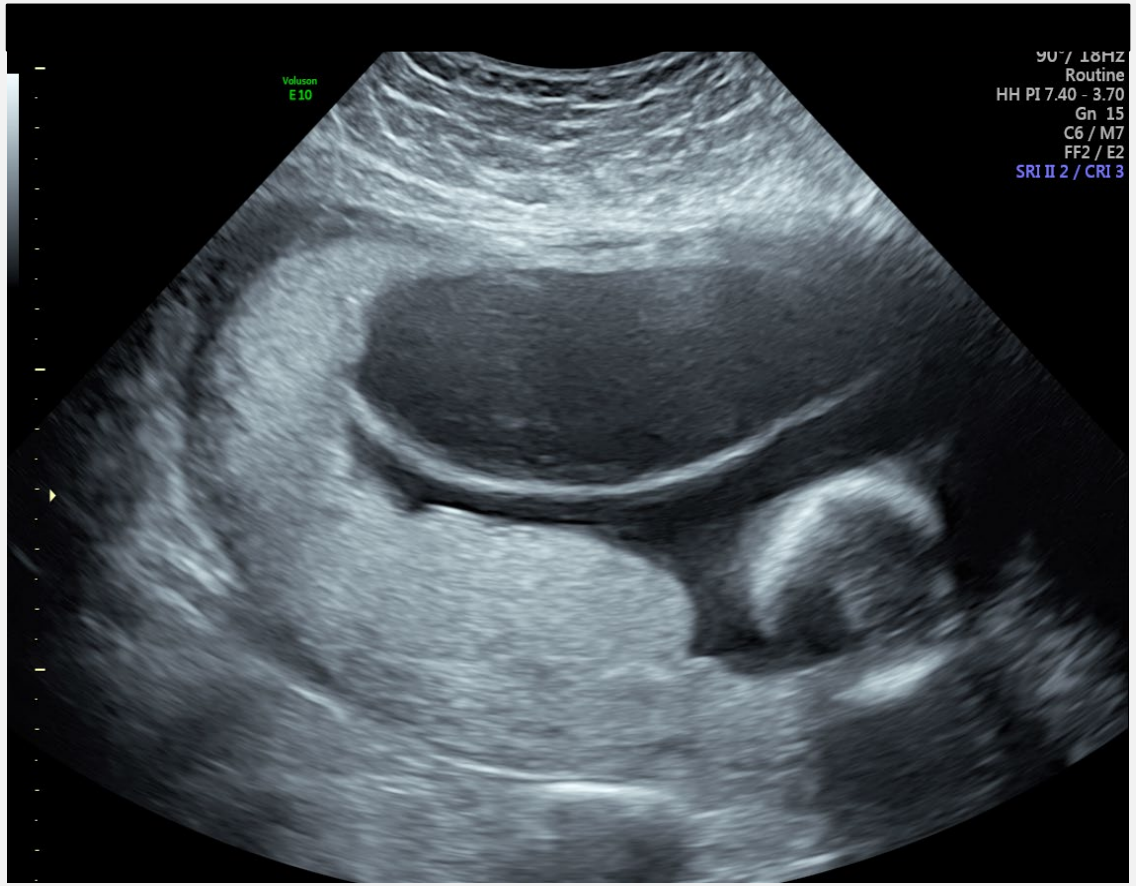


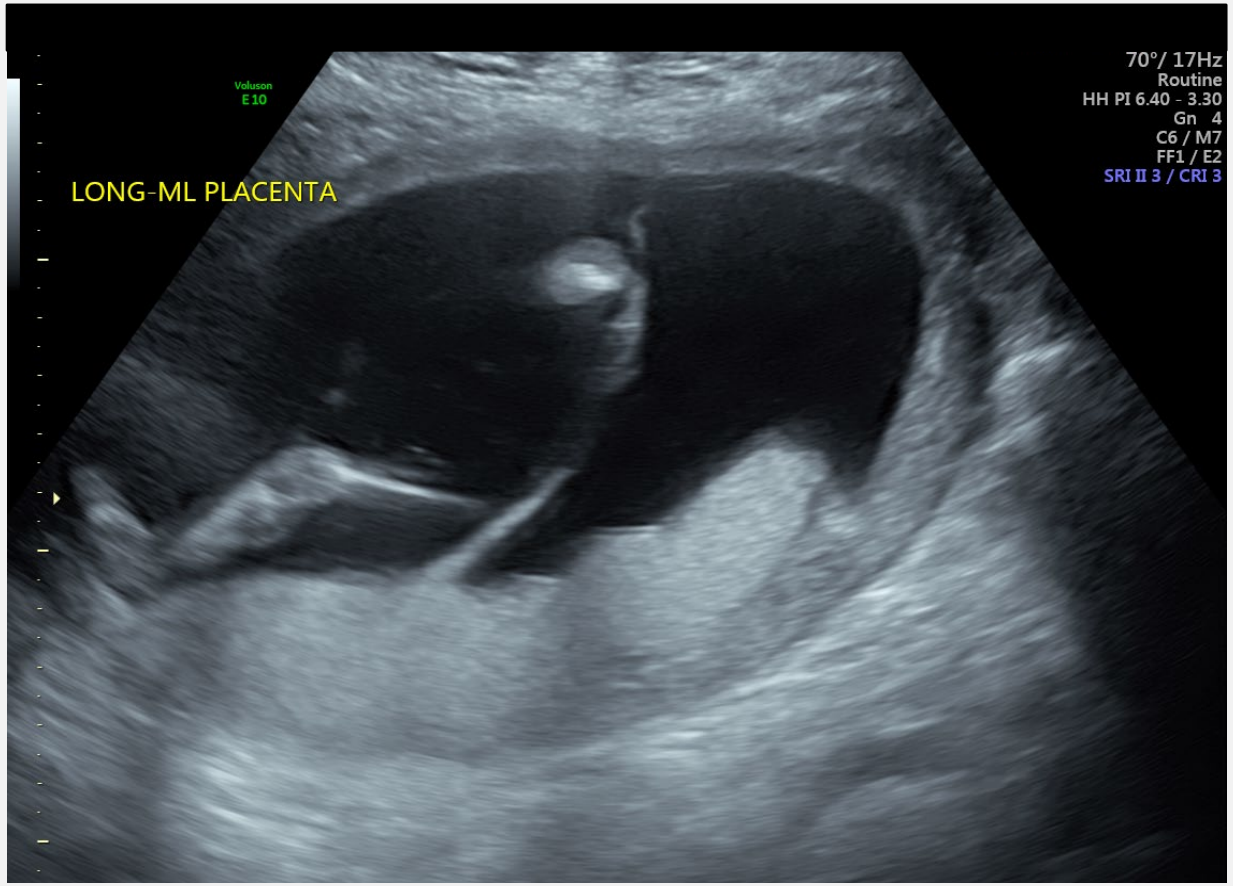
WHAT ARE POTENTIAL CONCERNS ARISING FROM MONO/DI PREGNANCIES?

- **Twin to Twin Transfusion Syndrome (10-15% of all mono/di gestations)**
- Twin Reversed Arterial Perfusion sequence
- **Twin Anemia Polycythemia Sequence**
- Selective Fetal Growth Restriction
  - Unequal placental sharing

CASE PRESENTATION

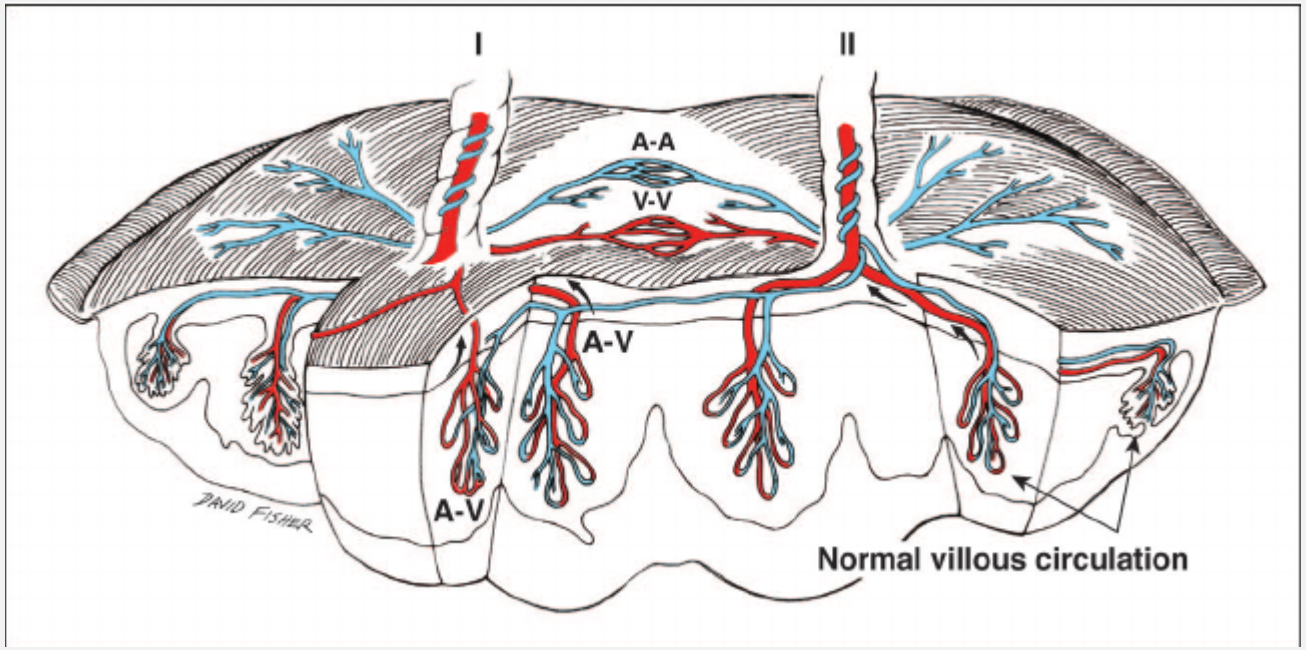
ULTRASOUND 16W5D





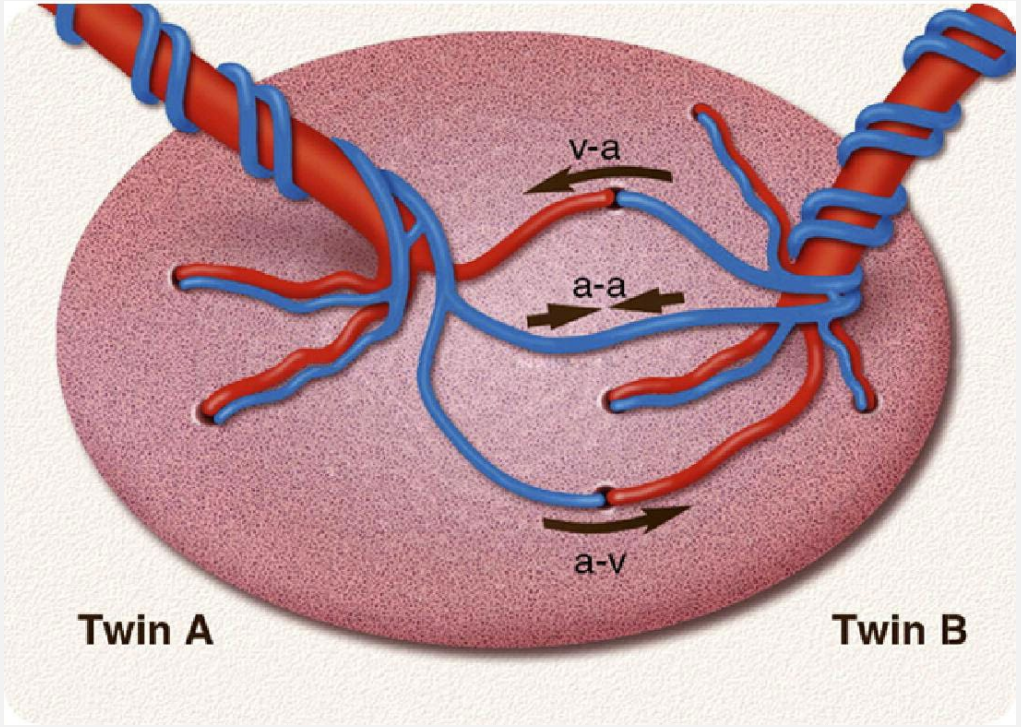
6 WEEKS LATER

PATHOPHYSIOLOGY OF TTTS/TAPS



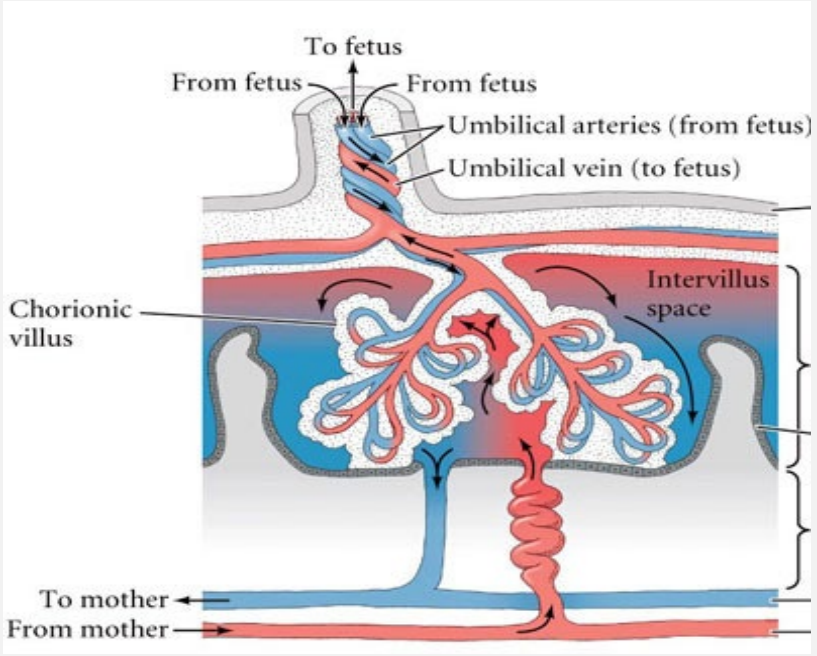
EVERY MONOCHORIONIC PREGNANCY HAS A CONGENITAL ANOMALY

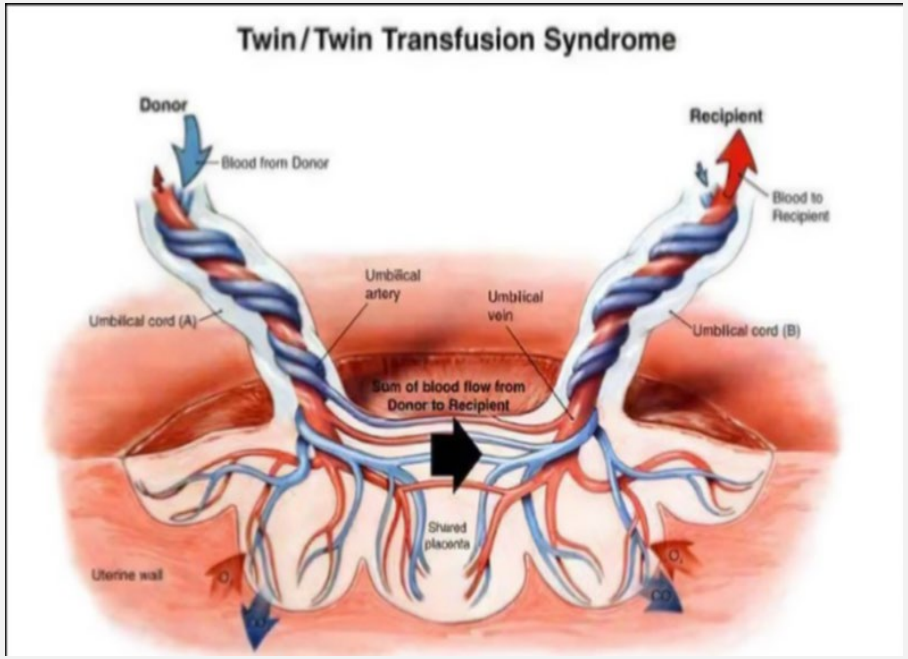
Imbalance of vascular anastomoses



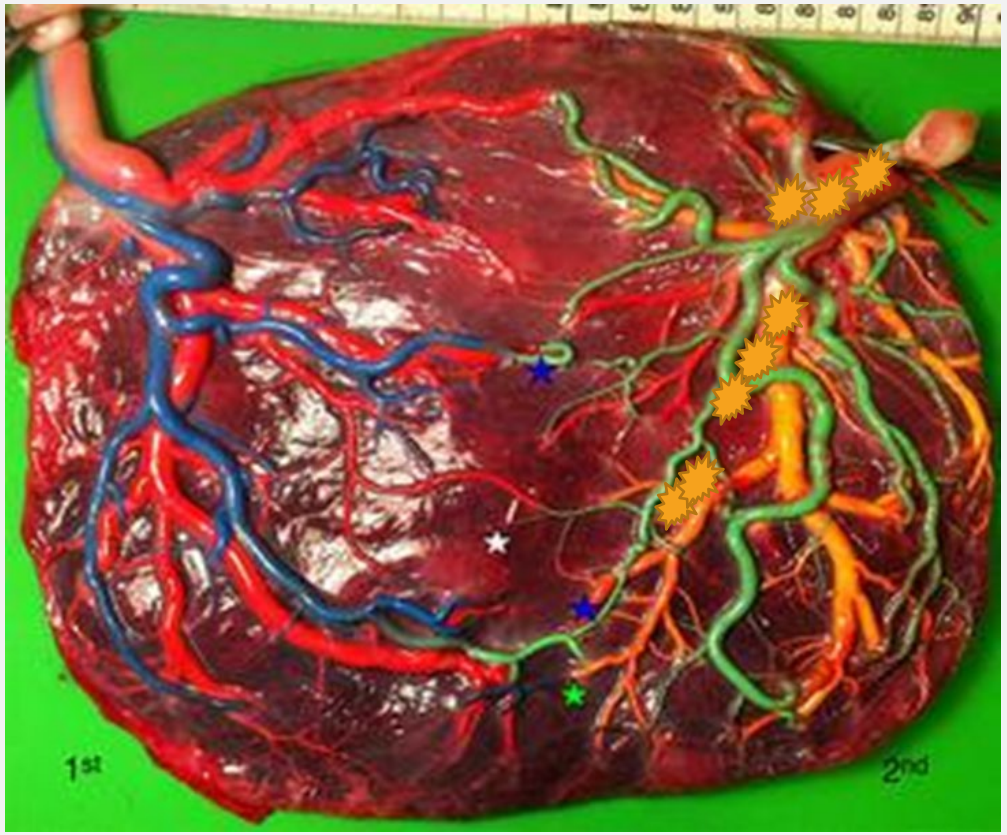
SMFM. Twin-twin transfusion syndrome. Am J Obstet Gynecol 2013

PATHOPHYSIOLOGY

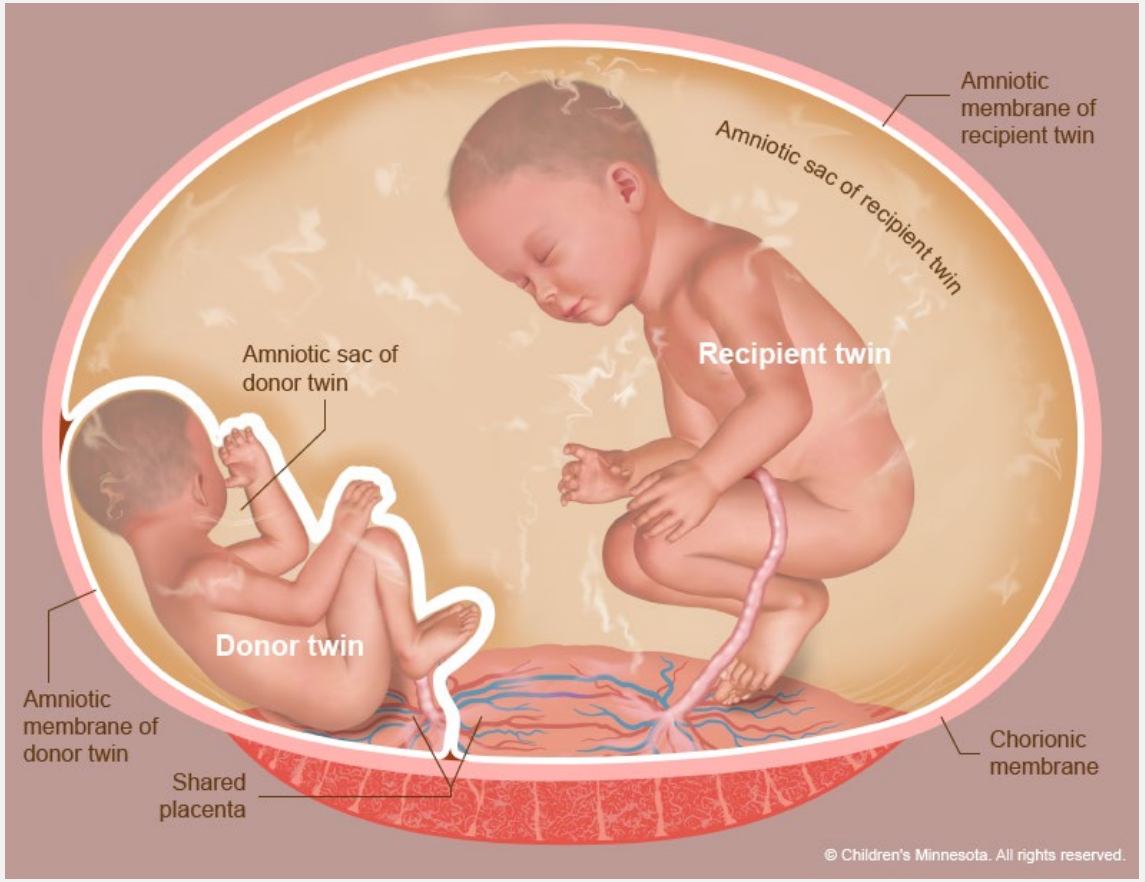




PATHOPHYSIOLOGY OF TTTS AND TAPS

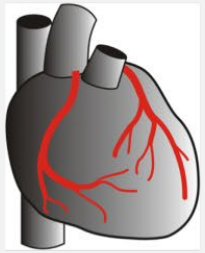


VOLUME IMBALANCE



Cardiac distension
Sympathetic stimulation
Angiotensin II

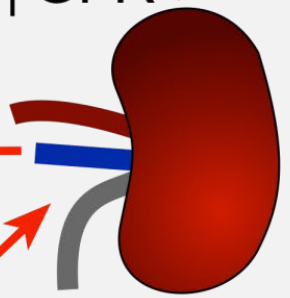
Recipient



ANP
BNP

↓Renin

↑GFR



↓Ang II &
Aldo

Vasodilation

Preload

Systemic Vascular Resistance

Blood
↓Pressure

Blood
↓Volume

Natriuresis
Diuresis

NATURAL PROGRESSION

- Ongoing volume overload in the Recipient can lead hypertensive cardiomyopathy
- Donor side, there is an upregulation in anti-angiogenic/vascular factors (endothelin 1) and elevated levels of RAAS mediators
- These hypertensive mediators are transferred to the Recipient through the AV anastomoses, even though its own RAAS system is down-regulated.
- Venous hypertension is a late stage of the process and results in movement of intravascular fluid into the interstitial spaces and functional lymphatic obstruction, leading to hydrops fetalis

SURVEILLANCE

- Starting At 16 Weeks GA
- Maternal symptoms (discomfort from overdistension, respiratory distress, preterm contractions)
- Cervical Lengths (transvaginal ultrasound monitoring)
- Evaluate amniotic fluid volume, presence of fetal bladders and Doppler interrogation of fetal vessels every 2 weeks (Doppler usually starts at 18 weeks)
- Monitor fetal growth every 3-4 weeks

TTTS STAGING

1

Stage 1: Polyhydramnios - vertical amniotic fluid pocket >8 cm in the recipient sac AND oligohydramnios - no vertical amniotic fluid pocket > 2 cm in the donor sac

2

Stage 2: Absent bladder filling in the donor

3

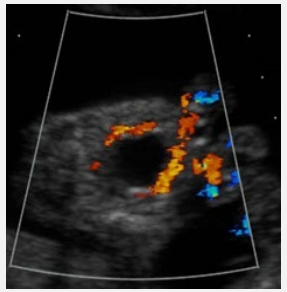
Stage 3: Critically abnormal cardiovascular function in either twin

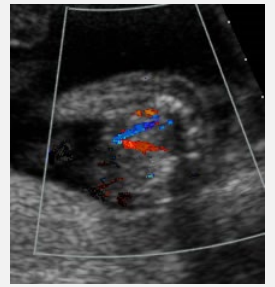
4

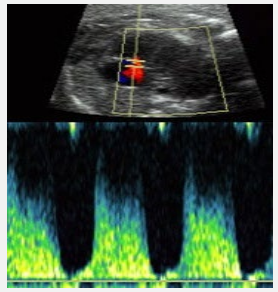
Stage 4: Evidence of overt heart failure (hydrops) in either twin

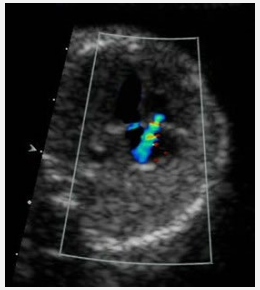
5

Stage 5: Death of one of the twins







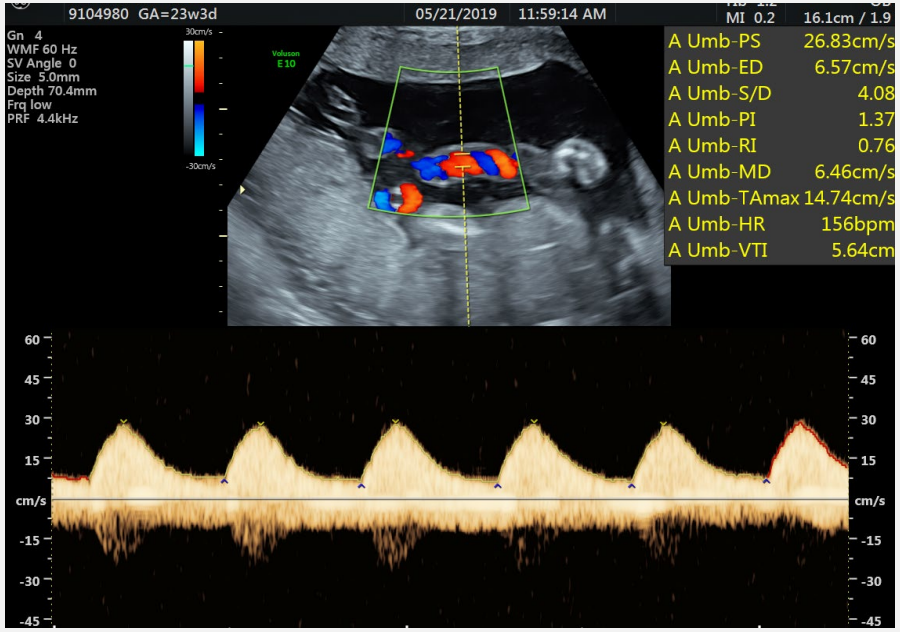


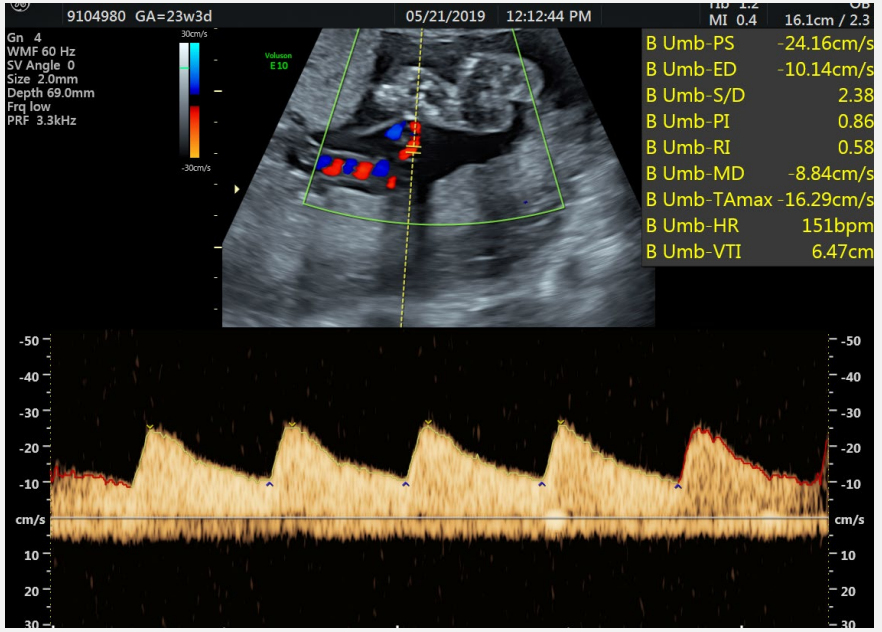
MODIFIED STAGING

- The Children's Hospital of Philadelphia and Cincinnati Children's have published data utilizing echocardiographic data in an effort to identify cases that may warrant medical intervention sooner than what they may have originally been intervened for based on the original staging criteria.
- Examples of some of the variables that are utilized:
  - AV valvular incompetence, ventricular wall thickening, and ventricular function as assessed by the myocardial performance index
- Predictive ability of these cardiac indices has been variable and use of these is limited to centers that have experience in obtaining this information.

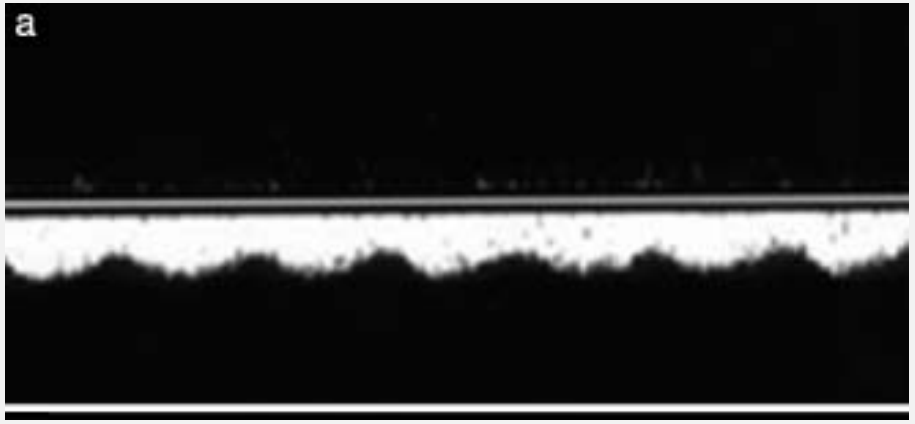
WHY DO WE EVALUATE FETAL VASCULATURE WITH DOPPLER?

UMBILICAL ARTERY DOPPLER

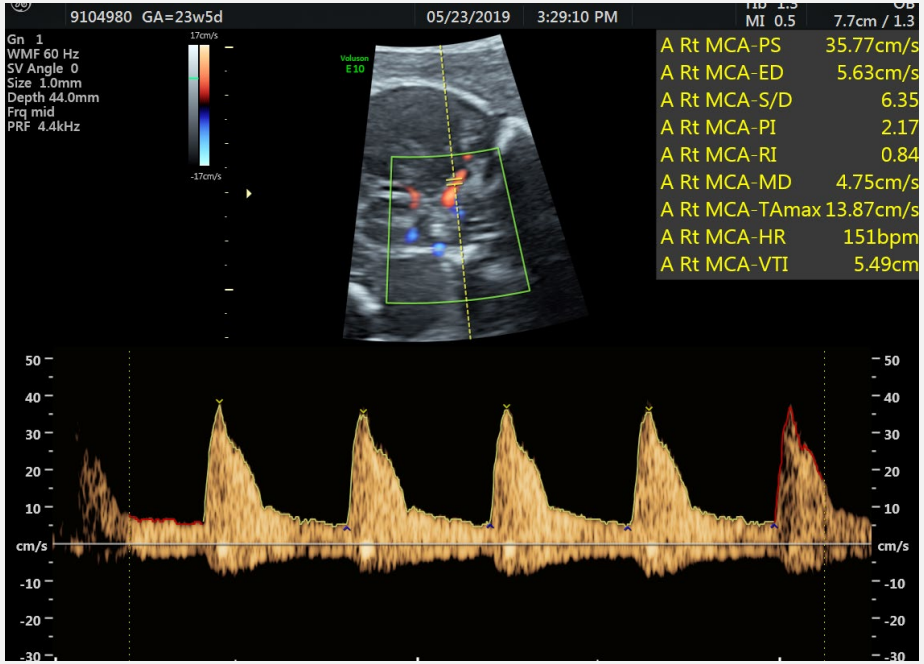


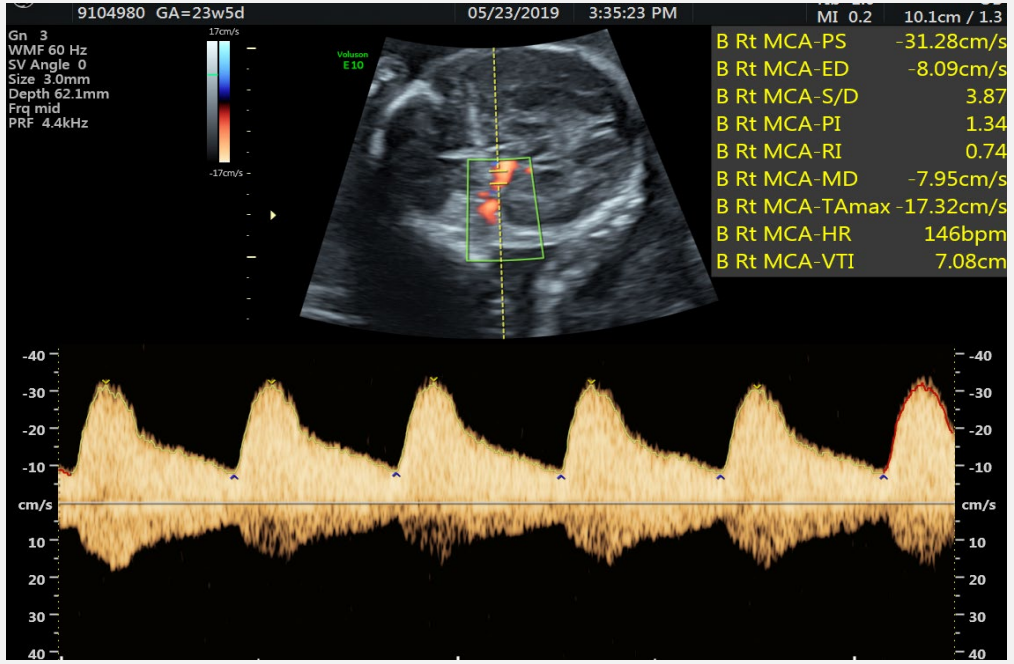


UMBILICAL VEIN DOPPER



MCA DOPPLERS



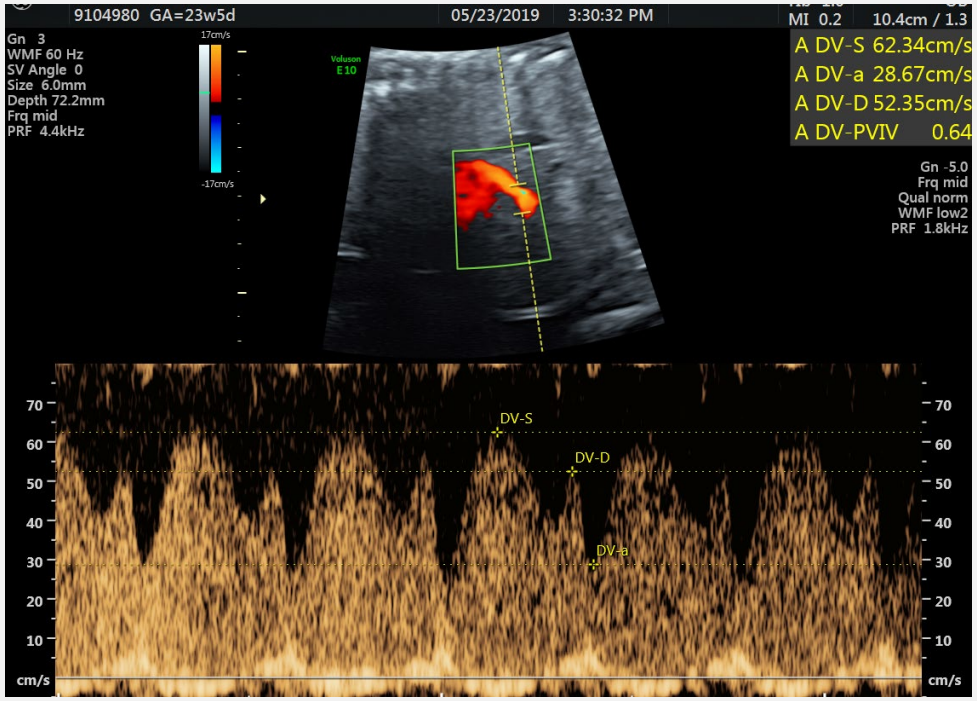


MCA-PSV

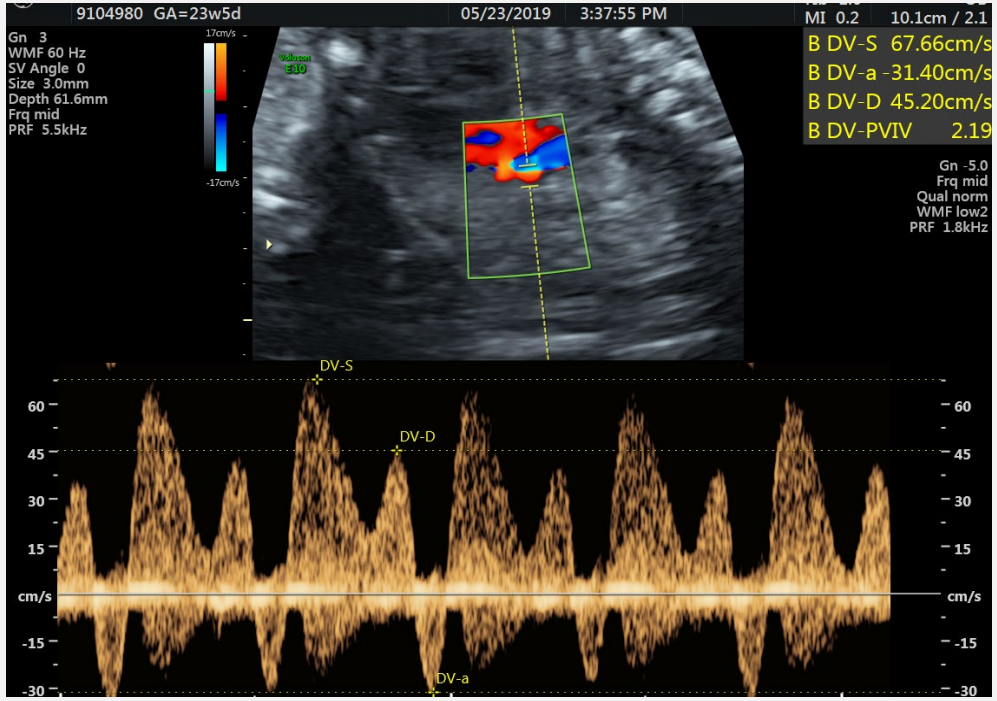
- Middle Cerebral Artery Peak Systolic Velocities (MCA-PSV)
- Discordant values are indicative of twin anemia polycythemia sequence (TAPS), a milder form of TTTS that occurs spontaneously in 5 percent of monochorionic twins.
- Discordancy is defined as MCA-PSV >1.5 multiples of the median (MoM) in one fetus in conjunction with a value of <1.0 MoM in the other.

DUCTUS VENOSUS

Donor



Recipient



OTHER CARDIAC VARIABLES

Alternative Predictive Scoring for TTTS

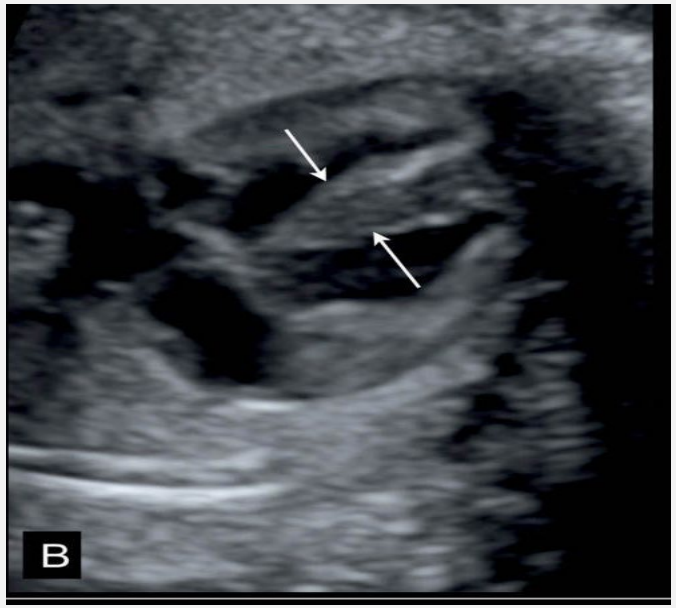
Assessment of Recipient Twin's Cardiac Status

VENTRICULAR HYPERTROPHY

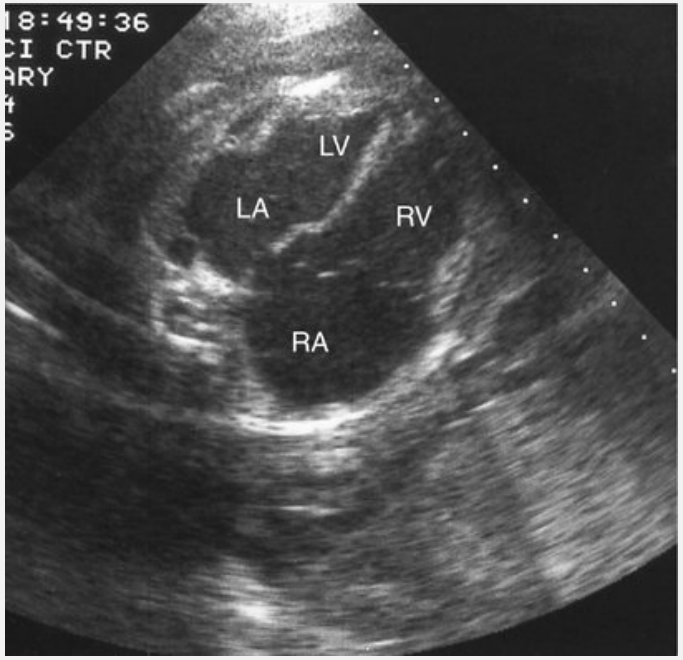
- Determined by qualitative assessment or by measurement.
  - Ventricular hypertrophy is present if the free walls of the ventricle or ventricular septum appear thickened

  OR

  - The right ventricle free wall ventricular septum thickness exceeds 2 SD from the expected mean for gestational age



CARDIOMEGALY



- Normal: cardiothoracic ratio is ≤1/3
- Mild: cardiothoracic ratio is >1/3 but <50%
- Mod-Severe: cardiothoracic ratio is ≥50%.

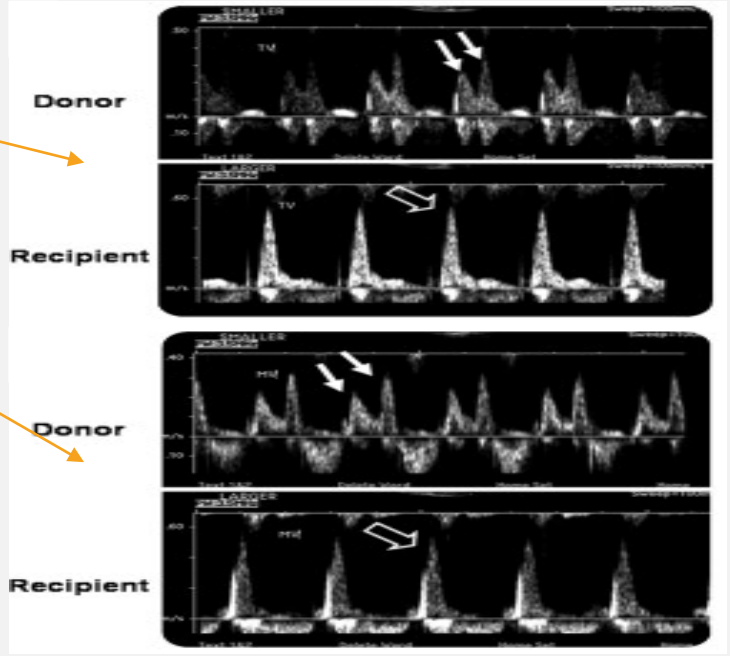
AV VALVE REGURGITATION

- Recipient twin assessment for mitral and tricuspid regurgitation
- If the regurgitant jet is >25% of the right atrial area (shown traced in the left image) then it is considered significant.

AV INFLOW INTERROGATION

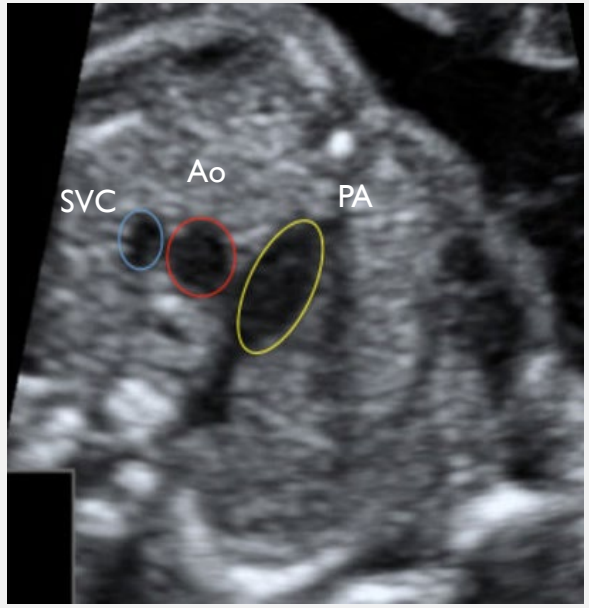
- Top image: inflow pattern across the TV valve
- Bottom image: inflow pattern across the mitral valve

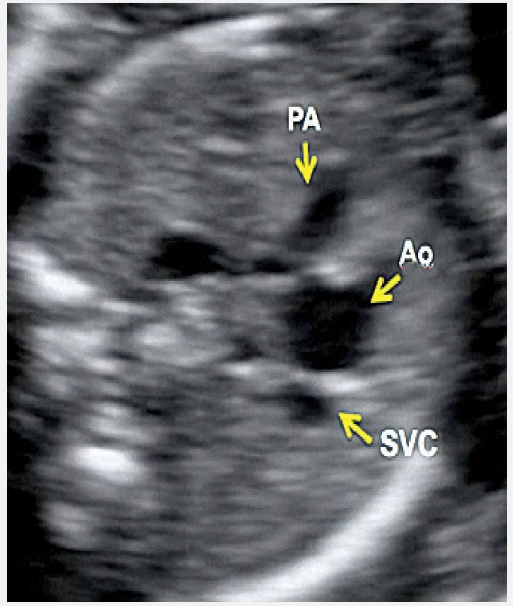
- Inflow across both valves normally elicits a 2-peak signal
- If diastolic ventricular compliance is abnormal, these 2 peaks will fuse together and form a single peak



ASSESS FOR RVOT OUTFLOW OBSTRUCTION

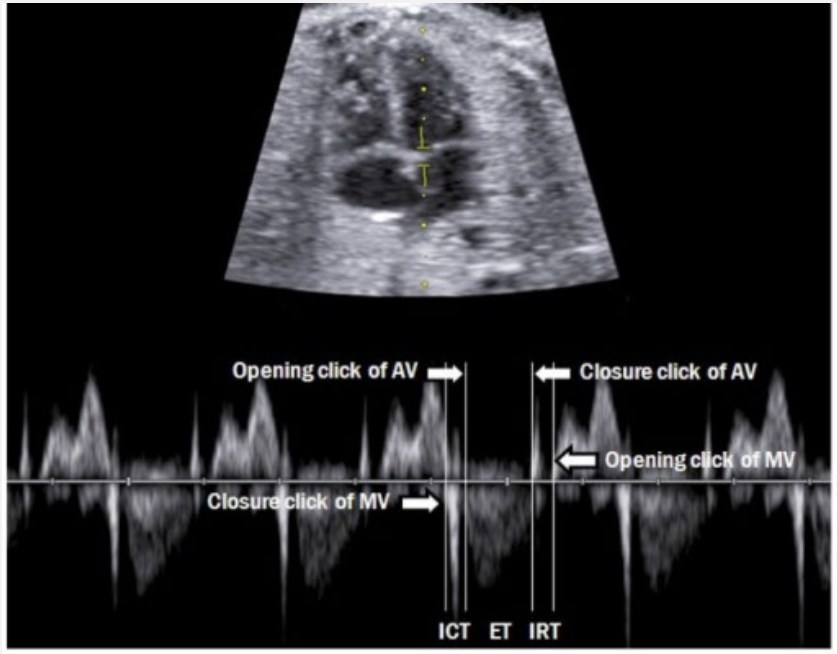
- PA is normally larger in diameter than the aorta
- As TTTS progresses, the pulmonary artery may not grow as well as expected. The pulmonary artery may be equal to the aorta in size, smaller than the aorta, or there may be frank right ventricular outflow tract obstruction
  - Subpulmonic or pulmonic stenosis





MYOCARDIAL PERFORMANCE INDEX

- MPI/Tei Index: ratio of combined ventricular isovolumic contraction (ICT) and isovolumic relaxation (IRT) times divided by the ejection time
- The greater the MPI, the greater the degree of ventricular dysfunction

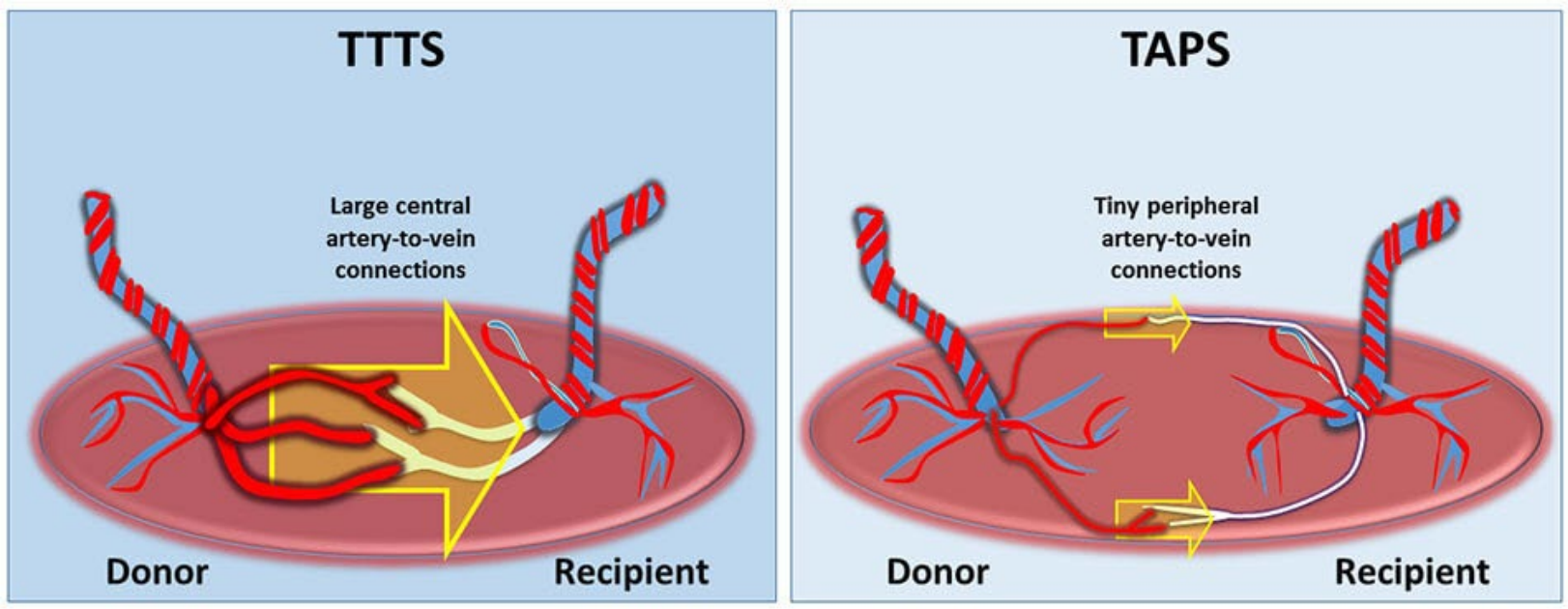


Mitral inflow and Aortic Outflow

RISKS OF TTTS

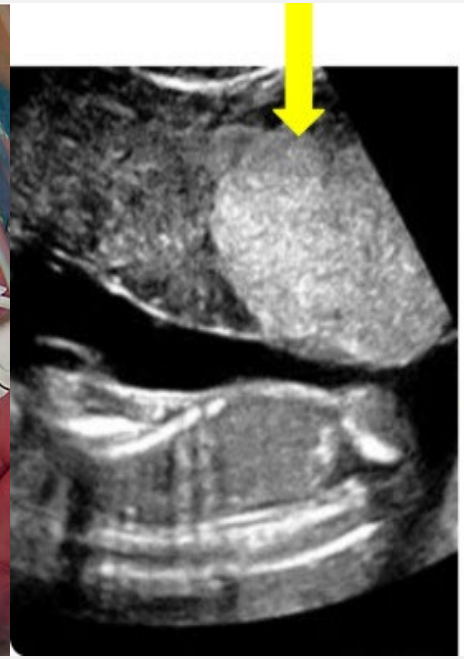
- 10-15% of monochorionic pregnancies will be complicated by TTTS
- Progression can take weeks but once it has started the disease process can progress rapidly
- Mean duration from diagnosis of stage I TTTS to a change in status was 11 days
- In those cases that progressed, the mean duration was 9 days

TWIN ANEMIA POLYCYTHEMIA SEQUENCE



TWIN ANEMIA POLYCYTHEMIA SEQUENCE (TAPS)

- Mild variant of TTTS
- Smaller/missed A-A or AV anastomoses results in a slow, but chronic transfusion syndrome resulting in a large inter-twin hemoglobin difference
- TAPS occurs in 2-13% of post laser cases



INTERVENTIONS

Amnioreduction and Fetoscopic Laser Ablation

WHEN TO INTERVENE AND WHICH METHOD IS BEST?

- Most Fetal Centers do not intervene for Type 1 TTTS unless there are concerns for cervical shortening, preterm labor or extreme maternal discomfort
- Data on pregnancy outcomes based on amnioreduction vs. laser ablation have yielded equivalent outcomes for Type 1 TTTS

Di Mascio D, Khalil A, D'Amico A, et al. Outcome of twin-twin transfusion syndrome according to Quintero stage of disease: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2020; 56:811.

FETOSCOPIC LASER ABLATION

- Fetoscopic laser ablation of placental anastomoses is the preferred procedure for definitive treatment of stage II to IV TTTS between 16 and 26 weeks of gestation

STAGE II-IV INTERVENTIONS 16-26 WEEKS

- Fetoscopic laser ablation of placental anastomoses is the preferred procedure for definitive treatment of stage II to IV TTTS between 16 and 26 weeks of gestation
- Preferred method due to studies demonstrating improved livebirths with the lowest risk for neurologic or cerebral injury through 6 years of age

Society for Maternal-Fetal Medicine, Simpson LL. Twin-twin transfusion syndrome. Am J Obstet Gynecol 2013; 208:3.

LASER ABLATION PROCEDURE

- Performed under local or general anesthetic (institutional dependent)
- Ultrasound prior to beginning the procedure
- Identify location of both umbilical cord insertion sites
- The suspected inter-twin vascular equator is located in the region between the two placental umbilical cord insertion sites.
- The lie of the "stuck" donor twin typically parallels this equator

LASER PHOTOCOAGULATION

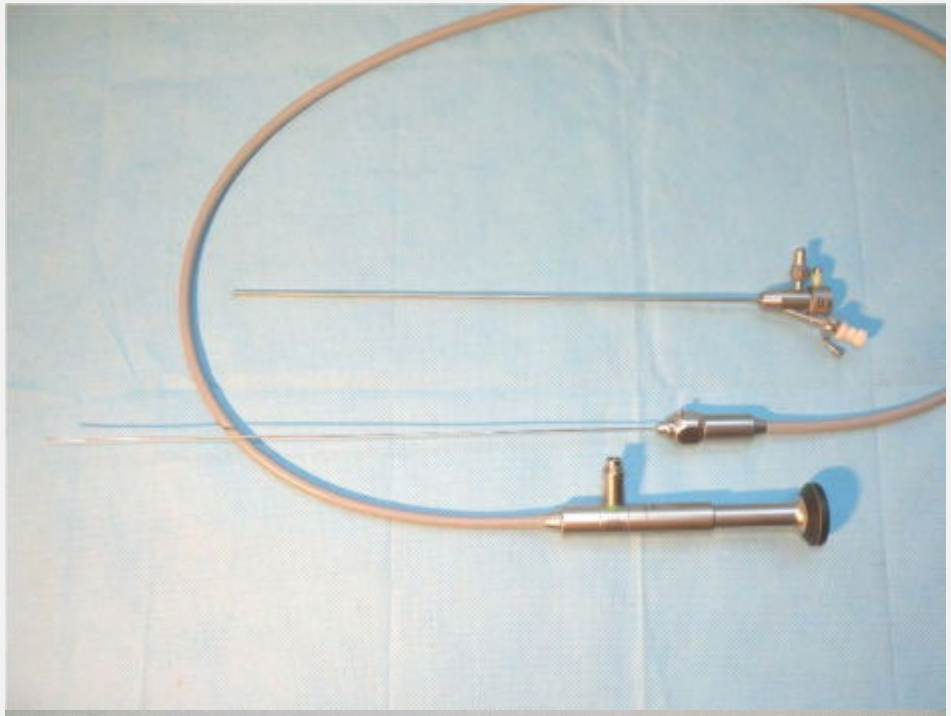
Scope Diameter is 2-3mm

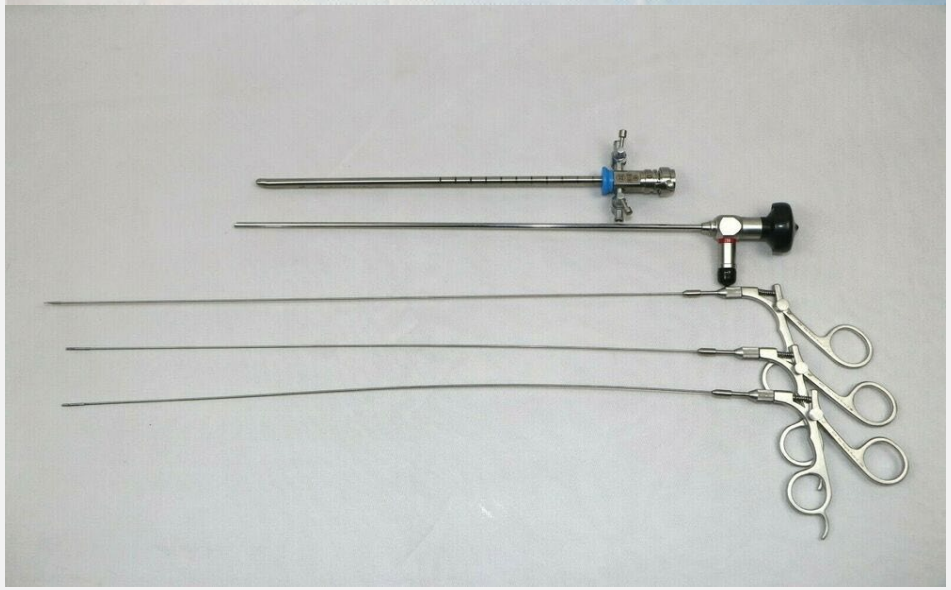
Single lens

Working Length is 20-30cm

Small operating chamber that allows laser fiber to be passed along length of the scope

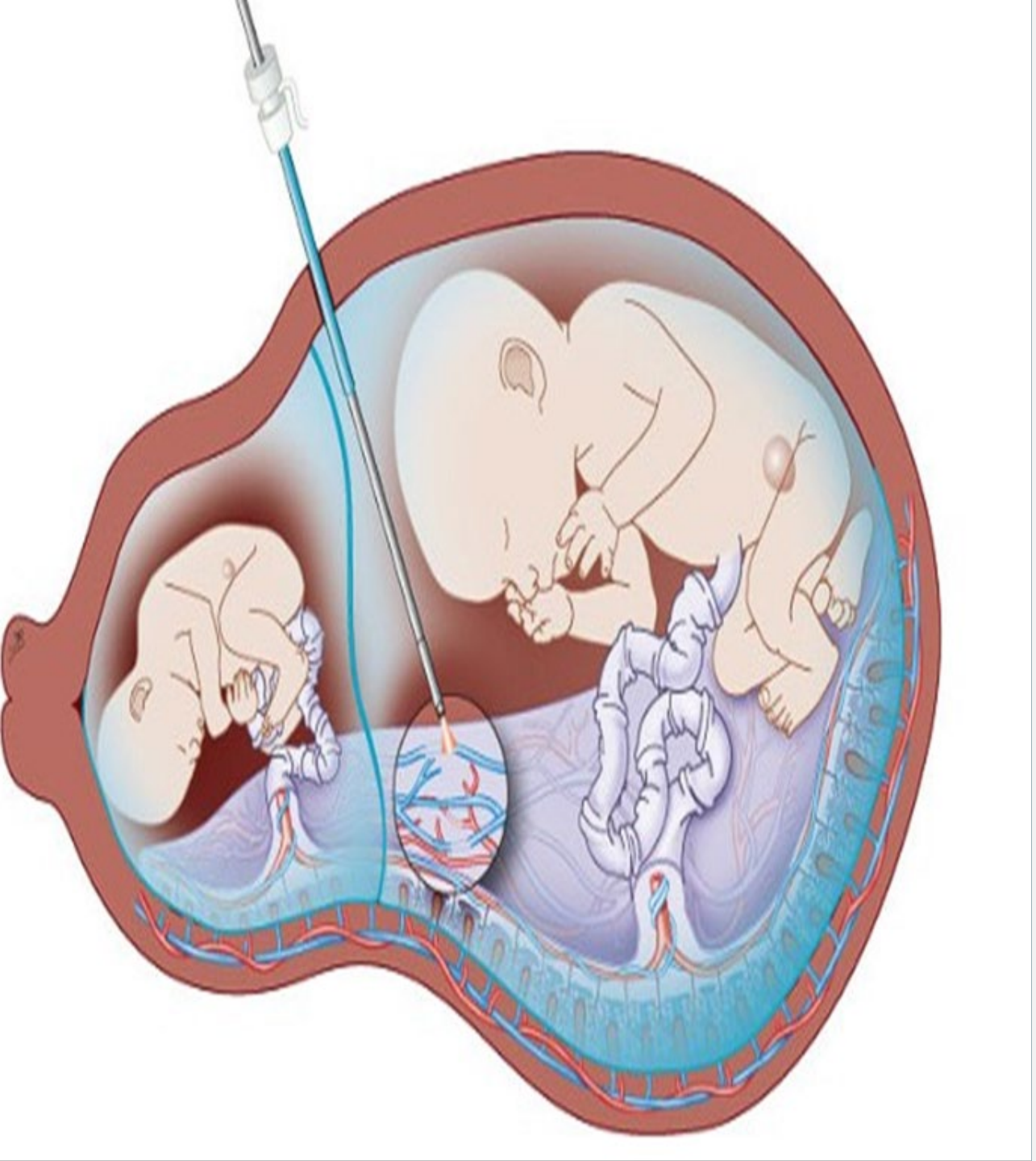
Another channel is present to allow for continuous irrigation





The inter-twin membrane on the placental surface is located as a landmark.

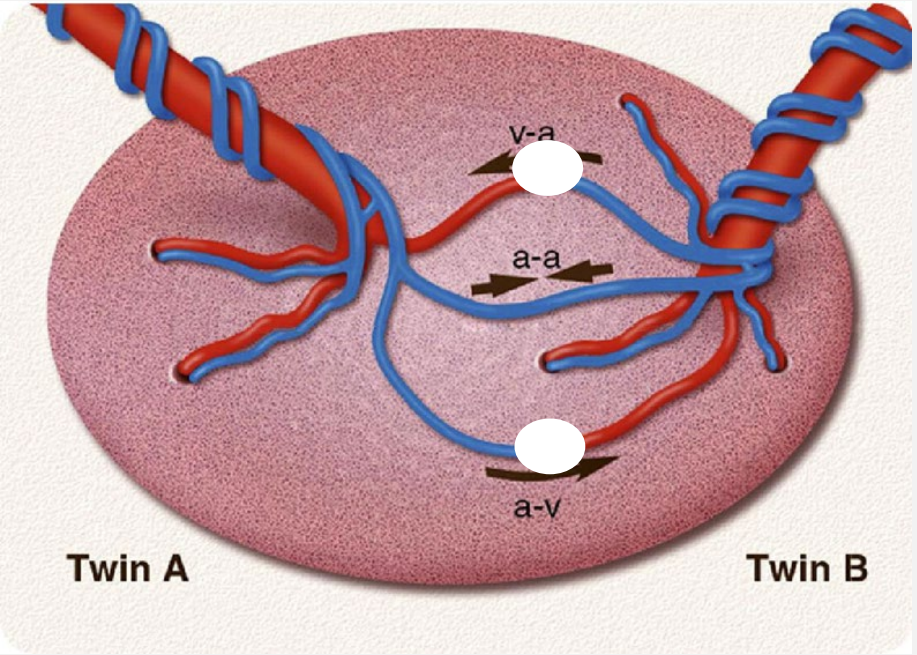
Once the vascular equator is found then “mapping” of the anastomoses occurs



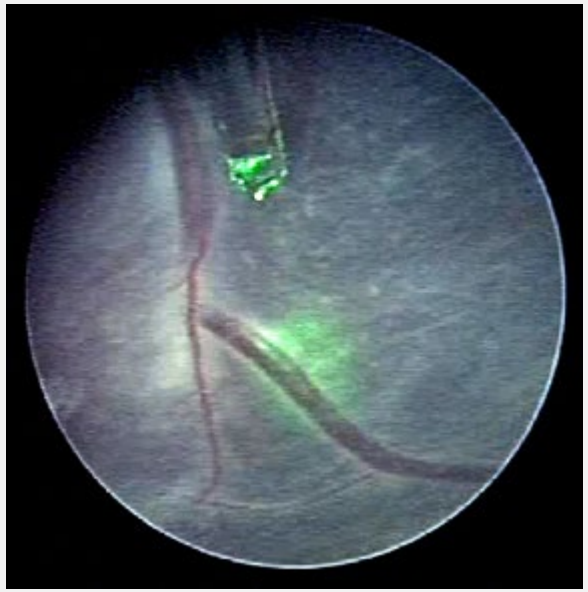
TECHNIQUES

- Sequential Selective Ablation
  - Anastomoses are coagulated in a specific sequential sequence
  - AV, donor artery to recipient vein, then VA, donor vein to recipient artery and lastly AA and VV anastomoses.
- Solomon (dichorionization)
  - After sequential selective ablation the entirety of the equator is ablated.
  - Decreased risks for TTTS recurrence and TAPS

PROCEDURE GOALS



LASER PHOTOCOAGULATION



FIRE THE LASER!

PROCEDURAL COMPLICATIONS

- Avg GA at delivery after fetoscopic laser ablation is 31-33W GA
- Preterm, Prelabor, Rupture of Membranes (PPROM)
  - Reports of risk being 7-40% occurring 1-3W from time of procedure
- Incidental Septostomy (tearing of the intertwin membrane) in 20% of cases
  - Cord entanglement, amniotic band syndrome resulting in loss of digits, limbs or in very rare cases demise of one twin due to cord constriction
- Loss of donor or recipient (10-30%) due to a variety of preexisting risk factors associated with TTTS pathology (i.e. hydrops fetalis)

POST-PROCEDURE COMPLICATIONS

- Persistence (failure) or recurrent TTTS: reported incidence is 0-16%
  - Residual anastomoses
  - Important to look closely at the placental margins for anastomoses
- Reverse TTTS (donor becomes recipient and vice versa): Rare

FREQUENCY OF AT LEAST ONE TWIN SURVIVING AFTER PROCEDURES

LASER

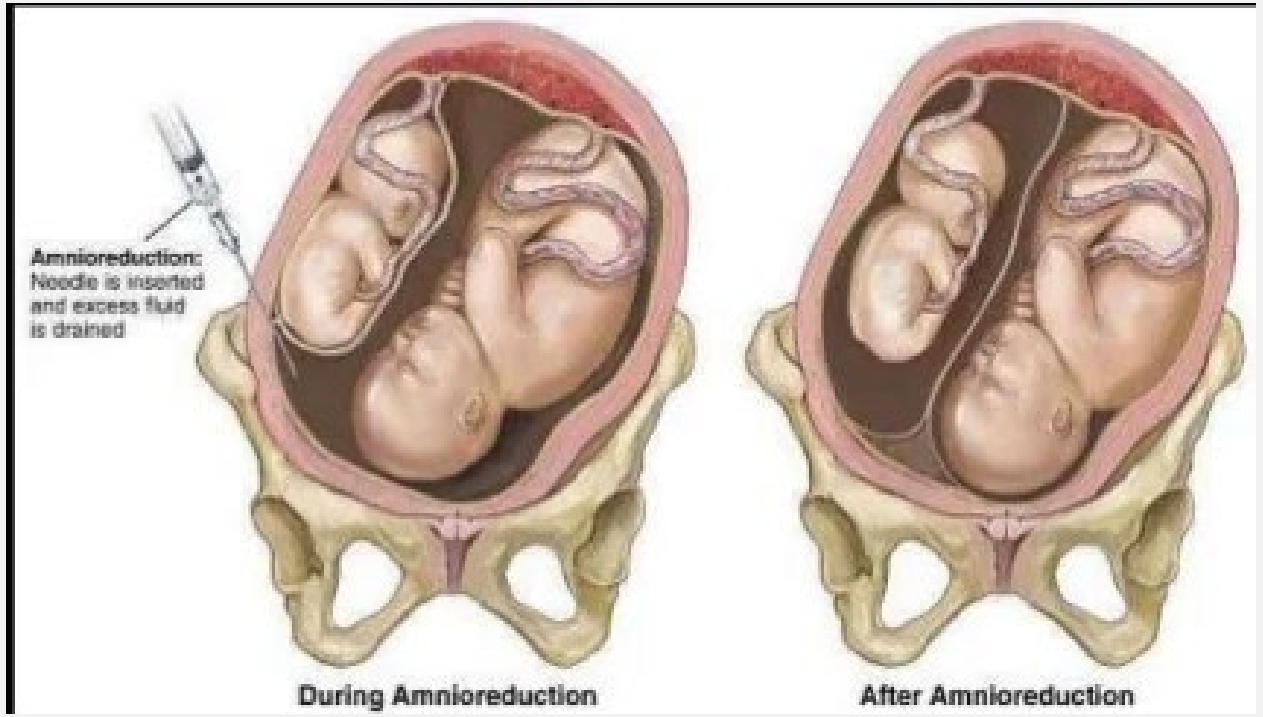
- The frequency of survival of at least one twin by stage was:
- Stage I – 86.9%
- Stage II – 85%
- Stage III – 81.5%
- Stage IV – 82.8%
- Stage V – 54.6%

AMNIOREDUCTION

- All cases were prior to 28 weeks but stages were not evaluated:
- One liveborn twin – 33%
- Cerebral injury observed in 25% of both recipient and donor twins at 4 weeks of life

POST-LASER PLACENTA

>26 WEEKS: AMNIOREDUCTION



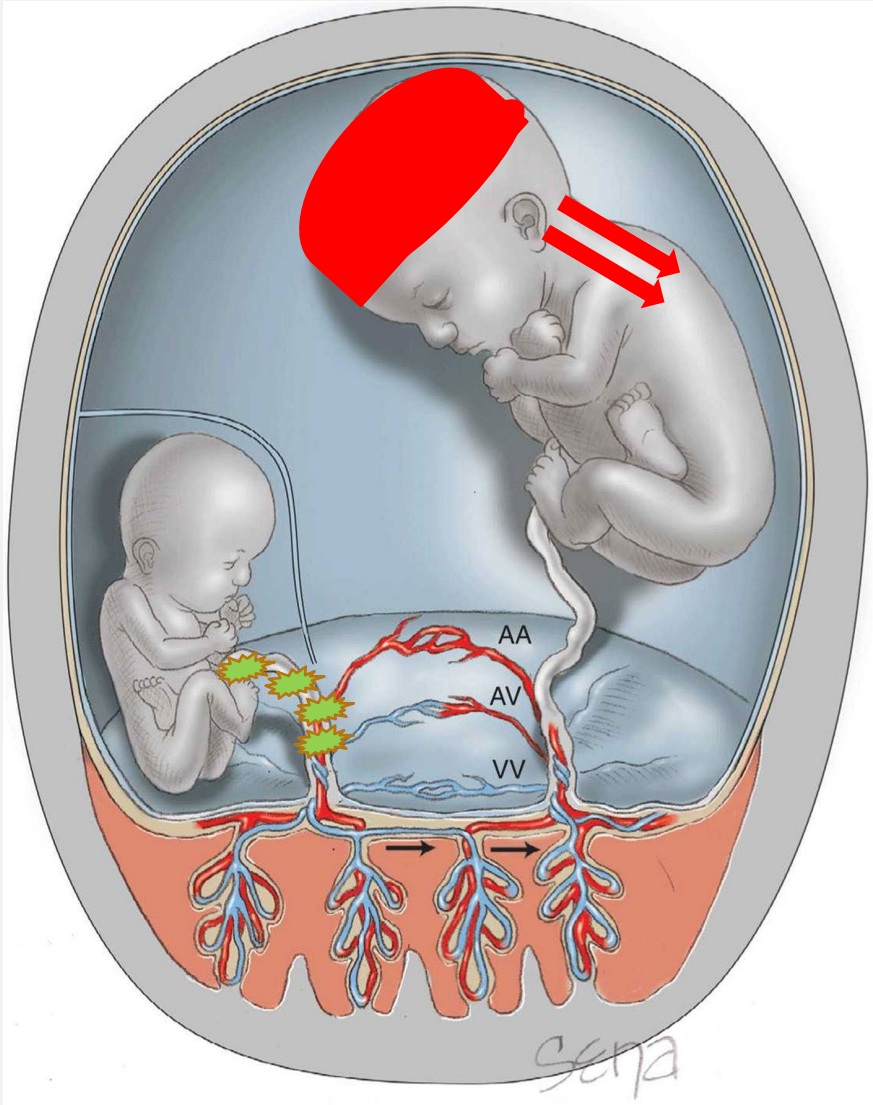
STAGE V TTTS (LOSS OF ONE BABY)

If one fetus has died, the major concerns for the co-twin are death (10 percent risk) or neurologic impairment (10 to 30 percent risk) due to their shared circulation

Watershed stroke

Ischemic Stroke

Other end organ damage



STAGE V TTTS SURVEILLANCE

- No interventions are warranted as the damage has likely already been done
- Performance of MCA-PSVs immediately following the loss of one twin can provide reassurance that major exsanguination has not occurred and the prognosis of the surviving twin may be good
  - Can perform an umbilical vein sampling to assess the fetal anemia status and an intrauterine fetal transfusion can be performed when severe fetal anemia is diagnosed
  - Have to be confident that death of the other twin was recent
- In most cases, there would be no benefit to delivery of the surviving twin due to significant risks for morbidity and mortality associated with premature delivery.
- Monitor growth every 3-4 weeks
- MRI is performed 4 weeks after loss of the other twin to assess for intracranial injury in surviving twin

DELIVERY TIMING

- Monochorionic, Dichorionic twins
  - We say 36W0D-36W6D
  - SMFM/ACOG: 34W0D-37W6D
  - North American Fetal Therapy Group: 37W0D-37W6D

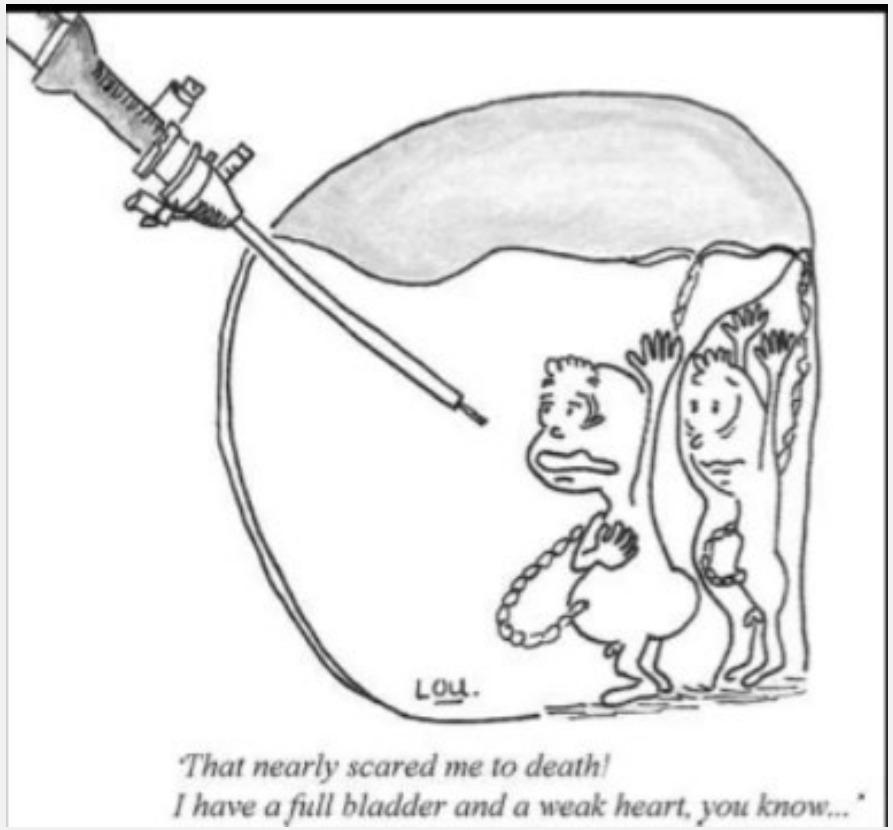
OUTCOME

- Underwent a fetoscopic laser ablation
  - <2 weeks later had lost one of the babies (stillbirth)
- Was there anything that could have been done to allow for the live birth of two healthy twins?

TAKE HOME POINTS

- Order a first trimester ultrasound or whenever the patient shows up for prenatal care
- Determining chorionicity is a big deal
- Obtain an ultrasound on any patient whom you know nothing about (personal twin anecdote)
- Delivery timing: think about risks for stillbirth vs. Neonatal death risks associated with co-morbidities

THANK YOU


LOU.
'That nearly scared me to death!
I have a full bladder and a weak heart, you know...'

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