Multifetal Gestation

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• No financial interests to disclose.
Multiples

- Maternal physiology
- Risks
- Twins
  - Specific risks
- Triplets
- Delivery timing
- Questions
Case 1

- 30 yo P1001
- Monochorionic/diamniotic twins
  - Risks?
  - Surveillance?
  - Delivery timing?
Case 2

- 22 yo P0
- Monoamniotic twins
  - Risks?
  - Surveillance?
  - Delivery timing?
Cardiovascular Changes of Pregnancy

- Cardiac Output Increased by 30-50%
- Twin Pregnancy: Add another 15%
- Starts Early and Peaks at 20 Weeks
- Increase in Stroke Volume
- Increase in Heart Rate
Cardiac Output Across Gestation

Cardiac Output Increased by 30-50%
Twin Pregnancy: Add another 15%
Starts Early and Peaks at 20 Weeks

Adapted from Uptodate - Citation Bonica 1994 Obstetrical Anesthesia
Epidemiology

- Of all twins... without ART
  - Dizygotic twins (~70%)
    - Ethnic variation in incidence of DZ twinning
  - Monozygotic twins (~30%)
    - Incidence of MZ twins is relatively stable worldwide at 3 to 5 per 1000 births
    - 70% MCDA, 30% DCDA
- Triplets+... 193.5/100,000 (1980s-90s)
  - 153.4/100,000 (2009)
Twinning

• Determine early in gestation
  – Location, fetal sex, insertion sites, thickness of membranes

• Why do we care about placentation?
  – Predicting risk…
    • Monochorionic, diamniotic
      – Risk of sharing a placenta; shunting, anastomosis
      – unequal blood distribution - TTTS
      – 15% occurrence rate
    • Monoamniotic (cord entanglement)
      – 1/10,000 of all pregnancies
        » 1-5% of monozygotic twins
2 placentas
2 amnions
2 chorions
(dizygotic twins or monozygotic twins with cleavage of zygote during first 3 days after fertilization)
Lambda sign/twin peak

1 placenta
2 amnions
1 chorion
(monozygotic twins with cleavage of zygote days 4-8 post-fertilization)
T sign

1 placenta
1 amnion
1 chorion
(monozygotic twins with cleavage of zygote days 8-12 post-fertilization)

*if split occurs after 12 days post-fertilization, conjoined twins result
Placentation

• Multiple gestations – (e.g. twins)
• Dependent on when zygote splits post-fertilization in monozygotic pregnancy
  • the earlier the split the more tissue each pregnancy gets to itself
    – <3 dichorionic
    – 3-8 diamniotic
    – 8-12 monoamniotic
    – >12 conjoined
  – Dichorionic placentation (two placentas, in all dizygotic and some monozygotic twins)
  – Monochorionic placentation
    • monozygotic twins develop with only one placenta
    • higher risk of complications during pregnancy
    • preeclampsia
    • shunting of blood from 1 twin to the other (TTTS)
  – Monoamniotic placentation
Dichorionic twin pregnancy (lambda sign)
Thick interdividing membrane of dichorionic twin pregnancy
Thin intertwin membrane characteristic of monochorionic diamniotic twin pregnancy
Risks during the pregnancy

- Preterm birth
- Anomalies
- GDM
- Preeclampsia
Prediction of preterm birth before 32 weeks of gestation in twins by sonographically determined cervical length

<table>
<thead>
<tr>
<th>Cut-off for cervical length (mm)</th>
<th>Sensitivity (percent)</th>
<th>Specificity (percent)</th>
<th>PPV (percent)</th>
<th>NPV (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assessment at 21 to 24 weeks of gestation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>42</td>
<td>85</td>
<td>22</td>
<td>94</td>
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<td>25</td>
<td>54</td>
<td>86</td>
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<td>30</td>
<td>46</td>
<td>89</td>
<td>19</td>
<td>97</td>
</tr>
<tr>
<td><strong>Assessment at 25 to 28 weeks of gestation</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>20</td>
<td>56</td>
<td>76</td>
<td>16</td>
<td>95</td>
</tr>
<tr>
<td>25</td>
<td>63 to 100</td>
<td>70 to 84</td>
<td>13 to 18</td>
<td>96 to 100</td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.

Data adapted from:
Nutrition

• NUTRITION — Women carrying multiple gestations should increase their daily dietary intake by about 300 kcal above that for a singleton pregnancy, or 600 kcal over that of a nonpregnant woman
• Institute of Medicine recommendations for weight gain
  • BMI <18.5 kg/m² (underweight) — no recommendation due to insufficient data
  • BMI 18.5 to 24.9 kg/m² (normal weight) — weight gain 37 to 54 lbs (16.8 to 24.5 kg)
  • BMI 25.0 to 29.9 kg/m² (overweight) — weight gain 31 to 50 lbs (14.1 to 22.7 kg)
  • BMI ≥30.0 kg/m² (obese) — weight gain 25 to 42 lbs (11.4 to 19.1 kg)
• These thresholds represent the 25th through 75th percentile weight gains in women who gave birth to twins weighing at least 2500 g and appear to be associated with a decreased risk of preterm birth and higher birth weights
• Dietary or vitamin/mineral supplementation - folate, etc
Society of Maternal-Fetal Medicine recommendations for nutrition in twin pregnancy are shown in the table.

<table>
<thead>
<tr>
<th>Intervention</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal weight/weight gain</td>
<td>Assess maternal pre gravid BMI, determine maternal BMI-specific weight gain goals</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
</tr>
<tr>
<td>Caloric requirements (kcal · kg⁻¹ · d⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal BMI</td>
<td>40-45</td>
<td>Alter as necessary for weight gain goal</td>
<td>Alter as necessary for weight gain goal</td>
</tr>
<tr>
<td>Underweight</td>
<td>42-50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>30-35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronutrient supplement (daily total intake)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVI with iron (30 mg elemental tablets)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>1500</td>
<td>2500</td>
<td>2500</td>
</tr>
<tr>
<td>Vitamin D (International units)</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>400</td>
<td>800</td>
<td>300</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>15</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>DHA/EPA (mg)</td>
<td>300-500</td>
<td>300-500</td>
<td>300-500</td>
</tr>
<tr>
<td>Follic acid (mg)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vitamin C/E (mg/international units)</td>
<td>500-1000/400</td>
<td>500-1000/400</td>
<td>500-1000/400</td>
</tr>
<tr>
<td>Nutritional consultation</td>
<td>Yes</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
</tr>
<tr>
<td>Laboratory nutritional assessment</td>
<td>Hemoglobin ferritin folate/B12 early screen for GDM (risk factors) vitamin D</td>
<td>Follow up abnormalities from first trimester</td>
<td>Hemoglobin ferritin GDM screen with or without vitamin D</td>
</tr>
<tr>
<td>Risk factor appropriate exercise or reduction in activity</td>
<td>Screen</td>
<td>Screen</td>
<td>Screen</td>
</tr>
</tbody>
</table>

BMI: body mass index; MVI: multivitamin; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; GDM: gestational diabetes mellitus.

Twinning Complications
TRAP sequence
- Occurs only in monochorionic twins
- 1 in 35,000 pregnancies
- Acardiac twin pregnancy
- Due to arterioarterial anastomoses resulting in a pump twin and a perfused twin
- Perfused twin – Abnl
- Pump twin -NL
• Perfused twin –
  – Reversed Doppler flow in umbilical cord present, this blood is low in oxygen and nutrients
  – Usually acardiac or has a rudimentary heart and its head and upper limbs are usually absent
  – Trunk and lower limbs may be well-developed, most internal organs are absent or malformed. It can be significantly larger than the pump twin due to hydrops fetalis

• Pump twin –
  – Not malformed, but is at high risk of perinatal morbidity/mortality from high output cardiac failure or preterm birth due to uterine overdistention related to the twin mass or polyhydramnios.

• Treatment - Separation of the two circulations is therapeutic for the pump twin and can be accomplished by fetoscopic laser coagulation of the placental vascular anastomoses or radiofrequency ablation of the umbilical cord of the acardiac twin
Conjoined Twins

- Only in monochorionic twins
- 1 in 50,000 pregnancies
- Conjoined twins are classified according to the site of union (eg, chest, head) with the suffix "pagus" (meaning fixed, eg thoracopagus)
- Sonogram - MA sac, contiguous skin, twins that stay in the same orientation to one another, fetal scoliosis, unusual limb positioning, and more than three vessels in the cord
- Associated congenital defects unrelated to the area of fusion are common
- Increased IUFD rate
- Anatomy sonogram, FE, MRI – used to determine extent of deformity and counsel the parents about prognosis
- Delivery of potentially viable infants is always by cesarean.
Case 3

• 24 yo P1001

• Triplets
  – Counseling on multifetal pregnancy reduction?

• Quadruplets
  – Counseling on multifetal pregnancy reduction?
Case 4

- 28 yo P2002
- **Monochorionic /diamniotic twins**
  - 1 twin normal
  - 1 twin anencephaly

- Management?
Multifetal pregnancy reduction and selective termination

- MFPR, selective termination
- 5-8% of pregnancy loss <24 weeks
- Selective fetal reduction —
  - Reduction of anomalous fetus to improve outcome of other fetuses
  - Anencephaly – risk of polyhydramnios and PTB increases risk to cotwin survival in MC/DA and DC/DA twin pregnancies
- MFPR
  - Triplets → Twins – Risks of morbidity/mortality <8% from prematurity as triplets average GA at delivery is 31 weeks (ACOG)
  - Quadruplets (and +) → triplets, twins
    - Risks of morbidity/mortality ≥8% from prematurity as quadruplets average GA at delivery is 29 weeks (ACOG) and infant mortality rate is high (>50%)
- Method – Medical (KCl, digoxin)
  - Laser photocoagulation, Radiofrequency ablation
• **TWIN-TWIN TRANSFUSION SYNDROME**
• **Diagnosis –**
• **MCDA twins**
• **Polyhydramnios/oligohydramnios**
• **Due to uncompensated vascular anastomoses in the placenta**
• **Intertwin differences in growth may present as early as the first trimester**
• **Prognosis for untreated severe cases is poor: perinatal mortality is 70 to 100 percent, survivors are at high risk of neurologic, cardiac, and renal impairment**
TTTS

- **Incidence**
  - 5-15% in monochorionic-diamniotic twin pregnancies
    - 6% of monoamniotic twin pregnancies
- **Possible in monoamniotic or dichorionic diamniotic twins, but rare**
- **Diagnosis**
  - Suspicion of monochorionic-diamniotic twin pregnancy
  - Polyhydramnios (>8cm) - recipient; oligohydramnios (<2cm) - donor
Etiology

- **TYPE OF ANASTOMOSIS**
- **A-V anastomosis:** unidirectional flow; intravillous (placental surface single unpaired artery carrying blood from donor twin to placental cotyledon together with single unpaired vein carrying blood from that cotyledon back to the recipient twin)
- **A-A, V-V anastomosis:** superficially located on chorionic plate, allow bidirectional flow, ‘saving type’ of anastomosis
- Less A-A and V-V anastomoses increases probability of A-V anastomoses leading to TTTS
- Discordant placental size or sharing of placenta
Classification

• Classification (no good system for prediction of progression or prognosis)
• Quintero staging system (good for monitoring disease progression, not predicting outcomes or determining which pregnancies will progress)
  • Stage I — + Poly/oligo (POS) ; +bladder in donor
  • Stage II — +POS; NO bladder seen in donor; normal Dopplers
  • Stage III — +POS; NO bladder seen in donor; abnormal Doppler (absent, REDV in donor umbilical artery; reversed ductus venousus flow; pulsatile umbilical vein venous flow in recipient)
  • Stage IV — + POS, hydrops in either twin
  • Stage V — Fetal demise of either or both twins
• Staging system based on presence of A-A anastomoses (Jain et al)
  – antenatal identification of A-A anastomosis, which is "protective" against TTTS
**Algorithm for screening for TTTS**

1. **MCDA pregnancy**

2. **First trimester:**
   - Confirm monochorionic, diamniotic placentaion
   - NT screening

3. **~16 weeks**
   - Start ultrasound surveillance with MVP in each sac, and fetal bladder in each fetus, every 2 weeks, until delivery

4. **MVP >2cm and <8cm in each sac**
   - **Yes**
     - Continue ultrasound surveillance every 2 weeks
   - **No**
     - MVP <2cm in 1 sac and MVP >8 cm in other sac: Diagnosis = TTTS

5. **See Figure 10**

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Treatment

• **Expectant management**
• **Amnioreduction**
• **Septostomy**
• **Selective feticide**
• **Fetoscopic laser ablation of vascular anastomoses (16-26 weeks)**
Treatment

- Treatment (prolonged neural outcomes not known in treatments, limits counseling patients)
- Amnioreduction (decrease pressure leading to less uterine distension, allows better placental blood flow, may help with maternal symptoms)
- Survival based on serial amnioreductions (2001 registry); (223 sets of twins; TTTS <28 wks) follow-up data until 4 weeks old; major findings included:
  - 78% born alive
  - 60% alive 4 weeks after birth
  - Abnormal neonatal cranial scan in ~25% recipients and donors
  - Better survival related to older gestational age, no Doppler abnormalities or hydrops, removal of less fluid, higher birthwt
  - Amnioreduction - may be appropriate if significant fluid discordance; more widely available; lower complication rate
Endoscopic Laser Surgery versus Serial AmниoReduction for Severe Twin-to-Twin Transfusion Syndrome

Marie-Victoire Senat, M.D., Jan Deprest, M.D., Ph.D., Michel Boulvain, M.D., Ph.D.,
Alain Paupe, M.D., Norbert Winer, M.D., and Yves Ville, M.D.

ABSTRACT

BACKGROUND
Monochorionic twin pregnancies complicated by severe twin-to-twin transfusion syndrome at midgestation can be treated by either serial amnioreduction (removal of large volumes of amniotic fluid) or selective fetoscopic laser coagulation of the communicating vessels on the chorionic plate. We conducted a randomized trial to compare the efficacy and safety of these two treatments.

METHODS
Pregnant women with severe twin-to-twin transfusion syndrome before 26 weeks of gestation were randomly assigned to laser therapy or amnioreduction. We assessed perinatal survival of at least one twin (a prespecified primary outcome), survival of at least one twin at six months of age, and survival without neurologic complications at six months of age on the basis of the number of pregnancies or the number of fetuses or infants, as appropriate.

RESULTS
The study was concluded early, after 72 women had been assigned to the laser group and 70 to the amnioreduction group, because a planned interim analysis demonstrated a significant benefit in the laser group. As compared with the amnioreduction group, the laser group had a higher likelihood of the survival of at least one twin to 28 days of age (76 percent vs. 56 percent; relative risk of the death of both fetuses, 0.63; 95 percent confidence interval, 0.25 to 0.93; P=0.009) and 6 months of age (P=0.002). Infants in the laser group also had a lower incidence of cystic periventricular leukomalacia (6 percent vs. 14 percent, P=0.02) and were more likely to be free of neurologic complications at six months of age (52 percent vs. 31 percent, P=0.003).

CONCLUSIONS
Endoscopic laser coagulation of anastomoses is a more effective first-line treatment than serial amnioreduction for severe twin-to-twin transfusion syndrome diagnosed before 26 weeks of gestation.
### TABLE 5
Randomized trial of laser photocoagulation vs amnioreduction (Eurofetus)\(^{65,77}\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laser, n = 72 pregnancies/ n = 144 twins</th>
<th>Amnioreduction, n = 70 pregnancies/ n = 140 twins(^a)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median gestational age at delivery, wk</td>
<td>33.3</td>
<td>29.0(^a)</td>
<td>.004</td>
</tr>
<tr>
<td>Survival of at least 1 twin at 6 mo of age</td>
<td>76% (55/72)</td>
<td>56% (36/70)(^a)</td>
<td>.009</td>
</tr>
<tr>
<td>All perinatal deaths up to 6 mo of age</td>
<td>44% (63/144)</td>
<td>61% (86/140)(^a)</td>
<td>.01</td>
</tr>
<tr>
<td>Cystic periventricular leukomalacia at 6 mo</td>
<td>6% (8/144)</td>
<td>14% (20/140)</td>
<td>.02</td>
</tr>
<tr>
<td>Alive and free of neurologic complications at 6 mo</td>
<td>52% (75/144)</td>
<td>31% (44/140)</td>
<td>.003</td>
</tr>
<tr>
<td>Normal neurologic development at 6 y(^b)</td>
<td>82% (60/73)</td>
<td>70% (33/47)</td>
<td>.12</td>
</tr>
</tbody>
</table>

\(^a\) Of women in amnioreduction group, 11 (16%) had voluntary termination of pregnancy between 21-25 wk; \(^b\) Includes only children delivered in France and still alive at 6 mo of age.


### TABLE 6
Randomized trial of laser photocoagulation vs amnioreduction (NICHD-sponsored)\(^{67}\)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Laser, n = 20 pregnancies/ n = 40 twins</th>
<th>Amnioreduction, n = 20 pregnancies/ n = 40 twin</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean gestational age at delivery, wk</td>
<td>30.5</td>
<td>30.2</td>
<td>NS</td>
</tr>
<tr>
<td>Survival of at least 1 twin at 30 d of age</td>
<td>65% (13/20)</td>
<td>75% (15/20)</td>
<td>.73</td>
</tr>
<tr>
<td>All perinatal deaths up to 30 d of age</td>
<td>55% (22/40)</td>
<td>40% (16/40)</td>
<td>.18</td>
</tr>
<tr>
<td>Recipient twin fetal mortality</td>
<td>70% (14/20)</td>
<td>35% (7/20)</td>
<td>.03</td>
</tr>
</tbody>
</table>

NICHD, Eunice Kennedy Shriver National Institute of Child Health and Human Development; NS, nonsignificant.

Laser Coagulation

- Laser coagulation (obliterate visible A-V anastomoses); amnioreduction done at end of surgery to buffer increases until the coagulation can take effect
- Appears to be an appropriate therapy in cases of significant discordance or when there is fetal myocardial dysfunction
- Eurofetus RCT (laser vs serial amnioreduction); interim analysis halted study as it showed better outcomes in the laser arm

- Overall perinatal survival (57 versus 41 percent)
- Survival of at least one twin to age 28 days (76 versus 56 percent)
- Survival without major neurologic morbidity at six months (52 versus 31 percent of the initial cohorts)
TTTS – Laser Photocoagulation - Complications

• Perioperative complications
  – PPROM – 7-17% (1-3 weeks post laser)
  – Amniotic fluid leakage into the maternal peritoneal cavity (7 percent),
  – Vaginal bleeding (4 percent),
  – Abruptio placentae (2 percent), and
  – Chorioamnionitis (2 percent).

• Amnioreduction – similar to above, lower rate of PPROM
TTTS - Other previously studied treatments

- Septostomy of amniotic membrane (does not address underlying pathophysiology); only big study limited by crossover of septostomy patients to amnioreduction arm
- Selective termination (difficult to tell which twin would be ultimately more severely affected)
- Medical – digoxin, prostaglandin synthase inhibitors (limited use)
TTTS

- Morbidity/Mortality
- Profound anemia, placental insufficiency of donor
- Heart failure from circulatory overload in recipient
- PTL (hydramnios) complications of prematurity
- Lethal congenital anomalies associated with monozygosity
- Survival depends on gestational age and severity at time of diagnosis (before 1990, 80-100% mortality)
- Death of one twin corresponds to 30-50% risk of mortality/neurologic damage to survivor
- Survival based on laser coagulation of A-V anastomoses
Neurodevelopmental outcome at 2 years in children born preterm treated by amnioreduction or fetoscopic laser surgery for twin-to-twin transfusion syndrome: comparison with dichorionic twins

Richard Lenclen, MD; Giuseppina Ciarlo, MD; Alain Paupe, MD; Laurence Bussieres, MD; Yves Ville, MD

OBJECTIVE: We sought to assess long-term neurodevelopment of children born prematurely treated for twin-to-twin transfusion syndrome and dichorionic (DC) twins.

STUDY DESIGN: In all, 21 and 88 children treated with amnioreduction (AR) and fetoscopic laser surgery (FLS), respectively, and 222 DC twins matched for gestational age at delivery were assessed with Ages and Stages Questionnaire assessment was similar in FLS and DC children but scores were lower ($P = .01$) and domains were more often abnormal (60% vs 27%; $P = .005$) following AR.

CONCLUSION: Neurodevelopmental outcome is similar in twin-to-twin transfusion syndrome survivors treated by FLS and in DC control subjects; but survivors treated with AR have an increased risk of neurodevelopmental delay at 2 years of age.

Key words: dichorionicity, laser surgery, monochorionicity, neurodevelopmental, outcome, twin-to-twin transfusion syndrome

Algorithm for management of TTTS

MCDA pregnancy with MVP < 2 cm in 1 sac and MVP < 8 cm in other sac: Diagnosis = TTTS

Do staging (Table 1): check fetal bladder, UA Doppler

Stage I

- Counseling. Consider expectant management, with fetal bladder, UA Doppler, and hydrops ultrasonographic checks at least once per week

Stage II, III, IV

- Counseling. Consider referral to fetal center for laser treatment at 16-25 6/7 weeks; if unable or outside eligibility criteria, consider amnioreduction

Stage V

- Counsel regarding co-twin 10% risk of death and 10-30% risk of neurologic complications. Consider expectant management.

MCDA, monochorionic diamniotic; MVP, maximum vertical pocket; TTTS, twin-twin transfusion syndrome; UA, umbilical artery.

Normal MC placenta (gestational age at delivery: 28 weeks) showing several AV and VA anastomoses (green and white stars, respectively) and 2 AA anastomoses (blue stars).

**Monochorionic twin placentas: Injection technique and analysis – Dec 2014**

Placentas monocoriónicas: técnicas de inyección y análisis

Depeng Zhao a, Suzanne F. de Villiers a, Dick Oepkes b, Enrico Lopriore a.
TAPS

- Twin Anemia/Polycythemia sequence
- Atypical chronic form of TTTS
- Large intertwin Hb discordance, without polyhydramnios/oligoxydramnios

Incidence –
- Spontaneous - 3-6% of previously uncomplicated MC/DA twins, diagnosed in 3rd trimester
- Following SFLP – 2-13% incidence

Uptodate
Fig. 5 – Spontaneous TAPS placenta (gestational age at delivery: 33 weeks) showing 3 small AV anastomoses (green stars) and 1 small AA anastomosis (blue star). Note the difference in color between the plethoric placental share of the recipient and the pale placental share of the donor.
TAPS

- **Twin Anemia/Polycythemia sequence**
- **Diagnosis** –
  - MCA Doppler >1.5MOMs in donor twin
  - MCA Doppler <0.8MOMs in recipient twin
  - Postnatal diagnosis – Hb difference of >8.0g/dL with intertwin reticulocyte ratio of >1.7 (Donor retic/Recipient retic) and a placental injection examination with small AV anastomoses
  - In post-laser TAPS, small arteriovenous anastomoses between the recipient and donor allow slow passage of red cells in a reverse manner so that the recipient twin becomes anemic and the donor twin becomes plethoric
- **Management** –
  - Laser Photocoagulation
  - IUT
  - Delivery
Risk of IUFD

- General rate of IUFD – 6/1000
- Twins - 12/1000 (OR 2.8)
- Triplets – 34/1000 (OR 2.8-3.7)
- GDM – treated – 6-35/1000 (OR 1.7-7)
- CHTN - 6-25/1000 (2.7)
- Lupus – 40-150/1000 (OR 6-20)

ACOG IUFD bulletin
Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice.

AU Kahn B; Lumey LH; Zybert PA; Lorenz JM; Cleary-Goldman J; D'Alton ME; Robinson JN SO


Table 3. Fetal Death Rate and Prospective Risk of Fetal Death for Singletons

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>10,906</td>
<td>11,061,599</td>
<td>3101</td>
<td>284.34 (275.90, 292.93)</td>
<td>0.28 (0.27, 0.29)</td>
<td>414.86 (403.91, 425.90)</td>
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<tr>
<td>25</td>
<td>11,692</td>
<td>11,050,693</td>
<td>2544</td>
<td>217.58 (210.16, 225.20)</td>
<td>0.23 (0.22, 0.24)</td>
<td>248.47 (239.67, 257.48)</td>
</tr>
<tr>
<td>26</td>
<td>13,285</td>
<td>11,039,001</td>
<td>2288</td>
<td>172.22 (165.86, 178.78)</td>
<td>0.21 (0.20, 0.22)</td>
<td>167.77 (160.86, 174.92)</td>
</tr>
<tr>
<td>27</td>
<td>13,756</td>
<td>11,025,716</td>
<td>2008</td>
<td>145.97 (140.14, 152.01)</td>
<td>0.18 (0.17, 0.19)</td>
<td>110.32 (104.74, 116.15)</td>
</tr>
<tr>
<td>28</td>
<td>15,569</td>
<td>11,011,960</td>
<td>2015</td>
<td>129.42 (124.21, 134.82)</td>
<td>0.18 (0.18, 0.19)</td>
<td>84.11 (79.52, 88.94)</td>
</tr>
<tr>
<td>29</td>
<td>17,431</td>
<td>10,996,391</td>
<td>1804</td>
<td>103.49 (99.03, 108.13)</td>
<td>0.16 (0.16, 0.17)</td>
<td>59.06 (55.44, 62.90)</td>
</tr>
<tr>
<td>30</td>
<td>23,078</td>
<td>10,978,960</td>
<td>1936</td>
<td>83.89 (80.36, 87.56)</td>
<td>0.18 (0.17, 0.19)</td>
<td>42.38 (39.72, 45.20)</td>
</tr>
<tr>
<td>31</td>
<td>27,728</td>
<td>10,955,882</td>
<td>1792</td>
<td>64.63 (61.78, 67.60)</td>
<td>0.16 (0.16, 0.17)</td>
<td>30.54 (28.49, 32.72)</td>
</tr>
<tr>
<td>32</td>
<td>39,551</td>
<td>10,928,154</td>
<td>1972</td>
<td>49.86 (47.75, 52.06)</td>
<td>0.18 (0.17, 0.19)</td>
<td>19.61 (18.25, 21.08)</td>
</tr>
<tr>
<td>33</td>
<td>61,653</td>
<td>10,888,603</td>
<td>1972</td>
<td>31.99 (30.62, 33.41)</td>
<td>0.18 (0.17, 0.19)</td>
<td>13.35 (12.46, 14.32)</td>
</tr>
<tr>
<td>34</td>
<td>125,999</td>
<td>10,826,950</td>
<td>2340</td>
<td>18.57 (17.84, 19.34)</td>
<td>0.22 (0.21, 0.23)</td>
<td>8.39 (7.90, 8.92)</td>
</tr>
<tr>
<td>35</td>
<td>231,475</td>
<td>10,700,951</td>
<td>2462</td>
<td>10.64 (10.22, 11.06)</td>
<td>0.23 (0.22, 0.24)</td>
<td>5.02 (4.73, 5.32)</td>
</tr>
<tr>
<td>36</td>
<td>418,129</td>
<td>10,469,476</td>
<td>2709</td>
<td>6.48 (6.24, 6.73)</td>
<td>0.26 (0.25, 0.27)</td>
<td>3.39 (3.22, 3.57)</td>
</tr>
<tr>
<td>37</td>
<td>819,233</td>
<td>10,051,347</td>
<td>2856</td>
<td>3.49 (3.36, 3.62)</td>
<td>0.28 (0.27, 0.29)</td>
<td>2.08 (1.98, 2.18)</td>
</tr>
<tr>
<td>38</td>
<td>1,686,122</td>
<td>9,232,114</td>
<td>3247</td>
<td>1.93 (1.86, 1.99)</td>
<td>0.35 (0.34, 0.36)</td>
<td>1.26 (1.21, 1.31)</td>
</tr>
<tr>
<td>39</td>
<td>2,654,221</td>
<td>7,545,992</td>
<td>2986</td>
<td>1.13 (1.09, 1.17)</td>
<td>0.40 (0.38, 0.41)</td>
<td>0.92 (0.89, 0.96)</td>
</tr>
<tr>
<td>40</td>
<td>2,590,504</td>
<td>4,891,771</td>
<td>2795</td>
<td>1.08 (1.04, 1.12)</td>
<td>0.57 (0.55, 0.59)</td>
<td>0.85 (0.82, 0.89)</td>
</tr>
<tr>
<td>41</td>
<td>1,438,442</td>
<td>2,301,267</td>
<td>1480</td>
<td>1.03 (0.98, 1.08)</td>
<td>0.64 (0.61, 0.68)</td>
<td>0.93 (0.88, 0.98)</td>
</tr>
<tr>
<td>42</td>
<td>493,493</td>
<td>862,825</td>
<td>647</td>
<td>1.31 (1.21, 1.42)</td>
<td>0.75 (0.69, 0.81)</td>
<td>1.15 (1.06, 1.25)</td>
</tr>
<tr>
<td>* 43+</td>
<td>369,332</td>
<td>369,332</td>
<td>453</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.12 (1.01, 1.23)</td>
</tr>
</tbody>
</table>

CI = confidence interval.

* Calculated for births of 24 weeks gestation or more.
Table 4. Fetal Death Rate and Prospective Risk of Fetal Death for Twins

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>2097</td>
<td>297,622</td>
<td>274</td>
<td>130.66 (116.68, 146.02)</td>
<td>0.92 (0.82, 1.04)</td>
<td>461.88 (438.82, 495.09)</td>
</tr>
<tr>
<td>25</td>
<td>2358</td>
<td>295,525</td>
<td>282</td>
<td>119.59 (106.91, 133.53)</td>
<td>0.95 (0.85, 1.07)</td>
<td>284.20 (264.98, 304.23)</td>
</tr>
<tr>
<td>26</td>
<td>2757</td>
<td>293,167</td>
<td>206</td>
<td>74.72 (63.31, 85.33)</td>
<td>0.70 (0.61, 0.81)</td>
<td>172.48 (158.13, 187.83)</td>
</tr>
<tr>
<td>27</td>
<td>3117</td>
<td>290,410</td>
<td>175</td>
<td>56.14 (48.45, 64.96)</td>
<td>0.60 (0.52, 0.70)</td>
<td>109.11 (98.19, 121.07)</td>
</tr>
<tr>
<td>28</td>
<td>3547</td>
<td>287,293</td>
<td>193</td>
<td>54.41 (47.29, 62.52)</td>
<td>0.67 (0.58, 0.78)</td>
<td>72.45 (64.02, 81.88)</td>
</tr>
<tr>
<td>29</td>
<td>4220</td>
<td>283,746</td>
<td>199</td>
<td>47.16 (41.05, 54.10)</td>
<td>0.70 (0.61, 0.81)</td>
<td>47.75 (41.46, 54.92)</td>
</tr>
<tr>
<td>30</td>
<td>5565</td>
<td>279,526</td>
<td>162</td>
<td>29.11 (24.92, 33.96)</td>
<td>0.58 (0.50, 0.68)</td>
<td>33.50 (28.94, 38.74)</td>
</tr>
<tr>
<td>31</td>
<td>7664</td>
<td>273,961</td>
<td>182</td>
<td>23.75 (20.51, 27.47)</td>
<td>0.66 (0.57, 0.77)</td>
<td>18.98 (16.06, 22.40)</td>
</tr>
<tr>
<td>32</td>
<td>10,619</td>
<td>266,297</td>
<td>187</td>
<td>17.61 (15.23, 20.34)</td>
<td>0.70 (0.61, 0.81)</td>
<td>13.13 (11.08, 15.56)</td>
</tr>
<tr>
<td>33</td>
<td>14,849</td>
<td>255,678</td>
<td>201</td>
<td>13.54 (11.77, 15.56)</td>
<td>0.79 (0.68, 0.90)</td>
<td>8.33 (6.95, 9.97)</td>
</tr>
<tr>
<td>34</td>
<td>23,262</td>
<td>240,829</td>
<td>220</td>
<td>9.46 (8.27, 10.81)</td>
<td>0.91 (0.80, 1.04)</td>
<td>5.82 (4.89, 6.91)</td>
</tr>
<tr>
<td>35</td>
<td>33,287</td>
<td>217,567</td>
<td>212</td>
<td>6.37 (5.56, 7.30)</td>
<td>0.97 (0.85, 1.12)</td>
<td>3.30 (2.72, 3.99)</td>
</tr>
<tr>
<td>36</td>
<td>45,405</td>
<td>184,280</td>
<td>205</td>
<td>4.51 (3.93, 5.19)</td>
<td>1.11 (0.97, 1.28)</td>
<td>2.88 (2.41, 3.43)</td>
</tr>
<tr>
<td>37</td>
<td>49,436</td>
<td>138,875</td>
<td>197</td>
<td>3.98 (3.46, 4.59)</td>
<td>1.42 (1.23, 1.63)</td>
<td>2.29 (1.90, 2.77)</td>
</tr>
<tr>
<td>38</td>
<td>41,859</td>
<td>89,439</td>
<td>136</td>
<td>3.25 (2.74, 3.85)</td>
<td>1.52 (1.28, 1.80)</td>
<td>2.06 (1.66, 2.56)</td>
</tr>
<tr>
<td>39</td>
<td>24,957</td>
<td>47,580</td>
<td>114</td>
<td>4.57 (3.79, 5.51)</td>
<td>2.40 (1.99, 2.89)</td>
<td>2.05 (1.54, 2.72)</td>
</tr>
<tr>
<td>40</td>
<td>11,895</td>
<td>22,623</td>
<td>70</td>
<td>5.88 (4.62, 7.47)</td>
<td>3.09 (2.43, 3.93)</td>
<td>3.30 (2.38, 4.55)</td>
</tr>
<tr>
<td>41+</td>
<td>10,728</td>
<td>10,728</td>
<td>54</td>
<td>5.03 (3.82, 6.61)</td>
<td>5.03 (3.82, 6.61)</td>
<td>4.22 (3.11, 5.69)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
* Calculated for births of 24 weeks gestation or more.

greater than for twins. In our data set, the prospective risk of fetal death for twins equaled the prospective risk of fetal death for postterm singletons by approximately 36 to 37 weeks’ gestation. The upswing in fetal death risk increases in the third trimester for twins and even more so for triplets.

We think it is more useful clinically to compare gestation-specific prospective risk of fetal death with gestation-specific fetal death rate.
**Table 5. Fetal Death Rate and Prospective Risk of Fetal Death for Triplets**

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>236</td>
<td>15,375</td>
<td>20</td>
<td>84.75 (53.83, 129.73)</td>
<td>1.30 (0.82, 2.05)</td>
<td>509.26 (440.73, 577.45)</td>
</tr>
<tr>
<td>25</td>
<td>280</td>
<td>15,139</td>
<td>13</td>
<td>46.43 (26.00, 79.99)</td>
<td>0.86 (0.48, 1.51)</td>
<td>247.19 (197.56, 304.25)</td>
</tr>
<tr>
<td>26</td>
<td>327</td>
<td>14,859</td>
<td>13</td>
<td>39.76 (22.24, 68.70)</td>
<td>0.87 (0.49, 1.54)</td>
<td>130.57 (96.34, 174.11)</td>
</tr>
<tr>
<td>27</td>
<td>485</td>
<td>14,532</td>
<td>15</td>
<td>30.93 (18.05, 51.66)</td>
<td>1.03 (0.60, 1.75)</td>
<td>104.26 (78.83, 136.34)</td>
</tr>
<tr>
<td>28</td>
<td>697</td>
<td>14,047</td>
<td>17</td>
<td>24.39 (14.73, 39.58)</td>
<td>1.21 (0.73, 1.98)</td>
<td>39.71 (26.83, 58.01)</td>
</tr>
<tr>
<td>29</td>
<td>648</td>
<td>13,350</td>
<td>13</td>
<td>20.06 (11.19, 34.98)</td>
<td>0.97 (0.54, 1.71)</td>
<td>26.77 (16.17, 43.41)</td>
</tr>
<tr>
<td>30</td>
<td>970</td>
<td>12,702</td>
<td>11</td>
<td>11.34 (5.97, 20.85)</td>
<td>0.87 (0.46, 1.60)</td>
<td>14.60 (8.33, 25.0)</td>
</tr>
<tr>
<td>31</td>
<td>1345</td>
<td>11,732</td>
<td>22</td>
<td>16.36 (10.53, 25.09)</td>
<td>1.88 (1.20, 2.89)</td>
<td>9.83 (5.47, 17.21)</td>
</tr>
<tr>
<td>32</td>
<td>1602</td>
<td>10,387</td>
<td>17</td>
<td>10.61 (6.40, 17.31)</td>
<td>1.64 (0.99, 2.68)</td>
<td>5.68 (2.77, 11.17)</td>
</tr>
<tr>
<td>33</td>
<td>2022</td>
<td>8785</td>
<td>9</td>
<td>4.45 (2.17, 8.76)</td>
<td>1.02 (0.50, 2.02)</td>
<td>5.96 (3.23, 10.71)</td>
</tr>
<tr>
<td>34</td>
<td>2342</td>
<td>6763</td>
<td>13</td>
<td>5.55 (3.09, 9.74)</td>
<td>1.92 (1.07, 3.38)</td>
<td>4.29 (2.18, 8.16)</td>
</tr>
<tr>
<td>35</td>
<td>1987</td>
<td>4421</td>
<td>18</td>
<td>9.06 (5.54, 14.58)</td>
<td>* 4.07 (2.49, 6.57)</td>
<td>4.57 (2.23, 9.00)</td>
</tr>
<tr>
<td>36</td>
<td>1249</td>
<td>2434</td>
<td>12</td>
<td>9.61 (5.21, 17.22)</td>
<td>4.93 (2.67, 8.86)</td>
<td>1.62 (0.28, 6.50)</td>
</tr>
<tr>
<td>37</td>
<td>502</td>
<td>1185</td>
<td>9</td>
<td>17.93 (8.77, 35.00)</td>
<td>7.59 (3.71, 14.92)</td>
<td>4.06 (0.70, 16.22)</td>
</tr>
<tr>
<td>38+</td>
<td>683</td>
<td>683</td>
<td>9</td>
<td>13.18 (6.44, 25.80)</td>
<td>13.18 (6.44, 25.80)</td>
<td>2.97 (0.51, 11.89)</td>
</tr>
</tbody>
</table>

CI = confidence interval.

* Calculated for births of 24 weeks gestation or more.
ANCS and NP magnesium

• If patient is at risk of delivering at <34 weeks, then ANCS are recommended

• If <32 weeks, then NP magnesium is recommended

• Late preterm (34 0/7-36 6/7 weeks) and rescue ANCS – Data is lacking
Delivery timing

- Di/di twins – 38 weeks
- MC/DA twins – 34-37 6/7 weeks
- Monoamnionitic twins – 32-34 weeks
- Triplets – 35-36 weeks
- Quadruplets – 34 weeks
- Mode – Increased risk of neurologic complications in vaginal breech delivery if EFW <1500 or nonpresenting twin is >15% bigger than presenting twin
End
Antenatal Betamethasone for Women at Risk for Late Preterm Delivery

Other issues -

- Delivery at 37+ weeks?
- EFW and breech?
- CD protective in extreme preterm?
- Discordant growth in twins, triplets
- Amnio vs laser for TTTS
- Cervical length
## Gestational age and birthweight characteristics of United States singleton, twin, and triplet live births

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of births</td>
<td>3,603,971</td>
<td>463,856</td>
<td>18,843</td>
</tr>
<tr>
<td>Mean gestational age (wk)</td>
<td>39.03</td>
<td>35.77</td>
<td>32.48</td>
</tr>
<tr>
<td>Percent very preterm (&lt;33 wk)</td>
<td>1.70</td>
<td>13.94</td>
<td>41.25</td>
</tr>
<tr>
<td>Percent preterm (&lt;37 wk)</td>
<td>9.43</td>
<td>50.74</td>
<td>91.03</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>3357</td>
<td>2389</td>
<td>1735</td>
</tr>
<tr>
<td>Percent very low birthweight (&lt;1,500 g)</td>
<td>1.10</td>
<td>10.12</td>
<td>31.88</td>
</tr>
<tr>
<td>Percent low birthweight (&lt;2,500 g)</td>
<td>6.06</td>
<td>52.24</td>
<td>91.52</td>
</tr>
<tr>
<td>Percent small for gestational age</td>
<td>9.38</td>
<td>35.63</td>
<td>36.57</td>
</tr>
</tbody>
</table>

TTTS – Uptodate
Risks during the pregnancy

• Preterm birth
Pregnancy Loss

- Early spontaneous reduction from twin to singleton pregnancy is common.
  - Increased risk for adverse pregnancy outcomes later in pregnancy?
  - In one study of 549 twin pregnancies, an initial ultrasound examination was performed 3.5 to 4.5 weeks after ovulation and repeated every two weeks until 12 weeks of gestation.
  - Spontaneous reduction of one sac (i.e., vanishing twin) occurred in 27 percent of pregnancies diagnosed as twins prior to 7 weeks of gestation; both sacs were lost in 9 percent. A vanishing twin may have implications for the remainder of the pregnancy.
  - For example, maternal analyte levels for Down syndrome screening may be affected.
• Rates of late fetal and infant death are shown in the table (table 1). Infant mortality in twins is five-fold higher than that of singletons (37 versus 7 per 1000 live births) \[33\], and twins account for 12 to 15 percent of neonatal deaths \[34\].

• Comparative outcomes of twin versus singleton pregnancies are shown in the table (table 2A-B). Interestingly, studies have consistently shown that, in pregnancies conceived using ART, the rate of early loss of the entire pregnancy is significantly lower for twin than singleton gestations.
Fetal and infant death rates in twin gestations (both fetuses alive at 20 weeks of gestation, n=150,386)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two surviving infants</td>
<td>93.7</td>
</tr>
<tr>
<td>One infant death, one surviving infant</td>
<td>2.3</td>
</tr>
<tr>
<td>Two infant deaths</td>
<td>1.5</td>
</tr>
<tr>
<td>One fetal death, one surviving infant</td>
<td>1.1</td>
</tr>
<tr>
<td>Two fetal deaths</td>
<td>1.1</td>
</tr>
<tr>
<td>One fetal death, one infant death</td>
<td>0.4</td>
</tr>
</tbody>
</table>

# Mortality per 1,000 live births by plurality

<table>
<thead>
<tr>
<th>Plurality</th>
<th>Infant deaths (birth to 1 year)</th>
<th>Neonatal deaths (birth to day 28)</th>
<th>Postneonatal (day 29 to 1 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singletons</td>
<td>11.2</td>
<td>7.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Twins</td>
<td>66.4</td>
<td>55.9</td>
<td>10.5</td>
</tr>
<tr>
<td>Triplets*</td>
<td>190.4</td>
<td>168.8</td>
<td>21.6</td>
</tr>
</tbody>
</table>

Prenatal Diagnosis Of Down Syndrome

- We suggest offering Down syndrome screening with the first-trimester combined test, which can provide fetus-specific risk assessment when chorionic villus sampling (CVS) is available.
- Each fetus of a multiple gestation is at the same risk of having trisomy 21 as a singleton fetus; this risk is based upon maternal age and family history. Since there are two fetuses at risk in twin pregnancy, the risk that one fetus of a DZ pregnancy is affected is twice that of a singleton pregnancy (if zygosity is unknown, multiply singleton risk by 5/3). The risk of an affected pregnancy is about the same for women age 31 to 33 carrying twins as for women age 35 carrying a singleton \[60,61\]. Age-based cutoffs for offering invasive testing are no longer recommended in singleton pregnancies, and should not be used in twin pregnancies either. All women should be offered the options of risk assessment and invasive testing.
- Determination of each fetus' risk also depends upon zygosity. As discussed above, this cannot always be determined with certainty before birth. For DZ twins, the pregnancy specific risk is calculated by summing the individual estimates of risk. By comparison, both MZ twins would be expected to be either affected or unaffected so their risk estimate is calculated differently \[62\]. As an example, given the same values for maternal age, maternal analyte levels, and nuchal translucency, the risk of carrying one or more fetuses with Down syndrome would be 1:140 if DZ and 1:1250 if MZ \[62\]. The method and calculations involved for prenatal screening of Down syndrome and neural tube defects in twin pregnancies were described by Wald \[62\].
Maternal serum analyte interpretation is problematic in twin pregnancies since both twins contribute to the analyte concentration, thus a fetus specific risk cannot be calculated. Maternal analyte levels can be adjusted for twin pregnancy; however, the detection rate for Down syndrome is lower than in singleton pregnancy (eg, integrated test: 93 percent detection in MC twins, 78 percent detection in DC twins, 95 percent detection in singletons; for the combined test detection rates are 84, 70, and 85 percent, respectively) [62].

Measurement of nuchal thickness can improve the detection rate and help identify which fetus is affected [63,64]. Using first-trimester combined risk assessment (nuchal translucency and analytes), a study by the Fetal Medicine Foundation reported identifying three of four fetuses with Down syndrome in DZ pregnancies discordant for the abnormality (detection rate 75 percent) [63]; by comparison, the detection rate was 90 percent in singleton pregnancies (5 percent false-positive rate) [65].

Of note, nuchal thickening in MC pregnancies may be an early sign of twin-twin transfusion syndrome.

An additional factor complicating prenatal diagnosis of MZ twins is that rarely these twins have different genotypes due to fetal mosaicism or confined placental mosaicism [68-72]. Moreover, fetuses with the same genotype may have different phenotypes; as an example, only one fetus of twins with Down syndrome may have increased nuchal translucency. For these reasons, both fetuses of an MZ pair should undergo karyotyping when karyotyping is performed, though this may not be possible when CVS is performed. In some cases, amniocytes as well as fetal blood may be needed to make an accurate diagnosis.
Diagnosis And Management Of Congenital Anomalies

- The incidence of congenital anomalies is significantly higher in MZ twins than in singletons or DZ twins.
- Twins are not predisposed to any specific type of congenital anomaly. Most twins with anomalies will have a normal cotwin. In a review of twin pairs in which at least one infant had an anomaly, the concordance rate for any one anomaly ranged from 3.6 to 18.8 percent, depending on the particular anomaly [78].
- The reported accuracy of ultrasound for detection of fetal anomalies in twins varies because of differences in ascertainment postnatally and at termination, definition of anomalies, and operator capability. Ultrasound examination can detect the majority of major malformations in twins, but should be performed by sonographers experienced in both anomaly detection and assessment of multiple gestation [79].
- The diagnosis of a congenital anomaly in one twin is especially problematic since decisions regarding monitoring, therapy, and delivery affect both fetuses.
- Expectant management, pregnancy termination, and selective reduction should all be discussed if a congenital anomaly is found. Women should be counseled about these options early in the pregnancy.
Conjoined twins
Growth issues, surveillance

- Di/di
- Mono/di
- Monoamniotic
When to deliver?

- **ACOG** – 38 weeks twins
  - **Creasy** –
    - Di/di 38 weeks
    - Mono/di 37 weeks
    - Monoamniotic – 32-34 weeks (Creasy)
Reestimating date of delivery in multifetal pregnancies. AU Minakami H; Sato I SO JAMA 1996 May 8;275(18):1432-4.

OBJECTIVE--To clarify the optimal estimated date of delivery for multifetal pregnancies. DESIGN, SUBJECTS, AND SETTING--A retrospective study of all 88,936 infants born of multifetal pregnancies and all 6,020,542 infants born of singleton pregnancies that occurred at 26 weeks or more of gestation between 1989 and 1993 in Japan. MAIN OUTCOME MEASURE--Incidence of stillbirth and early neonatal death according to gestational age at delivery. RESULTS--The mean +/- SD duration of pregnancy was 37.0 +/- 2.7 weeks for multifetal pregnancies and 39.6 +/- 1.6 weeks for singleton pregnancies. In multifetal pregnancies, the incidence of stillbirth and of early neonatal death gradually declined until 37 to 38 weeks' gestation and then increased. These parameters in singleton pregnancies declined until 39 weeks' gestation before increasing. The lowest incidence of perinatal death (Stillbirth plus early neonatal death) seen at 38 weeks' gestation in multifetal pregnancies corresponded to that seen at 43 weeks' gestation in singleton pregnancies (10.5 vs 9.7 per 1000 infants). The fist of perinatal death was more than 6 times as high for fetuses of multifetal pregnancies born at 37 weeks or later than for singleton fetuses born at 40 weeks or later (relative risk, 6.6; 95% confidence internal, 6.1 - 7.1). CONCLUSION--Fetuses of multifetal pregnancies are at an increased risk of death after reaching the normative gestational age for singleton pregnancies. Limiting the estimated date of delivery to 37 to 38 weeks may be appropriate in multifetal pregnancies. AD Department of Obstetrics and Gynecology, Jichi Medical School, Tochigi, Japan.
deliv single 41; twins 37-38, trip 36wk

- Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. AU Kahn B; Lumey LH; Zybert PA; Lorenz JM; Cleary-Goldman J; D'Alton ME; Robinson JN SO Obstet Gynecol 2003 Oct;102(4):685-92. OBJECTIVE: To evaluate the prospective risk of fetal death in singleton, twin, and triplet pregnancies and to compare this risk with fetal and neonatal death rates. METHODS: We analyzed 11,061,599 singleton, 297,622 twin, and 15,375 triplet gestations drawn from the 1995-1998 National Center for Health Statistics linked birth and death files. Prospective risk of fetal death was expressed as a proportion of all fetuses still at risk at a given gestational age and compared with fetal death rate. Fetal death risk and neonatal death rates were represented graphically for singletons, twins, and triplets. RESULTS: The prospective risk of fetal death at 24 weeks was 0.28 per 1000, 0.92 per 1000, and 1.30 per 1000 for singletons, twins, and triplets, respectively. At 40 weeks, the corresponding risk was 0.57 per 1000 and 3.09 per 1000 for singletons and twins, respectively and, at 38 or more weeks, 13.18 per 1000 for triplets. Plots of gestation-specific prospective risk of fetal death and neonatal mortality converged for singletons and twins at term but crossed for triplets at approximately 36 weeks' gestation. CONCLUSION: Prospective risk of fetal death is greater for triplets and twins than for singletons and greater for triplets than for twins during the third trimester. The pattern corroborates with uteroplacental insufficiency as a suspected underlying mechanism. When prospective risk of fetal death exceeds neonatal mortality risk, delivery might be indicated. When this model is used, this data set suggests that it might be reasonable to consider delivery of twins by 39 weeks and triplets by 36 weeks to improve perinatal outcome. AD Department of Obstetrics and Gynecology, University of Colorado, Denver, Colorado, USA
Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. AU Kahn B; Lumey LH; Zybert PA; Lorenz JM; Cleary-Goldman J; D'Alton ME; Robinson JN. Obstet Gynecol 2003 Oct;102(4):685-92.

Table 3. Fetal Death Rate and Prospective Risk of Fetal Death for Singletons

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>10,906</td>
<td>11,061,599</td>
<td>3101</td>
<td>284.34 (275.90, 292.93)</td>
<td>0.28 (0.27, 0.29)</td>
<td>414.86 (403.91, 425.90)</td>
</tr>
<tr>
<td>25</td>
<td>11,692</td>
<td>11,050,693</td>
<td>2544</td>
<td>217.58 (210.16, 225.20)</td>
<td>0.23 (0.22, 0.24)</td>
<td>248.47 (239.67, 257.48)</td>
</tr>
<tr>
<td>26</td>
<td>13,285</td>
<td>11,039,001</td>
<td>2288</td>
<td>172.22 (165.86, 178.78)</td>
<td>0.21 (0.20, 0.22)</td>
<td>167.77 (160.86, 174.92)</td>
</tr>
<tr>
<td>27</td>
<td>13,756</td>
<td>11,025,716</td>
<td>2008</td>
<td>145.97 (140.14, 152.01)</td>
<td>0.18 (0.17, 0.19)</td>
<td>110.32 (104.74, 116.15)</td>
</tr>
<tr>
<td>28</td>
<td>15,569</td>
<td>11,011,960</td>
<td>2015</td>
<td>129.42 (124.21, 134.82)</td>
<td>0.18 (0.17, 0.19)</td>
<td>84.11 (79.52, 88.94)</td>
</tr>
<tr>
<td>29</td>
<td>17,431</td>
<td>10,996,391</td>
<td>1804</td>
<td>103.49 (99.03, 108.13)</td>
<td>0.16 (0.16, 0.17)</td>
<td>59.06 (55.44, 62.90)</td>
</tr>
<tr>
<td>30</td>
<td>23,078</td>
<td>10,978,960</td>
<td>1936</td>
<td>83.89 (80.36, 87.56)</td>
<td>0.18 (0.17, 0.19)</td>
<td>42.38 (39.72, 45.20)</td>
</tr>
<tr>
<td>31</td>
<td>27,728</td>
<td>10,955,882</td>
<td>1792</td>
<td>64.63 (61.78, 67.60)</td>
<td>0.16 (0.16, 0.17)</td>
<td>30.54 (28.49, 32.72)</td>
</tr>
<tr>
<td>32</td>
<td>39,551</td>
<td>10,928,154</td>
<td>1972</td>
<td>49.86 (47.75, 52.06)</td>
<td>0.18 (0.17, 0.19)</td>
<td>19.61 (18.25, 21.08)</td>
</tr>
<tr>
<td>33</td>
<td>61,653</td>
<td>10,888,603</td>
<td>1972</td>
<td>31.99 (30.62, 33.41)</td>
<td>0.18 (0.17, 0.19)</td>
<td>13.35 (12.46, 14.32)</td>
</tr>
<tr>
<td>34</td>
<td>125,999</td>
<td>10,826,950</td>
<td>2340</td>
<td>18.57 (17.84, 19.34)</td>
<td>0.22 (0.21, 0.23)</td>
<td>8.39 (7.90, 8.92)</td>
</tr>
<tr>
<td>35</td>
<td>231,475</td>
<td>10,700,951</td>
<td>2462</td>
<td>10.64 (10.22, 11.06)</td>
<td>0.23 (0.22, 0.24)</td>
<td>5.02 (4.73, 5.32)</td>
</tr>
<tr>
<td>36</td>
<td>418,129</td>
<td>10,469,476</td>
<td>2709</td>
<td>6.48 (6.24, 6.73)</td>
<td>0.26 (0.25, 0.27)</td>
<td>3.39 (3.22, 3.57)</td>
</tr>
<tr>
<td>37</td>
<td>819,233</td>
<td>10,051,347</td>
<td>2856</td>
<td>3.49 (3.36, 3.62)</td>
<td>0.28 (0.27, 0.29)</td>
<td>2.08 (1.98, 2.18)</td>
</tr>
<tr>
<td>38</td>
<td>1,686,122</td>
<td>9,232,114</td>
<td>3247</td>
<td>1.93 (1.86, 1.99)</td>
<td>0.35 (0.34, 0.36)</td>
<td>1.26 (1.21, 1.31)</td>
</tr>
<tr>
<td>39</td>
<td>2,654,221</td>
<td>7,545,992</td>
<td>2986</td>
<td>1.13 (1.09, 1.17)</td>
<td>0.40 (0.38, 0.41)</td>
<td>0.92 (0.89, 0.96)</td>
</tr>
<tr>
<td>40</td>
<td>2,590,504</td>
<td>4,891,771</td>
<td>2795</td>
<td>1.08 (1.04, 1.12)</td>
<td>0.57 (0.55, 0.59)</td>
<td>0.85 (0.82, 0.89)</td>
</tr>
<tr>
<td>41</td>
<td>1,438,442</td>
<td>2,301,267</td>
<td>1480</td>
<td>1.03 (1.08, 1.08)</td>
<td>0.64 (0.61, 0.68)</td>
<td>0.93 (0.88, 0.98)</td>
</tr>
<tr>
<td>42</td>
<td>493,493</td>
<td>862,825</td>
<td>647</td>
<td>1.31 (1.21, 1.42)</td>
<td>0.75 (0.69, 0.81)</td>
<td>1.15 (1.06, 1.25)</td>
</tr>
<tr>
<td>43+</td>
<td>369,332</td>
<td>369,332</td>
<td>453</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.12 (1.01, 1.23)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
* Calculated for births of 24 weeks gestation or more.
greater than for twins. In our data set, the prospective risk of fetal death for twins equaled the prospective risk of fetal death for post-term singletons by approximately 36 to 37 weeks' gestation. The upswing in fetal death risk increases in the third trimester for twins and even more so for triplets.

We think it is more useful clinically to compare gestation-specific prospective risk of fetal death with gestation-specific neonatal death rates than to consider fetal death per 1000 births at each gestational age.
Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. AU Kahn B; Lumez LH; Zybert PA; Lorenz JM; Cleary-Goldman J; D'Alton ME; Robinson JN. SO Obstet Gynecol 2003 Oct;102(4):685-92.

### Table 5. Fetal Death Rate and Prospective Risk of Fetal Death for Triples

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>236</td>
<td>15,375</td>
<td>20</td>
<td>84.75 (53.83, 129.73)</td>
<td>1.30 (0.82, 2.05)</td>
<td>509.26 (440.73, 577.45)</td>
</tr>
<tr>
<td>25</td>
<td>280</td>
<td>15,139</td>
<td>13</td>
<td>46.43 (26.00, 79.99)</td>
<td>0.86 (0.48, 1.51)</td>
<td>247.19 (197.56, 304.25)</td>
</tr>
<tr>
<td>26</td>
<td>327</td>
<td>14,859</td>
<td>13</td>
<td>39.76 (22.24, 68.70)</td>
<td>0.87 (0.49, 1.54)</td>
<td>130.57 (96.34, 174.11)</td>
</tr>
<tr>
<td>27</td>
<td>485</td>
<td>14,532</td>
<td>15</td>
<td>30.93 (18.05, 51.66)</td>
<td>1.03 (0.60, 1.75)</td>
<td>104.26 (78.83, 136.34)</td>
</tr>
<tr>
<td>28</td>
<td>697</td>
<td>14,047</td>
<td>17</td>
<td>24.39 (14.73, 39.58)</td>
<td>1.21 (0.73, 1.98)</td>
<td>39.71 (26.83, 58.01)</td>
</tr>
<tr>
<td>29</td>
<td>648</td>
<td>13,350</td>
<td>13</td>
<td>20.06 (11.19, 34.98)</td>
<td>0.97 (0.54, 1.71)</td>
<td>26.77 (16.17, 43.41)</td>
</tr>
<tr>
<td>30</td>
<td>970</td>
<td>12,702</td>
<td>11</td>
<td>13.43 (5.97, 20.85)</td>
<td>0.87 (0.46, 1.60)</td>
<td>14.60 (8.33, 25.0)</td>
</tr>
<tr>
<td>31</td>
<td>1345</td>
<td>11,732</td>
<td>22</td>
<td>16.36 (10.53, 25.09)</td>
<td>1.88 (1.20, 2.89)</td>
<td>9.83 (5.47, 17.21)</td>
</tr>
<tr>
<td>32</td>
<td>1602</td>
<td>10,387</td>
<td>17</td>
<td>10.61 (6.40, 17.31)</td>
<td>1.64 (0.99, 2.68)</td>
<td>5.68 (2.77, 11.17)</td>
</tr>
<tr>
<td>33</td>
<td>2022</td>
<td>8785</td>
<td>9</td>
<td>4.45 (2.17, 8.76)</td>
<td>1.02 (0.50, 2.02)</td>
<td>5.96 (3.23, 10.71)</td>
</tr>
<tr>
<td>34</td>
<td>2342</td>
<td>6763</td>
<td>13</td>
<td>5.55 (3.09, 9.74)</td>
<td>1.92 (1.07, 3.38)</td>
<td>4.29 (2.18, 8.16)</td>
</tr>
<tr>
<td>35</td>
<td>1987</td>
<td>4421</td>
<td>18</td>
<td>9.06 (5.54, 14.58)</td>
<td>4.07 (2.49, 6.57)</td>
<td>4.57 (2.23, 9.00)</td>
</tr>
<tr>
<td>36</td>
<td>1249</td>
<td>2434</td>
<td>12</td>
<td>9.61 (5.21, 17.22)</td>
<td>4.93 (2.67, 8.86)</td>
<td>1.62 (0.28, 6.50)</td>
</tr>
<tr>
<td>37</td>
<td>502</td>
<td>1185</td>
<td>9</td>
<td>17.93 (8.77, 35.00)</td>
<td>7.59 (3.71, 14.92)</td>
<td>4.06 (0.70, 16.22)</td>
</tr>
<tr>
<td>38+</td>
<td>683</td>
<td>683</td>
<td>9</td>
<td>13.18 (6.44, 25.80)</td>
<td>13.18 (6.44, 25.80)</td>
<td>2.97 (0.51, 11.89)</td>
</tr>
</tbody>
</table>

CI = confidence interval.

* Calculated for births of 24 weeks gestation or more.
END
Other issues -

- Delivery at 37+ weeks?
- EFW and breech?
- CD protective in extreme preterm?
- Discordant growth in twins, triplets
- Amnio vs laser for TTTS
- Cervical length
• References:

• Creasy R, Resnik R. Maternal-Fetal Medicine Principles and Practice. 5th Edition

• Uptodate.com online source.
• No financial interests to disclose.
Multiples
Epidemiology

• United States, twin births accounted for 3.2 percent of live births in 2006 (Natl Vital Statistics)

• Of all twins…without ART
  – Dizygotic twins (~70%)
    • Ethnic variation in incidence of DZ twinning
  – Monozygotic twins (~30%)
    • Incidence of MZ twins is relatively stable worldwide at 3 to 5 per 1000 births
    • 70% MCDA, 30% DCDA

• Triplets…

• Quadruplets…
Placentation

- Multiple gestations – (e.g. twins)
- Dependent on when zygote splits post-fertilization in monozygotic pregnancy
  - the earlier the split the more tissue each pregnancy gets to itself
    - <3 dichorionic
    - 3-8 diamniotic
    - 8-12 monoamniotic
    - >12 conjoined
  - dichorionic placentation (two placentas, in all dizygotic and some monozygotic twins)
  - monochorionic placentation
    - monozygotic twins develop with only one placenta
    - higher risk of complications during pregnancy
    - preeclampsia
    - shunting of blood from 1 twin to the other (TTTS)
  - monoamniotic placentation
2 placentas
2 amnions
2 chorions
(dizygotic twins or monozygotic twins with cleavage of zygote during first 3 days after fertilization)
Lambda sign/twin peak

1 placenta
2 amnions
1 chorion
(monozygotic twins with cleavage of zygote days 4-8 post-fertilization)
T sign

1 placenta
1 amnion
1 chorion
(monozygotic twins with cleavage of zygote days 8-12 post-fertilization)

*if split occurs after 12 days post-fertilization, conjoined twins result
Twinning

• Determine early in gestation
  – Location, fetal sex, insertion sites, thickness of membranes

• Why do we care about placentation?
  – Predicting risk…
    • Monochorionic, diamniotic
      – Risk of sharing a placenta; shunting, anastomosis
      – unequal blood distribution - TTTS
      – 15% occurrence rate
    • Monoamniotic (cord entanglement)
      – 1/10,000 of all pregnancies
      » 1-5% of monozygotic twins
Dichorionic twin pregnancy (lambda sign)
Thick interdividing membrane of dichorionic twin pregnancy
Thin intertwin membrane characteristic of monochorionic diamniotic twin pregnancy.
Twin to twin transfusion syndrome (TTTS)

- Incidence
  - 15% in monochorionic-diamniotic twinpregs
- Diagnosis
  - Monochorionic-diamniotic pregnancy (same sex, thin membrane, no twin peak, 1 placenta)
  - Polyhydramnios (>8cm) - recipient; oligohydramnios (<2cm) - donor
- Etiology - TYPE OF ANASTOMOSIS, not necessarily number; discordant placental sharing
  - A-V- unidirectional flow; intravillous (placental surface single unpaired artery carrying blood from donor twin to placental cotyledon together with single unpaired vein carrying blood from that cotyledon back to the recipient twin)
  - A-A, V-V- superficial on chorionic plate; bidirectional flow; “protective”
  - Less A-A, V-V anastomoses increases probability of A-V anastomoses leading to TTTS
TTTS

- Classification (no good system for prediction of progression or prognosis)
- Quintero staging system (good for monitoring disease progression, not predicting outcomes)
- Stage I: + Poly/oligo (POS); +bladder in donor
- Stage II: +POS; NO bladder seen in donor; normal Dopplers
- Stage III: +POS; NO bladder seen in donor; abnormal Dopplers
- Stage IV: + POS, hydrops in either twin
- Stage V: Fetal demise of either or both twins
- Staging system based on presence of A-A anastamoses (Jain et al); not widely used
OUTLINE

• Delivery at 37+ weeks?
• EFW and breech?
• CD protective in extreme preterm?
• Discordant growth in twins, triplets
• Amnio vs laser for TTTS
• Cervical length
Twinning

- **Dizygotic**
  - 2 separate embryos
  - 2 separate placentas, not always obvious

- **Monozygotic**
  - Single embryo
  - May be single placenta, but most often not
Cardiovascular Changes of Pregnancy

- Cardiac Output Increased by 30-50%
- Twin Pregnancy: Add another 15%
- Starts Early and Peaks at 20 Weeks
- Increase in Stroke Volume
- Increase in Heart Rate
uptodate
Epidemiology

• United States, twin births accounted for 3.2 percent of live births in 2006 (Natl Vital Statistics)

• Of all twins... without ART
  – Dizygotic twins (~70%)
    • Ethnic variation in incidence of DZ twinning
  – Monozygotic twins (~30%)
    • Incidence of MZ twins is relatively stable worldwide at 3 to 5 per 1000 births
    • 70% MCDA, 30% DCDA

• Triplets...

• Quadruplets...
Epidemiology

• Triplets...
• Quadruplets...
Diagnosis
Placentation

- Multiple gestations – (e.g. twins)
- Dependent on when zygote splits post-fertilization in monozygotic pregnancy
  - the earlier the split the more tissue each pregnancy gets to itself
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  - dichorionic placentation (two placentas, in all dizygotic and some monozygotic twins)
  - monochorionic placentation
    - monozygotic twins develop with only one placenta
    - higher risk of complications during pregnancy
    - preeclampsia
    - shunting of blood from 1 twin to the other (TTTS)
  - monoamniotic placentation
Graph showing day of split and chorion/amnion
2 placentas  
2 amnions  
2 chorions  
(dizygotic twins or monozygotic twins with cleavage of zygote during first 3 days after fertilization)  
Lambda sign/twin peak

1 placenta  
2 amnions  
1 chorion  
(monozygotic twins with cleavage of zygote days 4-8 post-fertilization)  
T sign

1 placenta  
1 amnion  
1 chorion  
(monozygotic twins with cleavage of zygote days 8-12 post-fertilization)

*if split occurs after 12 days post-fertilization, conjoined twins result
Twinning

• Determine early in gestation
  – Location, fetal sex, insertion sites, thickness of membranes

• Why do we care about placentation?
  – Predicting risk…
    • Monochorionic, diamniotic
      – Risk of sharing a placenta; shunting, anastomosis
      – unequal blood distribution - TTTS
      – 15% occurrence rate
    • Monoamniotic (cord entanglement)
      – 1/10,000 of all pregnancies
        » 1-5% of monozygotic twins
Dichorionic twin pregnancy (lambda sign)
Thick interdividing membrane of dichorionic twin pregnancy
Thin intertwin membrane characteristic of monochorionic diamniotic twin pregnancy
## Gestational age and birthweight characteristics of United States singleton, twin, and triplet live births

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of births</td>
<td>3,603,971</td>
<td>463,856</td>
<td>18,843</td>
</tr>
<tr>
<td>Mean gestational age (wk)</td>
<td>39.03</td>
<td>35.77</td>
<td>32.48</td>
</tr>
<tr>
<td>Percent very preterm (&lt;33 wk)</td>
<td>1.70</td>
<td>13.94</td>
<td>41.25</td>
</tr>
<tr>
<td>Percent preterm (&lt;37 wk)</td>
<td>9.43</td>
<td>50.74</td>
<td>91.03</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td>3357</td>
<td>2389</td>
<td>1735</td>
</tr>
<tr>
<td>Percent very low birthweight (&lt;1,500 g)</td>
<td>1.10</td>
<td>10.12</td>
<td>31.88</td>
</tr>
<tr>
<td>Percent low birthweight (&lt;2,500 g)</td>
<td>6.06</td>
<td>52.24</td>
<td>91.52</td>
</tr>
<tr>
<td>Percent small for gestational age</td>
<td>9.38</td>
<td>35.63</td>
<td>36.57</td>
</tr>
</tbody>
</table>

Risks during the pregnancy

- Preterm birth
Pregnancy Loss

- Early spontaneous reduction from twin to singleton pregnancy is common.
  - Increased risk for adverse pregnancy outcomes later in pregnancy?
  - In one study of 549 twin pregnancies, an initial ultrasound examination was performed 3.5 to 4.5 weeks after ovulation and repeated every two weeks until 12 weeks of gestation.
  - Spontaneous reduction of one sac (ie, vanishing twin) occurred in 27 percent of pregnancies diagnosed as twins prior to 7 weeks of gestation; both sacs were lost in 9 percent. A vanishing twin may have implications for the remainder of the pregnancy.
  - For example, maternal analyte levels for Down syndrome screening may be affected
• Rates of late fetal and infant death are shown in the table (table 1). Infant mortality in twins is five-fold higher than that of singletons (37 versus 7 per 1000 live births) [33], and twins account for 12 to 15 percent of neonatal deaths [34].

• Comparative outcomes of twin versus singleton pregnancies are shown in the table (table 2A-B). Interestingly, studies have consistently shown that, in pregnancies conceived using ART, the rate of early loss of the entire pregnancy is significantly lower for twin than singleton gestations
Fetal and infant death rates in twin gestations (both fetuses alive at 20 weeks of gestation, n=150,386)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two surviving infants</td>
<td>93.7</td>
</tr>
<tr>
<td>One infant death, one surviving infant</td>
<td>2.3</td>
</tr>
<tr>
<td>Two infant deaths</td>
<td>1.5</td>
</tr>
<tr>
<td>One fetal death, one surviving infant</td>
<td>1.1</td>
</tr>
<tr>
<td>Two fetal deaths</td>
<td>1.1</td>
</tr>
<tr>
<td>One fetal death, one infant death</td>
<td>0.4</td>
</tr>
</tbody>
</table>

### Mortality per 1,000 live births by plurality

<table>
<thead>
<tr>
<th></th>
<th>Infant deaths (birth to 1 year)</th>
<th>Neonatal deaths (birth to day 28)</th>
<th>Postneonatal (day 29 to 1 year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singletons</td>
<td>11.2</td>
<td>7.8</td>
<td>3.4</td>
</tr>
<tr>
<td>Twins</td>
<td>66.4</td>
<td>55.9</td>
<td>10.5</td>
</tr>
<tr>
<td>Triplets*</td>
<td>190.4</td>
<td>168.8</td>
<td>21.6</td>
</tr>
</tbody>
</table>

Nutrition

- NUTRITION — Women carrying multiple gestations should increase their daily dietary intake by about 300 kcal above that for a singleton pregnancy, or 600 kcal over that of a nonpregnant woman [28]. The Institute of Medicine recommends the following cumulative weight gain by term for women carrying twins [36]:
  - BMI <18.5 kg/m2 (underweight) — no recommendation due to insufficient data
  - BMI 18.5 to 24.9 kg/m2 (normal weight) — weight gain 37 to 54 lbs (16.8 to 24.5 kg)
  - BMI 25.0 to 29.9 kg/m2 (overweight) — weight gain 31 to 50 lbs (14.1 to 22.7 kg)
  - BMI ≥30.0 kg/m2 (obese) — weight gain 25 to 42 lbs (11.4 to 19.1 kg)
- These thresholds represent the 25th through 75th percentile weight gains in women who gave birth to twins weighing at least 2500 g [36] and appear to be associated with a decreased risk of preterm birth and higher birth weights [37]. Other guidelines have also been developed [38].
- Dietary or vitamin/mineral supplementation should include adequate iron and folic acid. The Society of Maternal-Fetal Medicine recommendations for nutrition in twin pregnancy are shown in the table (table 3) [39].
<table>
<thead>
<tr>
<th>Intervention</th>
<th>First trimester</th>
<th>Second trimester</th>
<th>Third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal weight/weight gain</td>
<td>Assess maternal prepregnancy BMI, determine BMI-specific weight gain goals</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
<td>Assess/counsel re: maternal BMI-specific weight gain (each prenatal care visit)</td>
</tr>
<tr>
<td>Caloric requirements (kcal · kg⁻¹ · d⁻¹)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal BMI</td>
<td>40-45</td>
<td>Alter as necessary for weight gain goal</td>
<td>Alter as necessary for weight gain goal</td>
</tr>
<tr>
<td>Underweight</td>
<td>42-50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>30-35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronutrient supplement (daily total intake)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVI with iron (30 mg elemental tablets)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>1500</td>
<td>2500</td>
<td>2500</td>
</tr>
<tr>
<td>Vitamin D (International units)</td>
<td>1000</td>
<td>1000</td>
<td>1000</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>400</td>
<td>800</td>
<td>800</td>
</tr>
<tr>
<td>Zinc (mg)</td>
<td>15</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>DHA/EPA (mg)</td>
<td>300-500</td>
<td>300-500</td>
<td>300-500</td>
</tr>
<tr>
<td>Folic acid (mg)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vitamin C/E (mg/international units)</td>
<td>500-1000/400</td>
<td>500-1000/400</td>
<td>500-1000/400</td>
</tr>
<tr>
<td>Nutritional consultation</td>
<td>Yes</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
<td>Repeat if not at weight gain goal, anemia, GDM</td>
</tr>
<tr>
<td>Laboratory nutritional assessment</td>
<td>Hemoglobin ferritin folate/B12 early screen for GDM (risk factors) vitamin D</td>
<td>Follow up abnormalities from first trimester</td>
<td>Hemoglobin ferritin GDM screen with or without vitamin D</td>
</tr>
<tr>
<td>Risk factor appropriate exercise or reduction in activity</td>
<td>Screen</td>
<td>Screen</td>
<td>Screen</td>
</tr>
</tbody>
</table>

Prenatal Diagnosis Of Down Syndrome

• We suggest offering Down syndrome screening with the first-trimester combined test, which can provide fetus-specific risk assessment when chorionic villus sampling (CVS) is available.

• Each fetus of a multiple gestation is at the same risk of having trisomy 21 as a singleton fetus; this risk is based upon maternal age and family history. Since there are two fetuses at risk in twin pregnancy, the risk that one fetus of a DZ pregnancy is affected is twice that of a singleton pregnancy (if zygosity is unknown, multiply singleton risk by 5/3). The risk of an affected pregnancy is about the same for women age 31 to 33 carrying twins as for women age 35 carrying a singleton [60,61]. Age-based cutoffs for offering invasive testing are no longer recommended in singleton pregnancies, and should not be used in twin pregnancies either. All women should be offered the options of risk assessment and invasive testing.

• Determination of each fetus' risk also depends upon zygosity. As discussed above, this cannot always be determined with certainty before birth. For DZ twins, the pregnancy specific risk is calculated by summing the individual estimates of risk. By comparison, both MZ twins would be expected to be either affected or unaffected so their risk estimate is calculated differently [62]. As an example, given the same values for maternal age, maternal analyte levels, and nuchal translucency, the risk of carrying one or more fetuses with Down syndrome would be 1:140 if DZ and 1:1250 if MZ [62]. The method and calculations involved for prenatal screening of Down syndrome and neural tube defects in twin pregnancies were described by Wald [62].
Prenatal Diagnosis Of Down Syndrome

- Maternal serum analyte interpretation is problematic in twin pregnancies since both twins contribute to the analyte concentration, thus a fetus specific risk cannot be calculated. Maternal analyte levels can be adjusted for twin pregnancy; however, the detection rate for Down syndrome is lower than in singleton pregnancy (eg, integrated test: 93 percent detection in MC twins, 78 percent detection in DC twins, 95 percent detection in singletons; for the combined test detection rates are 84, 70, and 85 percent, respectively) [62].

- Measurement of nuchal thickness can improve the detection rate and help identify which fetus is affected [63,64]. Using first-trimester combined risk assessment (nuchal translucency and analytes), a study by the Fetal Medicine Foundation reported identifying three of four fetuses with Down syndrome in DZ pregnancies discordant for the abnormality (detection rate 75 percent) [63]; by comparison, the detection rate was 90 percent in singleton pregnancies (5 percent false-positive rate) [65].

- Of note, nuchal thickening in MC pregnancies may be an early sign of twin-twin transfusion syndrome

- An additional factor complicating prenatal diagnosis of MZ twins is that rarely these twins have different genotypes due to fetal mosaicism or confined placental mosaicism [68-72]. Moreover, fetuses with the same genotype may have different phenotypes; as an example, only one fetus of twins with Down syndrome may have increased nuchal translucency. For these reasons, both fetuses of an MZ pair should undergo karyotyping when karyotyping is performed, though this may not be possible when CVS is performed. In some cases, amniocytes as well as fetal blood may be needed to make an accurate diagnosis.
Diagnosis And Management Of Congenital Anomalies

- The incidence of congenital anomalies is significantly higher in MZ twins than in singletons or DZ twins.
- Twins are not predisposed to any specific type of congenital anomaly. Most twins with anomalies will have a normal cotwin. In a review of twin pairs in which at least one infant had an anomaly, the concordance rate for any one anomaly ranged from 3.6 to 18.8 percent, depending on the particular anomaly [78].
- The reported accuracy of ultrasound for detection of fetal anomalies in twins varies because of differences in ascertainment postnatally and at termination, definition of anomalies, and operator capability. Ultrasound examination can detect the majority of major malformations in twins, but should be performed by sonographers experienced in both anomaly detection and assessment of multiple gestation [79].
- The diagnosis of a congenital anomaly in one twin is especially problematic since decisions regarding monitoring, therapy, and delivery affect both fetuses.
- Expectant management, pregnancy termination, and selective reduction should all be discussed if congenital anomalies are present. Women who choose
TRAP

• TRAP sequence and conjoined twins — Twin reversed arterial perfusion (TRAP) sequence (also called acardia) and conjoined twins are rare anomalies unique to MC twins (incidence 1 in 35,000 pregnancies and 1 in 50,000 pregnancies, respectively) [80-82].

• TRAP sequence is due to arterioarterial anastomoses resulting in a pump twin and a perfused twin [83]. Reversed
Conjoined twins
Multifetal pregnancy reduction and selective termination

- MFPR vs selective termination
- 5-8% of pregnancy loss <24 weeks
- Selective fetal reduction — The timely diagnosis of a fetal anomaly allows the patient to consider selective termination of the anomalous fetus. This is a safe and effective option in expert hands, although there is a risk of miscarriage or preterm delivery of the normal co-twin. Because of these risks, expectant management may be a safer option if the twin with the anomaly is not expected to have prolonged survival or a favorable outcome (eg, trisomy 18) [88].
- Anencephaly is an exception since it is associated with polyhydramnios and preterm birth. If polyhydramnios develops in the anencephalic twin's sac of a DC twin pair, selective feticide or amniodrainage appears to result in longer gestation and higher birthweight in the viable twin than expectant management [89,90]. In our practice, we suggest selective termination whenever a fetal anomaly incompatible with survival is identified in one twin if this anomaly is associated with polyhydramnios. We do not recommend amnioreduction unless maternal respiratory compromise is present.
- As discussed above, selective termination of one twin (eg, anomalous fetus) with intracardiac injection of potassium chloride or digoxin is not considered in MC twins because feticide can result in death of the cotwin. Selective cord coagulation is an alternative approach in this setting, and avoids the intertwin risks associated with shared circulations [85].
Growth issues, surveillance

- Di/di
- Mono/di
- Monoamniotic
when to deliver?

- **ACOG** – 38 weeks twins
  - **Creasy** –
    - di/di 38 weeks
    - Mono/di 37 weeks
    - Monoamniotic – 32-34 weeks (Creasy)
Reestimating date of delivery in multifetal pregnancies. AU Minakami H; Sato I SO JAMA 1996 May 8;275(18):1432-4. OBJECTIVE--To clarify the optimal estimated date of delivery for multifetal pregnancies. DESIGN, SUBJECTS, AND SETTING--A retrospective study of all 88,936 infants born of multifetal pregnancies and all 6,020,542 infants born of singleton pregnancies that occurred at 26 weeks or more of gestation between 1989 and 1993 in Japan. MAIN OUTCOME MEASURE--Incidence of stillbirth and early neonatal death according to gestational age at delivery. RESULTS--The mean +/- SD duration of pregnancy was 37.0 +/- 2.7 weeks for multifetal pregnancies and 39.6 +/- 1.6 weeks for singleton pregnancies. In multifetal pregnancies, the incidence of stillbirth and of early neonatal death gradually declined until 37 to 38 weeks' gestation and then increased. These parameters in singleton pregnancies declined until 39 weeks' gestation before increasing. The lowest incidence of perinatal death (Stillbirth plus early neonatal death) seen at 38 weeks' gestation in multifetal pregnancies corresponded to that seen at 43 weeks' gestation in singleton pregnancies (10.5 vs 9.7 per 1000 infants). The fist of perinatal death was more than 6 times as high for fetuses of multifetal pregnancies born at 37 weeks or later than for singleton fetuses born at 40 weeks or later (relative risk, 6.6; 95% confidence interval, 6.1 - 7.1). CONCLUSION--Fetuses of multifetal pregnancies are at an increased risk of death after reaching the normative gestational age for singleton pregnancies. Limiting the estimated date of delivery to 37 to 38 weeks may be appropriate in multifetal pregnancies. AD Department of Obstetrics and Gynecology, Jichi Medical School, Tochigi, Japan.
Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice. AU Kahn B; Lumey LH; Zybert PA; Lorenz JM; Cleary-Goldman J; D'Alton ME; Robinson JN SO Obstet Gynecol 2003 Oct;102(4):685-92. OBJECTIVE: To evaluate the prospective risk of fetal death in singleton, twin, and triplet pregnancies and to compare this risk with fetal and neonatal death rates. METHODS: We analyzed 11,061,599 singleton, 297,622 twin, and 15,375 triplet gestations drawn from the 1995-1998 National Center for Health Statistics linked birth and death files. Prospective risk of fetal death was expressed as a proportion of all fetuses still at risk at a given gestational age and compared with fetal death rate. Fetal death risk and neonatal death rates were represented graphically for singletons, twins, and triplets. RESULTS: The prospective risk of fetal death at 24 weeks was 0.28 per 1000, 0.92 per 1000, and 1.30 per 1000 for singletons, twins, and triplets, respectively. At 40 weeks, the corresponding risk was 0.57 per 1000 and 3.09 per 1000 for singletons and twins, respectively and, at 38 or more weeks, 13.18 per 1000 for triplets. Plots of gestation-specific prospective risk of fetal death and neonatal mortality converged for singletons and twins at term but crossed for triplets at approximately 36 weeks' gestation. CONCLUSION: Prospective risk of fetal death is greater for triplets and twins than for singletons and greater for triplets than for twins during the third trimester. The pattern corroborates with uteroplacental insufficiency as a suspected underlying mechanism. When prospective risk of fetal death exceeds neonatal mortality risk, delivery might be indicated. When this model is used, this data set suggests that it might be reasonable to consider delivery of twins by 39 weeks and triplets by 36 weeks to improve perinatal outcome. AD Department of Obstetrics and Gynecology, University of Colorado, Denver, Colorado, USA
METHODS: We analyzed 11,061,599 singleton, 297,622 twin, and 15,375 triplet gestations drawn from the 1995-1998 National Center for Health Statistics linked birth and death files.

Table 3. Fetal Death Rate and Prospective Risk of Fetal Death for Singletons

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>10,906</td>
<td>11,061,599</td>
<td>3101</td>
<td>284.34 (275.90, 292.93)</td>
<td>0.28 (0.27, 0.29)</td>
<td>414.86 (403.91, 425.90)</td>
</tr>
<tr>
<td>25</td>
<td>11,692</td>
<td>11,050,693</td>
<td>2544</td>
<td>217.58 (210.16, 225.20)</td>
<td>0.23 (0.22, 0.24)</td>
<td>248.47 (239.67, 257.48)</td>
</tr>
<tr>
<td>26</td>
<td>13,285</td>
<td>11,035,001</td>
<td>2288</td>
<td>172.22 (165.86, 178.78)</td>
<td>0.21 (0.20, 0.22)</td>
<td>167.77 (160.86, 174.92)</td>
</tr>
<tr>
<td>27</td>
<td>13,756</td>
<td>11,025,716</td>
<td>2008</td>
<td>145.97 (140.14, 152.01)</td>
<td>0.18 (0.17, 0.19)</td>
<td>110.32 (104.74, 116.15)</td>
</tr>
<tr>
<td>28</td>
<td>15,569</td>
<td>11,011,960</td>
<td>2015</td>
<td>129.42 (124.21, 134.82)</td>
<td>0.18 (0.18, 0.19)</td>
<td>84.11 (79.52, 88.94)</td>
</tr>
<tr>
<td>29</td>
<td>17,431</td>
<td>10,996,391</td>
<td>1804</td>
<td>103.49 (99.03, 108.13)</td>
<td>0.16 (0.16, 0.17)</td>
<td>59.06 (55.44, 62.90)</td>
</tr>
<tr>
<td>30</td>
<td>23,078</td>
<td>10,978,960</td>
<td>1936</td>
<td>83.89 (80.36, 87.56)</td>
<td>0.18 (0.18, 0.19)</td>
<td>42.38 (39.72, 45.20)</td>
</tr>
<tr>
<td>31</td>
<td>27,728</td>
<td>10,955,882</td>
<td>1792</td>
<td>64.63 (61.78, 67.60)</td>
<td>0.16 (0.16, 0.17)</td>
<td>30.54 (28.49, 32.72)</td>
</tr>
<tr>
<td>32</td>
<td>39,551</td>
<td>10,928,154</td>
<td>1972</td>
<td>49.86 (47.75, 52.06)</td>
<td>0.18 (0.17, 0.19)</td>
<td>19.61 (18.25, 21.08)</td>
</tr>
<tr>
<td>33</td>
<td>61,653</td>
<td>10,868,003</td>
<td>1972</td>
<td>31.99 (30.62, 33.41)</td>
<td>0.18 (0.17, 0.19)</td>
<td>13.35 (12.46, 14.32)</td>
</tr>
<tr>
<td>34</td>
<td>125,999</td>
<td>10,826,950</td>
<td>2340</td>
<td>18.57 (17.84, 19.34)</td>
<td>0.22 (0.21, 0.23)</td>
<td>8.39 (7.90, 8.92)</td>
</tr>
<tr>
<td>35</td>
<td>231,475</td>
<td>10,700,951</td>
<td>2462</td>
<td>10.64 (10.22, 11.06)</td>
<td>0.23 (0.22, 0.24)</td>
<td>5.02 (4.73, 5.32)</td>
</tr>
<tr>
<td>36</td>
<td>418,129</td>
<td>10,469,476</td>
<td>2709</td>
<td>6.48 (6.24, 6.73)</td>
<td>0.26 (0.25, 0.27)</td>
<td>3.39 (3.22, 3.57)</td>
</tr>
<tr>
<td>37</td>
<td>819,233</td>
<td>10,051,347</td>
<td>2856</td>
<td>3.49 (3.36, 3.62)</td>
<td>0.28 (0.27, 0.29)</td>
<td>2.08 (1.98, 2.18)</td>
</tr>
<tr>
<td>38</td>
<td>1,686,122</td>
<td>9,232,114</td>
<td>3247</td>
<td>1.93 (1.86, 1.99)</td>
<td>0.35 (0.34, 0.36)</td>
<td>1.26 (1.21, 1.31)</td>
</tr>
<tr>
<td>39</td>
<td>2,654,221</td>
<td>7,545,992</td>
<td>2986</td>
<td>1.13 (1.09, 1.17)</td>
<td>0.40 (0.38, 0.41)</td>
<td>0.92 (0.89, 0.96)</td>
</tr>
<tr>
<td>40</td>
<td>2,590,504</td>
<td>4,891,771</td>
<td>2795</td>
<td>1.08 (1.04, 1.12)</td>
<td>0.57 (0.55, 0.59)</td>
<td>0.85 (0.82, 0.89)</td>
</tr>
<tr>
<td>41</td>
<td>1,438,442</td>
<td>2,301,267</td>
<td>1480</td>
<td>1.03 (0.98, 1.08)</td>
<td>0.64 (0.61, 0.68)</td>
<td>0.93 (0.88, 0.98)</td>
</tr>
<tr>
<td>42</td>
<td>493,493</td>
<td>862,825</td>
<td>647</td>
<td>1.31 (1.21, 1.42)</td>
<td>0.75 (0.69, 0.81)</td>
<td>1.15 (1.06, 1.25)</td>
</tr>
<tr>
<td>43+</td>
<td>369,332</td>
<td>369,332</td>
<td>453</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.23 (1.12, 1.35)</td>
<td>1.12 (1.01, 1.23)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
* Calculated for births of 24 weeks gestation or more.
METHODS: We analyzed 11,061,599 singleton, 297,622 twin, and 15,375 triplet gestations drawn from the 1995-1998 National Center for Health Statistics linked birth and death files.

Table 4. Fetal Death Rate and Prospective Risk of Fetal Death for Twins

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>2097</td>
<td>297,622</td>
<td>274</td>
<td>130.66 (116.68, 146.02)</td>
<td>0.92 (0.82, 1.04)</td>
<td>461.88 (438.82, 495.09)</td>
</tr>
<tr>
<td>25</td>
<td>2358</td>
<td>295,525</td>
<td>282</td>
<td>119.59 (106.91, 133.53)</td>
<td>0.95 (0.85, 1.07)</td>
<td>284.20 (264.98, 304.23)</td>
</tr>
<tr>
<td>26</td>
<td>2757</td>
<td>293,167</td>
<td>206</td>
<td>74.72 (63.31, 85.33)</td>
<td>0.70 (0.61, 0.81)</td>
<td>172.48 (158.13, 187.83)</td>
</tr>
<tr>
<td>27</td>
<td>3117</td>
<td>290,410</td>
<td>175</td>
<td>56.14 (48.45, 64.96)</td>
<td>0.60 (0.52, 0.70)</td>
<td>109.11 (98.19, 121.07)</td>
</tr>
<tr>
<td>28</td>
<td>3547</td>
<td>287,293</td>
<td>193</td>
<td>54.41 (47.29, 62.52)</td>
<td>0.67 (0.58, 0.78)</td>
<td>72.45 (64.02, 81.88)</td>
</tr>
<tr>
<td>29</td>
<td>4220</td>
<td>283,746</td>
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<td>47.16 (41.05, 54.10)</td>
<td>0.70 (0.61, 0.81)</td>
<td>47.75 (41.46, 54.92)</td>
</tr>
<tr>
<td>30</td>
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<td>279,526</td>
<td>162</td>
<td>29.11 (24.92, 33.96)</td>
<td>0.58 (0.50, 0.68)</td>
<td>33.50 (28.94, 38.74)</td>
</tr>
<tr>
<td>31</td>
<td>7664</td>
<td>273,961</td>
<td>182</td>
<td>23.75 (20.51, 27.47)</td>
<td>0.66 (0.57, 0.77)</td>
<td>18.98 (16.06, 22.40)</td>
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<tr>
<td>32</td>
<td>10,619</td>
<td>266,297</td>
<td>187</td>
<td>17.61 (15.23, 20.34)</td>
<td>0.70 (0.61, 0.81)</td>
<td>13.13 (11.08, 15.56)</td>
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<tr>
<td>33</td>
<td>14,849</td>
<td>255,678</td>
<td>201</td>
<td>13.54 (11.77, 15.56)</td>
<td>0.79 (0.68, 0.90)</td>
<td>8.33 (6.95, 9.97)</td>
</tr>
<tr>
<td>34</td>
<td>23,262</td>
<td>240,829</td>
<td>220</td>
<td>9.46 (8.27, 10.81)</td>
<td>0.91 (0.80, 1.04)</td>
<td>5.82 (4.89, 6.91)</td>
</tr>
<tr>
<td>35</td>
<td>33,287</td>
<td>217,567</td>
<td>212</td>
<td>6.37 (5.56, 7.30)</td>
<td>0.97 (0.85, 1.12)</td>
<td>3.30 (2.72, 3.99)</td>
</tr>
<tr>
<td>36</td>
<td>45,405</td>
<td>184,280</td>
<td>205</td>
<td>4.51 (3.93, 5.19)</td>
<td>1.11 (0.97, 1.28)</td>
<td>2.88 (2.41, 3.43)</td>
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<tr>
<td>37</td>
<td>49,436</td>
<td>138,875</td>
<td>197</td>
<td>3.98 (3.46, 4.59)</td>
<td>1.42 (1.23, 1.63)</td>
<td>2.29 (1.90, 2.77)</td>
</tr>
<tr>
<td>38</td>
<td>41,859</td>
<td>89,439</td>
<td>136</td>
<td>3.25 (2.74, 3.85)</td>
<td>1.52 (1.28, 1.80)</td>
<td>2.06 (1.66, 2.56)</td>
</tr>
<tr>
<td>39</td>
<td>24,957</td>
<td>47,580</td>
<td>114</td>
<td>4.57 (3.79, 5.51)</td>
<td>2.40 (1.99, 2.89)</td>
<td>2.05 (1.54, 2.72)</td>
</tr>
<tr>
<td>40</td>
<td>11,895</td>
<td>22,623</td>
<td>70</td>
<td>5.88 (4.62, 7.47)</td>
<td>3.09 (2.43, 3.93)</td>
<td>3.30 (2.38, 4.55)</td>
</tr>
<tr>
<td>41+</td>
<td>10,728</td>
<td>10,728</td>
<td>54</td>
<td>5.03 (3.82, 6.61)</td>
<td>5.03 (3.82, 6.61)</td>
<td>4.22 (3.11, 5.69)</td>
</tr>
</tbody>
</table>

CI = confidence interval.

* Calculated for births of 24 weeks gestation or more.

greater than for twins. In our data set, the prospective risk of fetal death for twins equaled the prospective risk of fetal death for postterm singletons by approximately 36 to 37 weeks' gestation. The upswing in fetal death risk increases in the third trimester for twins and even more so for triplets.

We think it is more useful clinically to compare gestation-specific prospective risk of fetal death with gestation-specific perinatal survival.
rates. METHODS: We analyzed 11,061,599 singleton, 297,622 twin, and 15,375 triplet gestations drawn from the 1995-1998 National Center for Health Statistics linked birth and death files.

Table 5. Fetal Death Rate and Prospective Risk of Fetal Death for Triples

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Deliveries</th>
<th>Fetuses at risk*</th>
<th>Fetal deaths</th>
<th>Fetal death rate (per 1000 deliveries) (95% CI)</th>
<th>Prospective risk of fetal death (per 1000 fetuses at risk) (95% CI)</th>
<th>Neonatal death rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>236</td>
<td>15,375</td>
<td>20</td>
<td>84.75 (53.83, 129.73)</td>
<td>1.30 (0.82, 2.05)</td>
<td>509.26 (440.73, 577.45)</td>
</tr>
<tr>
<td>25</td>
<td>280</td>
<td>15,139</td>
<td>13</td>
<td>46.43 (26.00, 79.99)</td>
<td>0.86 (0.48, 1.51)</td>
<td>247.19 (197.56, 304.25)</td>
</tr>
<tr>
<td>26</td>
<td>327</td>
<td>14,859</td>
<td>13</td>
<td>39.76 (22.24, 68.70)</td>
<td>0.87 (0.49, 1.54)</td>
<td>130.57 (96.34, 174.11)</td>
</tr>
<tr>
<td>27</td>
<td>485</td>
<td>14,532</td>
<td>15</td>
<td>30.93 (18.05, 51.66)</td>
<td>1.03 (0.60, 1.75)</td>
<td>104.26 (78.83, 136.34)</td>
</tr>
<tr>
<td>28</td>
<td>697</td>
<td>14,047</td>
<td>17</td>
<td>24.39 (14.73, 39.58)</td>
<td>1.21 (0.73, 1.98)</td>
<td>39.71 (26.83, 58.01)</td>
</tr>
<tr>
<td>29</td>
<td>648</td>
<td>13,350</td>
<td>17</td>
<td>20.06 (11.19, 34.98)</td>
<td>0.97 (0.54, 1.71)</td>
<td>26.77 (16.17, 43.41)</td>
</tr>
<tr>
<td>30</td>
<td>970</td>
<td>12,702</td>
<td>13</td>
<td>11.34 (5.97, 20.85)</td>
<td>0.87 (0.46, 1.60)</td>
<td>14.60 (8.33, 25.0)</td>
</tr>
<tr>
<td>31</td>
<td>1345</td>
<td>11,732</td>
<td>22</td>
<td>16.36 (10.53, 25.09)</td>
<td>1.88 (1.20, 2.89)</td>
<td>9.83 (5.47, 17.21)</td>
</tr>
<tr>
<td>32</td>
<td>1602</td>
<td>10,387</td>
<td>17</td>
<td>10.61 (6.40, 17.31)</td>
<td>1.64 (0.99, 2.68)</td>
<td>5.68 (2.77, 11.17)</td>
</tr>
<tr>
<td>33</td>
<td>2022</td>
<td>8785</td>
<td>9</td>
<td>4.45 (2.17, 8.76)</td>
<td>1.02 (0.50, 2.02)</td>
<td>5.96 (3.23, 10.71)</td>
</tr>
<tr>
<td>34</td>
<td>2342</td>
<td>6763</td>
<td>13</td>
<td>5.55 (3.09, 9.74)</td>
<td>1.92 (1.07, 3.38)</td>
<td>4.29 (2.18, 8.16)</td>
</tr>
<tr>
<td>35</td>
<td>1987</td>
<td>4421</td>
<td>18</td>
<td>9.06 (5.54, 14.58)</td>
<td>4.07 (2.49, 6.57)</td>
<td>4.57 (2.23, 9.00)</td>
</tr>
<tr>
<td>36</td>
<td>1249</td>
<td>2434</td>
<td>12</td>
<td>9.61 (5.21, 17.22)</td>
<td>4.93 (2.67, 8.86)</td>
<td>1.62 (0.28, 6.50)</td>
</tr>
<tr>
<td>37</td>
<td>502</td>
<td>1185</td>
<td>9</td>
<td>17.93 (8.77, 35.00)</td>
<td>7.59 (3.71, 14.92)</td>
<td>4.06 (0.70, 16.22)</td>
</tr>
<tr>
<td>38+</td>
<td>683</td>
<td>663</td>
<td>9</td>
<td>13.18 (6.44, 25.80)</td>
<td>13.18 (6.44, 25.80)</td>
<td>2.97 (0.51, 11.89)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
* Calculated for births of 24 weeks gestation or more.
Twin-twin transfusion syndrome

Farley

Uptodate; Creasy
• Incidence

• 5-15% in monochorionic-diamniotic twin preg

• Possible in monoamniotic or dichorionic diamniotic twins, but rare

• Diagnosis

• Suspicion of monochorionic-diamniotic twin pregnancy

• Polyhydramnios (>8cm) - recipient; oligohydramnios (<2cm) - donor
TWIN-TWIN TRANSFUSION SYNDROME —

Twin-twin transfusion syndrome (TTTS) occurs in 10 to 15 percent of MC twin pregnancies and 6 percent of monoamniotic twin pregnancies [122]. The diagnosis is primarily based upon ultrasonographic evidence of a single MC placenta with polyhydramnios/oligohydramnios sequence due to uncompensated vascular anastomoses in the placenta [44,68]. Intertwin differences in growth may present as early as the first trimester [123]. The prognosis for untreated
• Etiology
• -TYPE OF ANASTOMOSIS
• A-V anastomosis: unidirectional flow; intravillous (placental surface single unpaired artery carrying blood from donor twin to placental cotyledon together with single unpaired vein carrying blood from that cotyledon back to the recipient twin)
• A-A, V-V anastomosis: superficially located on chorionic plate, allow bidirectional flow, ‘saving type’ of anastomosis
• Less A-A and V-V anastomoses increases probability of A-V anastomoses leading to TTTS
• -Discordant placental size or sharing of placenta
• Classification (no good system for prediction of progression or prognosis)
• Quintero staging system (?good for monitoring disease progression, not predicting outcomes or determining which pregnancies will progress)
  • Stage I — + Poly/oligo (POS); + bladder in donor
  • Stage II — +POS; NO bladder seen in donor; normal Dopplers
  • Stage III — +POS; NO bladder seen in donor; abnormal Doppler (absent, REDV in donor umbilical artery; reversed ductus venous/s flow; pulsatile umbilical vein venous flow in recipient
  • Stage IV — +POS, hydrops in either twin
  • Stage V — Fetal demise of either or both twins
• Staging system based on presence of A-A anastamoses (Jain et al)
  – -antenatal identification of A-A anastomosis, which is "protective" against TTTS
• Natural history (progression 45%, stabilization 37%, regression in lower stages 18%)
• Treatment (prolonged neural outcomes not known in treatments, limits counseling patients)
• Amnioreduction (decrease pressure leading to less uterine distension, allows better placental blood flow, may help with maternal symptoms)
• Survival based on serial amnioreductions (2001 registry); (223 sets of twins; TTTS <28 wks) follow-up data until 4 weeks old; major findings included:
  • 78% born alive
  • 60% alive 4 weeks after birth
  • abnormal neonatal cranial scan in ~25% recipients and donors
  • better survival related to older gestational age, no Doppler abnormalities or hydrops, removal of less fluid, higher birthwt
• Amnioreduction - may be appropriate if significant fluid discordance; more widely available; lower complication rate
• Laser coagulation (obliterate visible A-V anastomoses); amnioreduction done at end of surgery to buffer increases until the coagulation can take effect
• appears to be an appropriate therapy in cases of significant discordance or when there is fetal myocardial dysfunction
• Eurofetus RCT (laser vs serial amnioreduction); interim analysis halted study as it showed better outcomes in the laser arm
• overall perinatal survival (57 versus 41 percent),
• survival of at least one twin to age 28 days (76 versus 56 percent)
• survival without major neurologic morbidity at six months (52 versus 31 percent of the initial cohorts)
• Septostomy of amniotic membrane (does not address underlying pathophysiology); only big study limited by crossover of septostomy patients to amnioreduction arm

• Selective termination (difficult to tell which twin would be ultimately more severely affected)

• Medical – digoxin, prostaglandin synthase inhibitors (limited use)
• Morbidity/Mortality
• profound anemia, placental insufficiency of donor
• heart failure from circulatory overload in recipient
• PTL (hydramnios) complications of prematurity
• lethal congenital anomalies associated with monozygosity
• Survival depends on gestational age and severity at time of diagnosis (before 1990, 80-100% mortality)
• Death of one twin corresponds to 30-50% risk of mortality/neurologic damage to survivor
• Survival based on laser coagulation of A-V anastomoses
Neurodevelopmental outcome at 2 years in children born preterm treated by amnioreduction or fetoscopic laser surgery for twin-to-twin transfusion syndrome: comparison with dichorionic twins

Richard Lenclen, MD; Giuseppina Ciarlo, MD; Alain Paupe, MD; Laurence Bussieres, MD; Yves Ville, MD

OBJECTIVE: We sought to assess long-term neurodevelopment of children born prematurely treated for twin-to-twin transfusion syndrome and dichorionic (DC) twins.

STUDY DESIGN: In all, 21 and 88 children treated with amnioreduction (AR) and fetoscopic laser surgery (FLS), respectively, and 222 DC twins matched for gestational age at delivery were assessed with Ages and Stages Questionnaire and standardized examination at 2 years of age.

RESULTS: Normal development was noted in 81% in the AR group, 88.6% in the FLS group, and 93.1% in the DC twins. Minor and major neurologic impairment was found in 9.5% and 9.5% following AR, in 6.8% and 4.6% of FLS children, and in 3.4% and 3.4% in DC twins, respectively. Ages and Stages Questionnaire assessment was similar in FLS and DC children but scores were lower ($P = .01$) and domains were more often abnormal (60% vs 27%; $P = .005$) following AR.

CONCLUSION: Neurodevelopmental outcome is similar in twin-to-twin transfusion syndrome survivors treated by FLS and in DC control subjects; but survivors treated with AR have an increased risk of neurodevelopmental delay at 2 years of age.

Key words: dichorionicity, laser surgery, monochorionicity, neurodevelopmental, outcome, twin-to-twin transfusion syndrome

Twin to twin transfusion syndrome (TTTS)

- Incidence
  - 15% in monochorionic-diamniotic twin pregnancies
- Diagnosis
  - Monochorionic-diamniotic pregnancy (same sex, thin membrane, no twin peak, 1 placenta)
  - Polyhydramnios (>8cm) - recipient; oligohydramnios (<2cm) - donor
- Etiology
  - TYPE OF ANASTOMOSIS, not necessarily number; discordant placental sharing
  - A-V: unidirectional flow; intravillous (placental surface single unpaired artery carrying blood from donor twin to placental cotyledon together with single unpaired vein carrying blood from that cotyledon back to the recipient twin)
  - A-A, V-V: superficial on chorionic plate; bidirectional flow; “protective”
  - Less A-A, V-V anastomoses increases probability of A-V anastomoses leading to TTTS
TTTS

- Classification (no good system for prediction of progression or prognosis)
- Quintero staging system (?good for monitoring disease progression, not predicting outcomes)
- Stage I:  + Poly/oligo (POS) ; +bladder in donor
- Stage II:  +POS; NO bladder seen in donor; normal Dopplers
- Stage III:  +POS; NO bladder seen in donor; abnormal Dopplers
- Stage IV:  + POS, hydrops in either twin
- Stage V:  Fetal demise of either or both twins
- Staging system based on presence of A-A anastamoses (Jain et al); not widely used
ttts

- Natural history (progression 45%, stabilization 37%, regression in lower stages 18%)
- Treatment (long term neurologic outcomes not known in treatments, limits counseling patients)
- Amnioreduction (decrease pressure leading to less uterine distension, allows better placental blood flow, may help with maternal symptoms)
- Survival based on serial amnioreductions (2001 registry); (223 sets of twins; TTTS <28 wks) follow-up data until 4 weeks old; major findings included:
  - 78% born alive
  - 60% alive 4 weeks after birth
  - abnormal neonatal cranial scan in ~25% recipients and donors
  - better survival related to older gestational age, no Doppler abnormalities or hydrops, removal of less fluid, higher birthwt
- Amnioreduction may be appropriate if significant fluid discordance; more widely available; lower complication rates; better for less severe disease?
- Laser coagulation to obliterate visible A-V anastomoses; amnioreduction done at end of surgery to buffer increases until the coagulation can take effect; YAG laser used
- Eurofetus RCT (laser vs serial amnioreduction); study halted(better outcomes in laser arm)
  - overall perinatal survival (57 versus 41 percent),
  - survival of at least one twin to age 28 days (76 versus 56 percent)
  - survival without major neurologic morbidity at six months (52 versus 31 percent of the initial cohorts); US study ongoing
- Septostomy of amniotic membrane (does not address underlying pathophysiology); only big study limited by crossover of septostomy patients to amnioreduction arm; may help in mild disease to decrease frequency of amnioreductions
- Selective termination (difficult to tell which twin would be ultimately more severely affected)
- Medical – digoxin, prostaglandin synthase inhibitors (limited use)
ttts

- Morbidity/Mortality
- profound anemia, placental insufficiency of donor
- heart failure from circulatory overload in recipient
- PTL (hydramnios) complications of prematurity
- lethal congenital anomalies associated with monozygosity twinning
- Survival depends on gestational age and severity at time of diagnosis (before 1990, 80-100% mortality)
• References:

• Creasy R, Resnik R.  Maternal-Fetal Medicine Principles and Practice. 5th Edition

• Uptodate.com online source.
Risks during the pregnancy

• Preterm birth
Prediction of preterm birth before 32 weeks of gestation in twins by sonographically determined cervical length

<table>
<thead>
<tr>
<th>Cut-off for cervical length (mm)</th>
<th>Sensitivity (percent)</th>
<th>Specificity (percent)</th>
<th>PPV (percent)</th>
<th>NPV (percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assessment at 21 to 24 weeks of gestation</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td><strong>Assessment at 25 to 28 weeks of gestation</strong></td>
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<td>63 to 100</td>
<td>70 to 84</td>
<td>13 to 18</td>
<td>96 to 100</td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.

Data adapted from: