Twins: New Guidelines  
*What you need to know*

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**Objective**

- To review the expected “standard of care” when managing twin pregnancies
  - to provide high-quality obstetric care
  - to avoid medical malpractice

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**Question 1**

Which of the following is **most** predictive of a twin pregnancy?

a. Larger than expected uterine size  
b. Strong family history of twins  
c. Severe hyperemesis  
d. Elevated serum βHCG  
e. Conceived via ovulation stimulation
Clinical Suspicion of Twins

- Larger than expected uterine size
- Strong family history of fraternal twins
- Severe hyperemesis gravidarum
- Elevated serum βHCG
- Assisted reproductive technologies

Prior to routine use of ultrasound, 10-15% of twins diagnosed in labor

Diagnosis and Dating of Twins

- Diagnosis best in the first trimester and dating optimal using crown-rump length
  - 20% of first trimester twin pregnancies result in singleton live births
  - Vanishing twin associated with favorable prognosis of surviving twin, similar to singleton pregnancy
- Multiple biometric measurements should be used beyond the first trimester
- If discrepancy in dates between the twins, date using the larger twin

Importance of Pregnancy Dating in Twins

- Timing for screening and diagnostic testing
- Accurate interpretation of twin growth
- Scheduling of twin deliveries
Question 2
Which of the following is **most** characteristic of dichorionic twins?
- a. Single placenta
- b. Same gender
- c. Two amnions
- d. T-sign
- e. Lack of a separating membrane

Types of Twins
- All dizygotic twins are dichorionic
- All monochorionic twins are monozygotic
- Not all monozygotic twins are monochorionic

Determination of Chorionicity
- Optimal in first trimester
  - close to 100% accuracy
- Incorrect assignment in up to 10% of cases when determined in second trimester

Wood et al., 1996; Lee et al., 2006
Determination of Chorionicity

- Gestational sacs
- Amniotic sacs
- Placenta number
- Intertwin membrane
  - thickness, layers, λ sign, T sign
- Gender

Importance of Chorionicity

Aneuploidy

Higher-Order Multiples

Discordant Growth

Prenatal Diagnosis in Twins

Goals in twin gestations are the same as for singletons

- To identify fetal abnormalities that could change a couple’s decision to continue a pregnancy or alter obstetric care – genetic, syndromic, and/or structural
- To identify fetuses that might benefit from fetal or early neonatal therapy

Graham and Simpson, 2005
Question 3

Which of the following is not associated with an increased nuchal translucency in a twin gestation?

a. Structural heart defect  
b. Fetal supraventricular tachycardia  
c. Turner syndrome  
d. Twin-twin transfusion syndrome  
e. Trisomy 21

First Trimester Risk Assessment

Trisomy 21 Screening in Twins: Detection Rate for 5% False Positive Rate*

<table>
<thead>
<tr>
<th>Twin Pregnancy</th>
<th>Nuchal Translucency</th>
<th>Combined with free BHCG &amp; PAPP-A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monochorionic</td>
<td>73%</td>
<td>84%</td>
</tr>
<tr>
<td>Dichorionic</td>
<td>68%</td>
<td>70%</td>
</tr>
<tr>
<td>All twins</td>
<td>69%</td>
<td>72%</td>
</tr>
<tr>
<td>Singletons</td>
<td>73%</td>
<td>85%</td>
</tr>
</tbody>
</table>

* All tests include maternal age

Wald et al, 2003; Cleary-Goldman et al, 2005

Diagnostic Prenatal Testing

CVS  
- 10-13 weeks gestation
  - Sample each placenta separately
  - 2% of samples show cross contamination
  - Pregnancy loss data limited for twins (for singletons 1%)

Amniocentesis  
- ≥ 15 weeks gestation
  - Double needle approach
  - Indigo carmine into first sac after withdrawing fluid
  - Attributable risk for pregnancy loss 1.6-1.9% (for singletons 0.6-1.0%)

ACOG Committee Opinion 640, 2015

- Cell-free DNA screening for fetal aneuploidy – not a diagnostic test
- It is not recommended for women with multiple gestations

Strickland et al, 2003; Wapner et al, 1993; Wapner, 1995; Cahill et al, 2009

Ghidini et al, 1993; Wapner et al, 1993; Wapner, 1995; Cahill et al, 2009
**Importance of Nuchal Translucency in Twins**

- Aneuploidy
- Structural malformations
- Twin-twin transfusion syndrome
  
  
  
  - PPV 30%

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**Twin Anatomy: Fetal Anomalies**

- Background risk for singletons
  
  - 2% overall
- Rate same per fetus for dizygotic twins
  
  - 4% overall
- Rate 2 to 3 times higher for monozygotic twins
  
  - 4-6% per fetus, 8-12% overall
    
    - rate of congenital heart disease increased
    
    - 2-3% per fetus, 6% overall

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**Question 4**

Fetal echocardiography is recommended for all of the following twin pregnancies except:

- a. Spontaneous monochorionic diamniotic twins
- b. Monoamniotic twins
- c. Clomid induced dichorionic twins
- d. Twins with twin-twin transfusion syndrome
- e. IVF conceived dichorionic twins
Screening for Fetal Malformations

- Imaging more difficult with greater number of fetuses
- Discordant twin anomalies are the norm
  - Only 10% of DC and 20% of MC twins have concordant defects
- Fetal echocardiography is now indicated for all
  - IVF conceived pregnancies
  - Monochorionic twins
- Only ¼ to ½ of all major anomalies detected prior to birth

Structural Anomalies in Twins

Management of discordant twin anomalies depends on a number of factors:
- Gestational age at diagnosis
- Placenta
- Type of defect
  - Lethal vs nonlethal
  - Potential for pregnancy complications

Importance of Placental Evaluation

- Placental location
  - Previa
    - 40% higher in twin births (3.9 per 1,000 live births)
  - Placental cord insertion more likely to be abnormal in twins
    - Marginal
    - Velamentous
    - Vasa previa
A velamentous placental cord insertion in a monochorionic twin pregnancy is a strong sonographic marker for which of the following?

- TAPS (twin anemia-polycythemia sequence)
- Unequal placental sharing with discordant growth
- TRAP (twin reversed arterial perfusion)
- TTTS (twin-twin transfusion syndrome)

**Velamentous Placental Cord Insertion**

- 10% of twins (1% of singletons)
- Marker for TTTS (OR 7.5, 95% CI 2.14-26.5) and unequal placental sharing (OR 38, 95% CI 3.4-266.5)
- 2% associated with vasa previa; detection rate > 90-95% with routine use of transvaginal ultrasound using color and pulsed Doppler in midtrimester
- Perinatal mortality of vasa previa
  - ~ 50% in undiagnosed cases
  - < 5% in cases identified prenatally

Simpson et al. ACOG 2011;54:145
Derbala et al., 2007

**PCI: Ultrasound and Pathology**

- Vasa Previa
- Velamentous PCI with intertwin anastomoses
• Identify patients at risk for preterm delivery
  - Mean gestational age for live born twins = 35.4 weeks
• Potential clinical value for all twin gestations
• Transvaginal approach proven to be optimal approach to assess cervix

Importance of Cervical Length

Meta-Analysis of 21 Twins Studies

- Transvaginal cervical length ≤20 mm at 20-24 wk performed best as predictor of spontaneous preterm birth in asymptomatic women with twins

<table>
<thead>
<tr>
<th>Spontaneous Preterm Birth</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive LR</th>
<th>Negative LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;28 weeks</td>
<td>35%</td>
<td>93%</td>
<td>5.2</td>
<td>0.69</td>
</tr>
<tr>
<td>&lt;32 weeks</td>
<td>39%</td>
<td>96%</td>
<td>10.1</td>
<td>0.64</td>
</tr>
<tr>
<td>&lt;34 weeks</td>
<td>29%</td>
<td>97%</td>
<td>9.0</td>
<td>0.74</td>
</tr>
</tbody>
</table>

- Cervical length >35 mm at 20-24 wk, high likelihood of delivery ≥34 wk, PPV >95%

Conde-Agudelo et al, 2010

Question 6

Of the following, which is the best management of a short cervix in a twin pregnancy?

- a. Weekly IM 17P injections
- b. Pessary
- c. Shirodkar cerclage
- d. Vaginal progesterone
- e. Routine prenatal care
Cervical Length

- Baseline assessment and serial assessments for patients at risk
  - All twin pregnancies
- Optimal cervical length threshold and frequency of follow-up assessments uncertain
  - ≤20 mm, two week intervals
- Management of patient with twins and a short cervix remains controversial

Preterm Delivery in Twins

**No role for . . .**
- Prophylactic cerclage
- Prophylactic bed rest
- Prophylactic tocolysis
- Prophylactic 17P
- Home uterine activity monitoring

**But if short cervix, may be role for . . .**
- Vaginal progesterone

**And if preterm labor, there is a role for . . .**
- Antenatal steroids ± tocolysis
- Magnesium sulfate for neuroprotection
  - Decrease risk of CP

Importance of Twin Growth

- Detection of intrauterine fetal growth restriction
- Diagnosis of twin discordance
- Identify cases for increased surveillance
- Twin growth impacts delivery planning
**Evaluation of Twin Growth**

- Fetuses of a multiple gestation tend not to grow at the same rate as singletons.
  - Individual biometric measurements close to that of singletons up to 30 weeks; twin growth slows after 30 weeks.
- Main determinants of growth: genetic potential and placental function.
  - Assume same for monochorionic pregnancies.
  - Likely to be different for dichorionic pregnancies.
- Risk for adverse outcomes with birth weights <5th %ile.
  - 7.5% for monochorionic pregnancies.
  - 1.7% for dichorionic pregnancies.

**Twin Discordance**

Discordance = \( \frac{\text{EFW of larger twin} - \text{EFW of smaller twin}}{\text{EFW of larger twin}} \)

- 20-25% discordance considered to be significant.
- Disparate abdominal circumferences early sonographic sign.
  - Intertwin AC \( \geq 20 \text{ mm at } >24 \text{ weeks} \) has a positive predictive value of >80% to detect 20% or more discordance in birth weight.

**Causes of Discordant Growth**

- Structural anomalies.
- Chromosomal abnormalities.
- Genetic syndromes.
- Discordant congenital infection.
- Unfavorable placental implantation.
- Unfavorable cord insertion site.
- Placental abruption.
- Complications of monochorionic placentation.

*Monthly ultrasounds for fetal growth recommended for all twin pregnancies.*
Importance of Ultrasound in Monochorionic Twins

- Monoamniotic twins
- Conjoined twins
- Twin reversed arterial perfusion (TRAP) syndrome
- Twin reversed arterial perfusion syndrome (TRAPS)
- Twin-to-twin transfusion syndrome (TTTS)
- Unequal placental sharing (UPS) with discordant twin growth or selective intrauterine growth restriction (sIUGR)
- Twin anemia-polycythemia sequence (TAPS)
- Single twin demise in the second or third trimester

Potential Complications in Monochorionic Twins

- Monoamniotic twins
- Conjoined twins
- Twin reversed arterial perfusion (TRAP) syndrome

**Twin-twin transfusion syndrome (TTTS)**
- Unequal placental sharing (UPS) with discordant twin growth or selective intrauterine growth restriction (sIUGR)
- Twin anemia-polycythemia sequence (TAPS)
- Single twin demise in the second or third trimester

**Question 7**

Of the following, which is **not** a criterion in the staging of twin-twin transfusion syndrome?

- a. 20% discordant twin growth
- b. Non-visualization of the fetal bladder
- c. Polyhydramnios-oligohydramnios sequence
- d. Demise of one twin
- e. Reversed end-diastolic flow in umbilical artery
Twin-Twin Transfusion Syndrome

- Complicates 8-10% of monochorionic diamniotic twin gestations
- Untreated TTTS developing before the third trimester has a perinatal mortality rate of >70%
  - 15-50% risk of handicap in survivors

Simpson et al. ACOG 2011:204:145

Twin-Twin Transfusion Syndrome

<table>
<thead>
<tr>
<th>Stage</th>
<th>Ultrasound Assessment</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Amniotic fluid</td>
<td>MVP &lt;2 cm in donor sac; MVP &gt;8 cm in recipient sac</td>
</tr>
<tr>
<td>II</td>
<td>Fetal bladder</td>
<td>Nonvisualization of fetal bladder in donor twin over 60 minutes of observation</td>
</tr>
<tr>
<td>III</td>
<td>Doppler studies</td>
<td>Absent or reversed umbilical artery diastolic flow, reversed ductus venosus a-wave flow, pulsatile umbilical vein flow</td>
</tr>
<tr>
<td>IV</td>
<td>Fetal hydrops</td>
<td>Hydrops in one or both twins</td>
</tr>
<tr>
<td>V</td>
<td>Fetal cardiac activity</td>
<td>Fetal demise in one or both twins</td>
</tr>
</tbody>
</table>


TNTS Outcomes

<table>
<thead>
<tr>
<th>TTTS Outcomes</th>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
<th>Stage IV</th>
<th>Normal Neurologic Outcome at 6 months and 6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resolution</td>
<td>27%</td>
<td>10%</td>
<td>1%</td>
<td>–</td>
<td>31% 70%</td>
</tr>
<tr>
<td>Amnioreduction</td>
<td>90%</td>
<td>80%</td>
<td>48%</td>
<td>26%</td>
<td>52% 82%</td>
</tr>
<tr>
<td>At least one survivor</td>
<td>50%</td>
<td>48%</td>
<td>20%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Two survivors</td>
<td>52%</td>
<td>82%</td>
<td>66%</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Laser</td>
<td>86%</td>
<td>84%</td>
<td>78%</td>
<td>62%</td>
<td>86% 82%</td>
</tr>
<tr>
<td>At least one survivor</td>
<td>92%</td>
<td>82%</td>
<td>66%</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Two survivors</td>
<td>95%</td>
<td>82%</td>
<td>66%</td>
<td>52%</td>
<td></td>
</tr>
</tbody>
</table>


- In over 1000 published cases of laser performed for TTTS from six different centers, there were:
  - Two survivors: 50%
  - Single survivor: 30%
  - No survivors: 20%
- Normal neurologic development at 2 years of age: 80-90%

Simpson et al. ACOG 2011:204:145
**TTTS or UPS: Clues to getting it right . . .**

- **Growth discordance >20%**
  - UPS more likely than TTTS
  - EFW <10th %ile
  - 100% of sIUGR
  - 50% of TTTS

- **Amniotic fluid discrepancy**
  - In UPS with sIUGR
    - oligohydramnios in IUGR twin
    - normal fluid in AGA twin
  - In TTTS
    - oligohydramnios MVP ≤2 cm in one sac
    - polyhydramnios MVP ≥8 cm in second sac

- **Cardiac dysfunction**
  - In sIUGR, findings in the smaller twin
  - In TTTS, findings in the larger twin

- **Placenta Pathology: UPS vs TTTS**

- **Recommendations for Ultrasound in Twins**

<table>
<thead>
<tr>
<th>Timing</th>
<th>Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st trimester</td>
<td>Determination of chorionicity</td>
</tr>
<tr>
<td></td>
<td>Measurement of crown rump lengths</td>
</tr>
<tr>
<td>11-13 weeks</td>
<td>Measurement of nuchal translucency</td>
</tr>
<tr>
<td>16-26 weeks</td>
<td>Screen MC twins every other week for TTTS</td>
</tr>
<tr>
<td>18-20 weeks</td>
<td>Screen for structural anomalies</td>
</tr>
<tr>
<td></td>
<td>Assessment of cervical length</td>
</tr>
<tr>
<td>20-22 weeks</td>
<td>Fetal echocardiography for IVF and MC twins</td>
</tr>
<tr>
<td>24 weeks to delivery</td>
<td>Serial determination of twin growth and discordance</td>
</tr>
<tr>
<td></td>
<td>Assessment of cervical length as indicated</td>
</tr>
<tr>
<td></td>
<td>Antenatal fetal testing as indicated</td>
</tr>
</tbody>
</table>
Evaluation of Fetal Well-Being in Twins

- Evidence-based recommendations for antenatal testing in multiples are lacking
- Antenatal testing usually performed in twins with recognized complications:
  - IUGR
  - Discordant growth
  - Amniotic fluid abnormalities
  - Structural malformations
- Optimal frequency of testing uncertain

Proposed Antenatal Testing in Twins

Uncomplicated DC twins: weekly testing starting at 32-36 weeks
Uncomplicated MCDA twins: weekly testing starting at 28-32 weeks
Monoamniotic twins: daily NST of both fetuses starting at 24-28 weeks

Complicated twins:
- weekly testing starting at time of diagnosis or at 24-28 weeks
- twice weekly testing if oligohydramnios or abnormal Dopplers identified in twins with IUGR
- if absent end diastolic flow in umbilical artery, daily testing
- if reversed end-diastolic flow, hospital admission, daily testing, consideration of delivery depending on gestational age

Columbia University Medical Center 2006

Question 8

At what gestational age does the risk of stillbirth begin to increase exponentially in ongoing twin pregnancies?

- a. 34 weeks
- b. 36 weeks
- c. 38 weeks
- d. 40 weeks
Prospective Risk of Stillbirth in Twins

- Risk of stillbirth increases from 1:3333 at 28 weeks to 1:69 at ≥ 39 weeks gestation
- Stillbirth risk in multiples at 39 weeks surpasses that of post-term singletons (1:526)

Twin Chorionicity and Risk of Stillbirth

- Retrospective cohort analysis of 1000 consecutive twin deliveries ≥ 24 weeks
  - 196 monochorionic-diamniotic
  - 804 dichorionic-diamniotic
- Stillbirth occurred in
  - 7 (3.6%) MCDA
  - 9 (1.1%) DCDA
- MC twins had higher risk of SB compared to DC twins both overall and at each gestational age >24 weeks
- Risk persisted in the subset of 771 apparently normal twins

Unexpected Late Fetal Death in MCDA Twins

- 151 uncomplicated MCDA
- Elective delivery at 36-37 weeks
  - 10 unexpected deaths >24 weeks affecting 7 patients
  - 3 double demises and 4 single twin demise (all within 2 weeks of normal scan)
  - median gestational age 34w1d (28w-36w3d)
- Overall risk of late fetal death in uncomplicated MCDA twins:
  - 4.6% per pregnancy
  - 3.3% per fetus
  - Exceeds 1% risk in singletons

Exceeds 1% risk in singletons
Delivery of Twins: Recommendations*

<table>
<thead>
<tr>
<th>Placentaion</th>
<th>Gestational Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dichorionic, uncomplicated</td>
<td>38w0d – 38w6d</td>
</tr>
<tr>
<td>Dichorionic with isolated IUGR</td>
<td>36w0d – 37w6d</td>
</tr>
<tr>
<td>Monochorionic diamniotic, uncomplicated</td>
<td>34w0d – 37w6d</td>
</tr>
<tr>
<td>Monochorionic diamniotic with isolated IUGR</td>
<td>32w0d – 37w6d</td>
</tr>
<tr>
<td>Monoamniotic</td>
<td>34 weeks</td>
</tr>
</tbody>
</table>

* Timing of delivery should be individualized in the presence of maternal and/or fetal co-morbidities and/or abnormal antenatal testing

ACOG Committee Opinion Number 560, 2013

Summary

- In order to provide high-quality obstetric care of twins, need to diagnose early, counsel extensively, follow closely, and base management on best current evidence