PART 1

Obstetrics

CHAPTER 1

Multiple Gestations

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OVERALL BOTTOM LINE

- The incidence of twin gestation has risen due to advancing maternal age and the use of assisted reproductive techniques (ART).
- There are increased risks of a twin gestation, including preterm labor, preterm delivery, low birth weight, fetal growth restriction, gestational diabetes, preeclampsia, and need for cesarean delivery.
- Twin gestations require increased surveillance due to these increased risks.

Background

Definition of disease

- Twin gestation refers to an intrauterine gestation of two fetuses.

Disease classification

- Dizygotic twins occur after ovulation and fertilization of two different oocytes. This type of twins has two placentas and two amniotic sacs (Figure 1.1).
- Monozygotic twins result from ovulation and fertilization of one single oocyte, with subsequent division. Depending on what day the embryo splits, these monozygotic twins are further classified as the following:
  - Dichorionic/diamniotic (Day 1–3)
  - Monochorionic/diamniotic (Day 4–8) (Figure 1.2)
  - Monochorionic/monoamniotic (Day 8–13)
  - Conjoined twins (Day 13–15)

Incidence/prevalence

- The natural incidence of twins is 1/80.
- The incidence of multiple gestation increased by 76% from 1980 to 2009 due to ART and has since stabilized.
- Twins now account for 3% of live births.

Economic impact

- Twin gestations are associated with higher cost, which is mostly related to the increased rate of preterm delivery. The cost of a premature infant is up to 10 times greater than that of a term infant in the first year.

Mount Sinai Expert Guides: Obstetrics and Gynecology, First Edition. Edited by Rhoda Sperling.

Companion Website: www.wiley.com/go/sperling/mountsinai/obstetricsandgynecology

Predictive/risk factors

Risk factor	Contribution
Assisted reproductive technology	Accounts for 1/3 of all twin pregnancies
Maternal age	Fourfold increase from age 15 to age 35
Family history	Increased risk of dizygotic twins

Prevention

BOTTOM LINE/CLINICAL PEARLS

- The incidence of twin gestation has stabilized over time as the number of embryos transferred with ART has decreased. Single embryo transfer has become an increasingly common practice.

Screening

- Ultrasound in the first or early second trimester is essential in diagnosing twin gestation and establishing chorionicity (Figures 1.1 and 1.2).

Primary prevention

- Single embryo transfer to decrease the number of twin gestations that result from in vitro fertilization is an important prevention method. Splitting of an embryo into a monozygotic twin gestation, whether spontaneous or after ART, is not preventable.

Secondary prevention

- After a twin gestation is diagnosed, a multifetal pregnancy reduction procedure can be performed, resulting in a single fetus and improved pregnancy outcomes.
- Multifetal pregnancy reduction to a singleton gestation is associated with higher birth weights and lower rates of preterm deliveries.

Diagnosis

BOTTOM LINE/CLINICAL PEARLS

- The diagnosis of twins is made with ultrasound.
- This ultrasound should be done in the first or early second trimester in order to most accurately establish chorionicity, which has important implications for the pregnancy.

Typical presentation

- Twin gestation may be suspected if uterine size measures larger than would be expected for a given gestational age.
- Diagnosis can be confirmed only with ultrasound.

Clinical diagnosis

History

- Age
- Family history of twin gestation
- Use of ART

Physical examination

- Clinical examination of uterine size with bimanual exam and measurement of fundal height

Laboratory diagnosis

List of diagnostic tests

- The risk of aneuploidy is higher in dizygotic twins. The mathematical probability that a single fetus is affected is doubled in a twin gestation.
  - The chance that a 33-year-old with twins has one fetus with Down syndrome is equivalent to the chance that a 35-year-old has a singleton fetus with Down syndrome.
- All pregnant patients are counseled on options for genetic screening (serum screening such as sequential or quad screen) or diagnostic testing (chorionic villus sampling or amniocentesis).
- Even in a singleton pregnancy, serum screening is never diagnostic, but this screening is even further limited in twin gestations.
  - Analyte levels in maternal serum for twins are estimated using mathematical models.
  - Analyte levels in maternal serum from each fetus are averaged together, possibly normalizing the levels and masking an affected fetus.
  - First trimester serum screening combined with nuchal translucency measurements identifies 75–85% of pregnancies with Down syndrome and 66% of pregnancies with trisomy 18 in twins.
  - Second trimester serum screening identifies 63% of pregnancies with Down syndrome in twins.
- Noninvasive prenatal screening (NIPS), which analyzes cell-free fetal DNA in maternal serum, is not recommended for multiple gestations.
- Invasive testing with chorionic villus sampling (CVS) or amniocentesis remain the only two options for diagnostic testing.
  - CVS samples the chorionic villi and may be performed as early at 9 weeks.
    - CVS may be more technically challenging in a twin gestation. There is an approximately 1% rate of sampling error, meaning that one fetus was sampled twice.
  - Amniocentesis is performed by sampling the amniotic fluid and is done after 15 weeks.
    - To avoid sampling error, once a needle is inserted into the first amniotic sac, indigo carmine is injected into this sac, which results in blue colored fluid. This needle is then removed and a second needle inserted into the second sac. If the fluid is clear, it is confirmed that the second sac has been entered. If the fluid is blue, this indicates that the same sac has just been entered a second time.
    - There is approximately a 1.8% pregnancy loss rate prior to 24 weeks after amniocentesis in twins.

List of imaging techniques

- Ultrasound is the primary imaging modality used in the surveillance of all pregnancies, including twin gestation.

Potential pitfalls/common errors made regarding diagnosis of disease

- Ultrasound should be performed in the first or early second trimester for the most accurate determination of chorionicity. It is essential that chorionicity is accurately established, as monochorionic twins and dichorionic twins are at risk for different complications and need to be monitored and managed differently.

Treatment

Treatment rationale

- There have been several interventions that have been studied in an attempt to decrease the rate of preterm delivery in twins that have not found to be beneficial:
  - Prophylactic cerclage: not beneficial, not recommended
  - Cerclage for short cervix: not only not beneficial but actually DOUBLES the rate of spontaneous preterm delivery and is therefore not recommended

- Bed rest: not beneficial, not recommended
- Prophylactic tocolytics: not beneficial, not recommended
- Prophylactic pessary: not beneficial, not recommended
- Prophylactic use of progesterone: not beneficial, not recommended

- Twin pregnancies require increased surveillance to detect signs of preterm labor. There are several beneficial interventions if a patient is found to be in preterm labor that are discussed in the following sections.

When to hospitalize

- There are several indications for hospitalization of twins:
  - Preterm labor, advanced cervical exam, preeclampsia/gestational hypertension, bleeding, fetal growth restriction
  - Twins are at higher risk for all of the aforementioned complications, but once they are diagnosed, they are often managed similarly to the way singletons are managed.

Managing the hospitalized patient

- Management of preterm labor in twin gestation:
  - Tocolytics: Data are limited in twin gestations, though a 48-hour course to enable the administration of corticosteroids seem to be beneficial in twins as well. First-line agents include calcium channel blockers and nonsteroidal anti-inflammatory agents (indomethacin).
  - Corticosteroids: Administration of steroids between 24 and 34 weeks has been shown to decrease the incidence of neonatal death, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis in singleton gestations. Based on this evidence, the National Institutes of Health recommends that they should be administered in multiple gestations as well.
  - Magnesium sulfate: Administration has been shown to reduce the incidence of cerebral palsy when given prior to delivery when it is occurs less than 32 weeks.

Table of treatment

Treatment	Comments
Medical	When a patient with twins is admitted for preterm labor, administration of corticosteroids (if between 24–34 weeks), tocolytics (if between 24–34 weeks), and magnesium sulfate prior to delivery (if less than 32 weeks) is recommended.
Surgical	Cerclage is not recommended in twin gestations, as it leads to worse outcomes. There is a higher rate of cesarean delivery in twin gestations, although vaginal delivery is possible if the presenting fetus (typically fetus A) is in cephalic presentation.
Radiological	The use of ultrasound is essential to the management of twin gestation. Early ultrasound to establish chorionicity, then second trimester anatomic survey, and then serial growth ultrasounds to look for growth restriction or twin to twin transfusion syndrome are employed.
Psychological (includes cognitive, behavioral, etc., therapies)	Mothers who give birth to twins are at increased risk of postpartum depression; therefore, it is important to administer a depression scale at their postpartum visit and treat as necessary.

Prevention/management of complications

- Prevention is aimed at early identification of complications for which twins are at risk.
  - Preterm delivery: cervical length screening to identify patients at risk for preterm delivery is reasonable in order to optimize outcomes with steroids and magnesium sulfate if preterm delivery is imminent.

- Preeclampsia: blood pressure should be taken at each visit and patients counseled on signs and symptoms of preeclampsia.
- Gestational diabetes: all patients should be screened for gestational diabetes and early screen should be considered in patients with risk factors.
- Twin to twin transfusion syndrome: this complication is unique to monochorionic twins. Screening for this is with ultrasound that is performed every 2 weeks starting at 16 weeks in monochorionic gestations.
- Growth discordance/restriction: all twin gestations should be followed with serial growth ultrasounds to detect differences in weight or selective growth restriction.

CLINICAL PEARLS

- Chorionicity is best established in the first or early second trimester.
- Twin gestations are at an increased risk for spontaneous abortion, genetic abnormalities, growth restriction, preeclampsia, gestational diabetes, and cesarean delivery and patients should be counseled accordingly.
- Multifetal pregnancy reduction has been shown to improve outcomes and may be offered to patients with multiple gestation.

Prognosis

BOTTOM LINE/CLINICAL PEARLS

- Twins are at increased risk for preterm delivery and the neonatal complications that accompany it. Twin gestations delivery earlier on average, even with treatment of preterm labor.
- The following table compares delivery timing and infant morbidity in singleton versus twin gestation.

Outcomes in singleton versus twin gestations

	Singletons	Twins
Mean gestational age at delivery	38.7 weeks	35.3 weeks
Mean birth weight	3296 g	2336 g
Percentage who deliver <32 weeks	1.6	11.4
Percentage who deliver <37 weeks	10.4	58.8
Rate of cerebral palsy (per 1000 live births)	1.6	7

Reading list

American College of Obstetricians and Gynecologists. Multifetal gestations: twin, triplet and higher-order multifetal pregnancies. Practice bulletin no. 169. *Obstet Gynecol* 2016;e131-46.

Society for Maternal Fetal Medicine Publications Committee. Prenatal aneuploidy screening using cell-free DNA. Consult series no. 36. *Am J Obstet Gynecol* 2015;212:711-6.

Stone J, Ferrara L, Kamrath J, et al. Contemporary outcomes with the latest 1000 cases of multifetal pregnancy reduction (MPR). *Am J Obstet Gynecol* 2008 Oct;199(4):408.e1-4. doi: 10.1016/j.ajog.2008.05.020

Suggested websites

American College of Obstetricians and Gynecologists. www.acog.org
Society for Maternal-Fetal Medicine. www.smfm.org

Guidelines

National society guidelines

Title	Source	Date/full reference
Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies	American College of Obstetricians and Gynecologists	American College of Obstetricians and Gynecologists. Multifetal gestations: twin, triplet and higher-order multifetal pregnancies. Practice bulletin no. 169. *Obstet Gynecol* 2016;e131-46.

Images

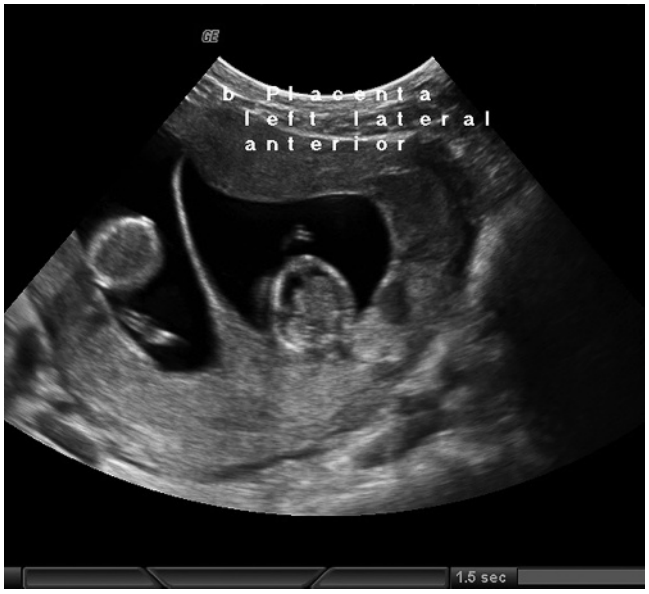

Figure 1.1 "Twin peak" or Lambda sign characteristic of a dichorionic diamniotic gestation. This sonographic sign is used to help establish chorionicity. Another sonographic feature of a dichorionic diamniotic gestation is two placentas. If the fetal sex is discordant, the pregnancy is dichorionic.

Figure 1.2 "T sign" characteristic of monochorionic diamniotic gestation. This sonographic feature is 100% sensitive and >98% specific for the diagnosis of monochorionic gestation.

Additional material for this chapter can be found online at:
www.wiley.com/go/sperling/mountsinai/obstetricsandgynecology

This includes multiple choice questions, advice for patients, and ICD codes.