Objectives

• Determine chorionicity in twins.
• Diagnose complications specific to monochorionic diamniotic gestations
• Monitor twin pregnancies with ultrasound techniques

Why are we so concerned about twins?

1% of live births
10-15% of perinatal death
23% of low birth weight babies
25% of most NICU census
Expenditure: 6x singleton

Mean GA of delivery

<table>
<thead>
<tr>
<th>Number of fetuses</th>
<th>Weeks of gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
</tr>
<tr>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>29 1/2</td>
</tr>
</tbody>
</table>

Cerebral palsy

5% to 10% of all cerebral palsy cases occur in twins which is more than 4-times the observed frequency in the general population


Twins in the USA

Twins in the USA

The twin birth rate was 35.9 per 1,000 in 2014, which was not significantly higher than the rate for 2013 (33.7), but was a new high for the nation. The triplet and higher-order multiple birth rate (triplet+) dropped another 5% in 2014 to 113.5 per 100,000 births and is down by more than 40% since the 1998 high.

Accessed 6/5/2017

Increasing multiples

Rate of monozygosity = 3-times higher in pregnancies conceived after ART, compared to spontaneous conceptions

Twins

• Etiology
• Diagnosis
• Placenta	on
• Aneuploidy screening
• Cervical

Twins – Etiology

• Monozygotic: 30%, sporadic, similar throughout the world (1:250 pregnancies)
• Dizygotic: 70%, increases with maternal age (>30), parity, ovulation induction, more common in some families, some ethnicities

Nigeria: The Yoruba have the highest rate of twinning in the world, at 45–50 twin sets per 1,000 live births. It is due to high consumption of a specific type of yam containing a natural phytoestrogen

Chorionicity/Amnionicity

<table>
<thead>
<tr>
<th>Days Post Concept</th>
<th>Stage</th>
<th>Placenta</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td></td>
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</tr>
<tr>
<td>3-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;13</td>
<td></td>
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</tr>
</tbody>
</table>
Etiology

Classification

Dizygotic (70%)

Monozygotic (30%)

DiC-DiA (8%)

MonoC-DiA (20%)

MonoC-MonoA (1%)

Monozygotic (30%)

Dizygotic (70%)

If your patient asks: fetuses are the same gender, does it mean they are identical?

43% of same-sex twins are monozygotic

Accuracy of Diagnosis

- Before ultrasound 25-50%
- Indicated ultrasound 75%
- Routine ultrasound 90%

Twins - Diagnosis

- Routine scan
- Clinical suspicion
- Reproductive technologies
- Note: number of sacs, yolk sacs, fetuses, location of placenta, presence and type of membrane, heartbeat

Chorionicity/Amnionicity

Why?

- Mortality x 3-4 in monochorionic twins
- Twin-twin transfusion
- Cord entanglement
- Conjoined twins (1/50,000 births)
- Co-twin death

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Perinatal mortality

<table>
<thead>
<tr>
<th>Type of twinning</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>DiC-DiA</td>
<td>8.9%</td>
</tr>
<tr>
<td>MonoC-DiA</td>
<td>25%</td>
</tr>
<tr>
<td>MonoC-MonoA</td>
<td>50-60%</td>
</tr>
<tr>
<td>Conjoined twins</td>
<td>&gt;90%</td>
</tr>
</tbody>
</table>

Twins-mortality

- Fatal loss (<24 weeks):
  - Dichorionic: 12.1%
  - Monochorionic: 4.8%
- Fatal loss (>24 weeks):
  - Dichorionic: 2.8%
  - Monochorionic: 1.6%

Chorionicity/Amnionicity

- When?: 1st Trimester
Chorionicity/Amnionicity

How?

- Dividing Membrane
- Placenta
- Fetal Sex

Diagnosis of chorionicity

- Dichorionic membranes
  - Typically well defined
  - Definite measurable width (usually greater than 2mm)

Twins: sonographic determination of Chorionicity/Amnionicity (I)

**Early Pregnancy**
- Number of sacs
- Number of fetuses/sac
- Width/number of membranes
- Location of yolk sac
- Number of placentas
- Twin peak or lambda sign (10-14 weeks)

**Diagnosis of chorionicity**

Early in pregnancy ultrasound imaging can distinguish between MC and DC twin pregnancies with more than 90% accuracy (lambda or twin peak sign vs. T sign)


**The lambda (twin peak) sign**

- Extension of placental tissue into the base of the inter-twin membrane

The lambda (twin peak) sign (cont.)

- Best at 10-14 weeks
- Lambda sign present: >90% predictive value for dichorionicity
- T-sign present:  
  - sens = 100%
  - spec = 98.2% for prediction of monochorionicity

Twin peak  
T-sign

Twins: sonographic determination of Chorionicity/Amnionicity (II)

- DC-DA
  - 2 separate rings/sacs
  - 2 placentas
  - Opposite sex (DZ)
  - Positive twin peak/lambda (99% accurate)
  - Thick membrane, 4 layers

Twins: sonographic determination of Chorionicity/Amnionicity (III)

- MC-DA (70% of MZ)
  - Single placenta
  - Same sex
  - Thin, elusive membrane
  - T sign

Twins: sonographic determination of Chorionicity/Amnionicity (IV)

- MC-MA
  - 1% of all monozygotic twins
  - Single embryo splits at day 8-10
  - High perinatal mortality (cord accidents)
  - Ultrasound
    - Same sac (no membrane)
    - One yolk sac
MC/MA

Twins: sonographic determination of Chorionicity/Amnionicity (V)

- Later Pregnancy
- Fetal Sex
- Number of placentas
- Membrane width (< or > 2mm)
- Lambda sign
Twins: sonographic determination of Chorionicity/Amnionicity (VI)

- Gender
- Opposite
- DZ (DC)
- Same
- # Placentas
- 1
- DC or MC
- Twin peak (10-14 wks)
- DC
- MC

Anomalies Unique to Multiple Gestations

- Conjoined twins
  - 1 per 33,000-165,000 births and 1 per 200,000 live births
  - Zygote splits after 13-15 days
  - Most Common (>50%):
    - Thoracoamphalopagus (ie, joined at the chest, abdomen, or both) - 74%
    - Thoracopagus or xiphopagus (ie, joined at the chest) - 40%
    - Omphalopagus (ie, joined at the abdomen) - 34%

Complications Unique to Multiple Gestations

- “Vanishing-twin” syndrome
- Growth discordancy
- Twin-twin transfusion syndrome: TTTS
- Twin-reversed arterial perfusion sequence: TRAP (Acardiac twin is previous, less scientific, but still used nomenclature)
- Fetal anomalies
Twins – Complications

“50% of 1st trimester multiple gestations result in the birth of a singleton”

Varan, 1979

Vanishing Twin

• Sac smaller than normal
• Irregular margins
• Crescent shaped
• Incomplete trophoblastic ring

Growth discordancy

- Constitutional
- Genetic
- Placental

Early Growth Discordancy

- Difference in CRL may be 1st sign of chromosome abnormality, major congenital anomaly or imminent demise (Cheeth, 1992; Weisman, 1994)
- <8 weeks, >3mm difference is associated with 50% risk of demise of smaller twin (Dickey, 1992)
- Use the larger twin CRL to determine gestational age.
- Label the twins and be consistent
Monochorionic Twins

- ↑ after IVF potential causes
  - Lower maternal age
  - Ovulation induction
  - Length of embryo culture
  - Cultivation media conditions
  - Manipulation of zona pellucida
  - Hereditary factors
  - Ovarian function

Monochorionic twins - Risks

- Twin-Twin Transfusion Syndrome - TTTS
- Twin Anemia Polycythemia Sequence - TAPS
- Twin reversed arterial perfusion - TRAP
- Selective Fetal Growth Restriction - FGR
- Discordance for fetal anomalies
- Death of a twin

Twin-twin transfusion syndrome

- 10-15% monochorionic twins
- 50% perinatal mortality in monochorionic twins
- Unbalanced AV shunt
- Mortality = 40-100% if untreated, 15-50% handicap
- Donor: small, oligohydramnios
- Recipient: large, polyhydramnios


### Quintero’s stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Oligo and Polyhydramnios</th>
<th>Absent Urine in Donor Bladder</th>
<th>Abnormal Doppler Blood Flows</th>
<th>Hydrops Fetalis</th>
<th>Fetal Demise</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>*</td>
<td>–</td>
<td>–</td>
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<tr>
<td>II</td>
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<tr>
<td>III</td>
<td>*</td>
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<tr>
<td>IV</td>
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<td>–</td>
</tr>
<tr>
<td>V</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>


### TTTS

- Polyhydramnios (>8cm)
- Oligohydramnios (<2cm)

### What doppler velocimetry is used?

- Umbilical artery doppler velocimetry: Absent or reversed flow
- Ductus venosus-reversal of a wave
- Umbilical vein-pulsatile flow
Can we predict TTTS?

- Inter twin CRL discrepancy + isolated increased nuchal translucency: present x 3 more frequently in cases of TTTS
- TTTS: more common when abnormal DV blood velocity waveform detected during the 11-13+6 week exam


TTTS: treatment

- Conservative-Stage I
- Amnioreduction-laser not available or after 26 weeks
- Amniotic septostomy
- Selective feticide-bipolar diathermy, Radiofrequency ablation, or laser of umbilical cord
- Laser obliteration of placental anastomoses
  - Acceptable for stage I
  - Recommendation stage II

TAPS

Twin Anemia-Polycythemia Sequence

- Large inter-twin hemoglobin differences in the absence of amniotic fluid discordance
- Few, minuscule AV placental anastomoses (diameter <1mm) with a slow blood transfusion from donor to recipient, leading gradually to highly discordant Hb levels

TAPS

- Affects 3-5% monochorionic twins after 26 weeks
- Affects up to 16% monochorionic twins after fetoscopic laser for TTTS
- Diagnosed by discordance in fetal middle cerebral artery peak systolic velocity (MCA-PSV) measurements
- Optimal treatment, timing, and surveillance have not been determined.


TAPS-Perinatal outcome

- Not well known (only case reports and small series)
- Vary according to severity
- May range from double intrauterine fetal demise to two healthy neonates without major morbidity at birth besides large intertwin hemoglobin differences
- Most: severe anemia in donor requiring blood transfusion, and severe polycythemia in recipient requiring partial exchange transfusion.
- Cases of severe cerebral injury in TAPS have also been described


Growth discordancy in MC twin

- Inter-twin crown-rump length (CRL) difference greater than 10%: increases the risk for discordant fetal growth or TTTS
- CRL difference of less than 10%: excellent prognosis in terms of perinatal outcome
Selective Fetal Growth Restriction

- Disproportionate sharing in conjunction with abnormal vascular connections
- Two definitions
  - One fetus <20% EFW with or without intertwin discordancy
  - Intertwin discordancy >25%
- OK to use 20% weight differential to identify women at risk
- Routine growth scans Q4 weeks
- After diagnosis, doppler velocimetry Q1-2 weeks

Monochorionic twins – Death of One Fetus

- Co-fetal death: 12-25%
- Neurological morbidity: 25%

Monochorionic twins – Death of One Fetus

- Survivor follow up
  - Delivery usually not indicated
  - Serial growth ultrasounds
  - MCA doppler velocimetry to screen for anemia Q2-4 weeks
  - Neuroimaging 4-6 weeks after event

Monochorionic Antenatal testing

- Q2 week US for MVP, bladder visualization beginning at 16 weeks
- Anatomy ultrasound and fetal ECHO at 18-22 weeks
- Q4 week growth after anatomy scan
- Doppler velocimetry-be consistent

MonoC-monoA complications

1) unequal sharing of the placenta (discordant fetal growth with IUGR, metabolic compromise and death)
2) chronic unidirectional blood shunting through placental vascular anastomoses (TTTS or twin reverse arterial perfusion [TRAP] and death)
3) conjoined twinning and cord entanglement (can also lead to death)


MonoC-monoA

[Diagram showing classification of monozygotic twins]

Twin Reverse Arterial Perfusion (TRAP), a.k.a. acardiac twin

- Due to unidirectional arterio-arterial placental anastomosis
- Responsible for secondary fetal cardiac hypoplasia and amorphic development: one twin pumps blood for both fetuses of a MC twin pregnancy.
- TRAP occurs in both MCMA and MCDA twin pregnancies
- Overall pregnancy loss rate estimated at 50% (due to high output cardiac failure and preterm delivery)
- Can be diagnosed in 1st trimester


TRAP sequence (Acardia)

- One twin has absent, rudimentary or nonfunctioning heart
- 5 types. Most common (60-75%): acardius acephalus.
  - Head is absent, trunk and limbs +/- developed.
- Pathophysiology: a to a anastomoses between umbilical arteries, early in embryogenesis.
  - One twin becomes "pump", other "perfused" by retrograde, deoxygenated blood.
  - Lower body gets "better" blood and develops preferentially.

TRAP sequence (Acardia)

- Most common (75%)
  - Monochorionic-diamnionic
- Less common (25%)
  - Mono-mono
- Trisomy in 10% of "pump" twin
- "Pump" twin at risk of CHF
- Complications: polyhydramnios, preterm labor
A cardiac twin

Risk of Chromosomal Abnormalities
- MZ twins: almost always genetically identical, thus risk of each fetus = singleton-age-related risk
- DZ twins: each twin has independent risk
  - Approximately 2x age-related risk

Risk of Chromosomal Abnormalities
- ART/ICSI associated with increased risk of aneuploidy.
Aneuploidy Screening

- More and more pregnancies in women > 35
- ↑ Incidence of multiple gestations
- Risk of one twin, the other or both, to have trisomy 21 is 80% higher than singleton at same maternal age (risk comparable to patient 2-4 years older)

Aneuploidy screening options with ultrasound

- First trimester screening
- Nuchal translucency must obtained in both fetuses
- Not useful if there is a vanishing twin.

Diagnostic testing

- CVS or amniocentesis
- Loss rate—2-3.5% vs 1.5-3.1%
Do all monozygotic twins have same karyotype?

Heterokaryotypia - a discordance in karyotype due to either an early postzygotic chromosomal rescue in one fetus or a mitotic error that leads to one trisomic fetus with a normal co-twin


Malformations in Twins

- Birth Defects x 2 Singletons
- MZ >> DZ
- Cardiac (PDA, single ventricle, VSD), CNS, facial clefts, GI abdominal defects
  - Monochorionic twins have 5% risk of cardiac malformation → Fetal ECHO

Fetal Anomalies

- Twin "A": 7.3%
- Twin "B": 9.4%
- (2.5% in singletons)
Management of Pregnancy with 1 Anomalous Twin

- Continuation
- Termination
- Selective Reduction

Selective Reduction

- Fetal Abnormality
  - Chromosomal (50%)
  - Structural (43%)
  - Other (7%)

Pregnancy Losses after Selective Reduction

- 8 unintended (4%)
  - 4/164 twins
  - 4/164 triplets
  - No losses in 4 quads
- Mean GA at delivery = 37.1 weeks
Fetal Reduction

- Initially to reduce high order multiples
- Usually to twins
- Increasingly to singleton

Outcome - Loss

- Complete loss rate: 4.7%
- 46% of losses >8 weeks
- Chance of loss
  - 1% within 4 weeks
  - 1.5% 4-8 weeks
  - 2.1% >8 weeks

Outcome – Loss (cont.)

<table>
<thead>
<tr>
<th>Starting # fetuses</th>
<th>Loss rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>3</td>
<td>5.1</td>
</tr>
<tr>
<td>4</td>
<td>5.5</td>
</tr>
<tr>
<td>6+</td>
<td>11.0</td>
</tr>
</tbody>
</table>

Outcome – GA at Delivery

Mean GA: 36.2 weeks

Decrease in PTD when reduced to singleton compared to twins


Reduced vs. Non-Reduced Twins

• Decreased risk of PTB <37 weeks


Uncomplicated DC/DA Twins

Uncomplicated MC


Cervical length in twins

- 21 studies (16 in asymptomatic women and 5 in symptomatic women) with a total of 3523 women
- CL ≤ 20 mm at 20-24 weeks: most accurate in predicting PTB <32 and <34 weeks (pooled sens, spec, + and - LR of 39% and 29%, 96% and 97%, 10.1 and 9.0, and 0.64 and 0.74, respectively).
- CL ≤ 25 mm at 20-24 weeks: pooled + LR of 9.6 to predict preterm birth <28 weeks' gestation.
- Most twins are delivered by 37 weeks


Identical quads