



Reviewed By
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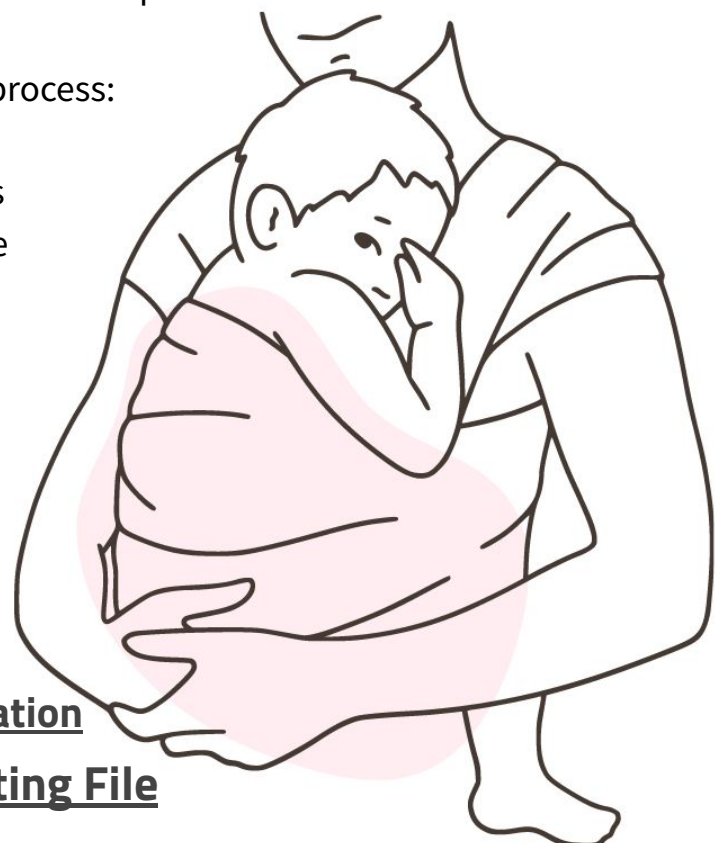


Video Case

Multiple Pregnancy

Objectives:

- List the risk factors for multiple pregnancy.
- Identify the incidence of multiple pregnancy.
- Describe the classification of twinning (dizygotic and monozygotic) and relation between timing of cleavage and the nature of the membranes in twin gestations.
- Describe how to diagnose multiple pregnancy.
- Mention delivery options for multiple pregnancy.
- List the potential maternal and fetal risks of multiple pregnancies
- Describe the abnormalities of twinning process:
 - a. Conjoined twins
 - b. Placental vascular anastomoses
 - c. Twin-twin transfusion syndrome
 - d. Fetal malformations



- Slides
- **Important**
- **Golden notes**
- Extra
- **439 Doctor's notes**
- **441 Doctor's notes**
- **441 Female Presentation**
- **Reference**

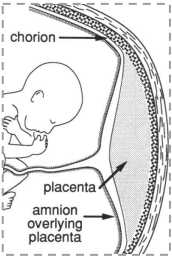
Female presentation

Video Case | Editing File

Multiple Gestation

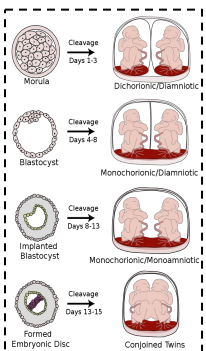
- Multiple gestations are defined as any pregnancy in which two or more embryos or fetuses occupy the uterus simultaneously.
- Since 1980, there has been a 70% increase in the frequency of twins, and a 400% increase in triplet and higher order birth.
 - Twins account for around 3.5% of all births in the United States, approximately $\frac{2}{3}$ of **spontaneously conceived twins are fraternal** and $\frac{1}{3}$ are identical (monozygotic).
 - The frequency of **monozygotic** twinning, which **depends on** a very infrequent biologic event (**embryo splitting**), is constant in all populations studied at about 1 in 250 births.
 - The frequency of **dizygotic** twinning, which **arises from multiple ovulations in the mother**. It rates are markedly different in various populations

Types :

	<u>Monozygotic / Identical Twins</u>	<u>Dizygotic / Fraternal Twins (non identical)</u>	
Definition	It result when a single fertilized ovum divides after conception. (one zygote)	It result when 2 separate ovums in a single menstrual cycle fertilized by 2 separate sperms (two zygotes)	
Chorionicity & Amnionicity 	Chorionicity & amnionicity will depend on the time at which the embryo divides The earlier the embryo splits, the more separate the membranes and placentas will be , If division / cleavage occur within:		
	9-12 days after fertilization	4-8 days after fertilization	First 3 days after fertilization
	Monochorionic & Monoamniotic : 1 placenta + 1 sac	Monochorionic & Diamniotic : 1 placenta + 2 sac	Dichorionic & Diamniotic : 2 placenta + 2 sac
	This is the rarest one , and highest risk bc risk of umbilical cord entanglement resulting in a net mortality 50%	It is the most common in monozygotic twins	This is the lowest risk

In Monozygotic twins :

- If division occurs **within 4-8 days** when the chorion has already formed, the result will be **monozygotic, diamniotic twins**.
- If division occurs **after 8 days**, when both amnion and chorion have already formed, the result will be **monozygotic, monoamniotic twins**.
 - If division occurs **after 12 days**, after the embryonic disc has completely formed, **cleavage of the embryo will be incomplete**, resulting in **conjoined twins**.





Risk Factors

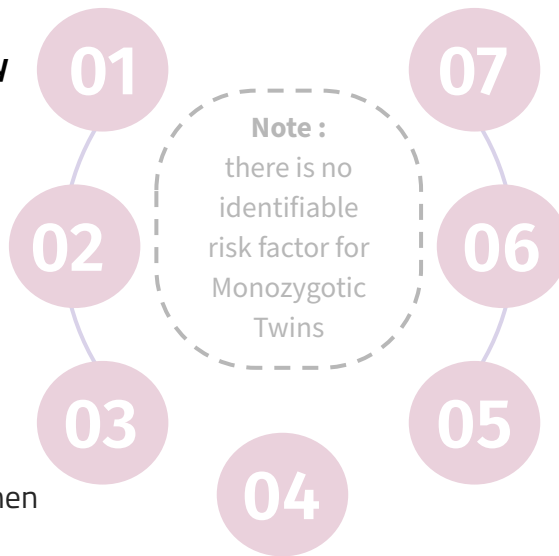
History of assisted technology

Ovulation induction agent / Use of fertility drugs ex:

- Clomiphene Citrate
- Menopausal Gonadotropin

Increased maternal age :

Twins are twice as common in women over 35 as in women at 25 years of age.



“IVF” has a 30% risk

Race (higher among Africans)

Family history of twins

Multiparous



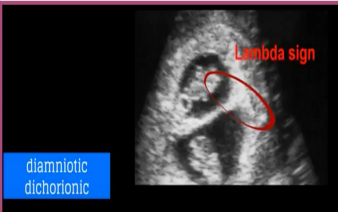
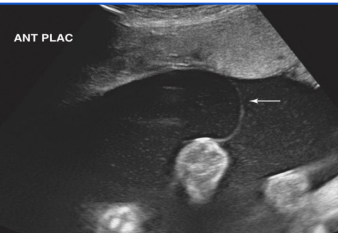
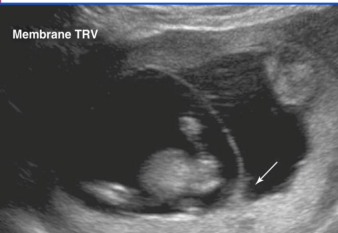


Diagnosis

By Early **Ultrasound** (as early as **6 weeks**) can determine :

- **Estimate the gestational age**
- **The number of fetuses**
- **Determine the zygosity, US may helpful** for example :
 - Imaging of discordant fetal gender confirms a dizygotic gestation, or Monochorionic placentas confirms monozygotic. However, **The definitive Dx of zygosity** may require **detailed examination of placenta after delivery**, HLA typing, and **DNA analysis**.
 - **Determining zygosity is the most important after determine fetuses number** because the prognosis and expected morbidity with twins is strongly dependent on zygosity.
- **Determine the chorionicity**
 - Chorionicity should be determined as early in the pregnancy as possible optimally in the late first or early second trimester **because it will be difficult to assess the chorio and which type is it later.**

Note : Identical twins share the same genomes and are always of the same sex.

		
No membrane between fetus	Thin 2 layers membrane between fetus	Thick 4 layers membrane between fetus (lambda sign)
		

MONOCHORIONIC TWIN PLACENTATION	DICHORIONIC TWIN PLACENTATION
<ul style="list-style-type: none"> Monoamniotic Monochorionic (conjoined twins, with one cord) Monoamniotic Monochorionic (torked cord) Monoamniotic Monochorionic Diamniotic Monochorionic 	<ul style="list-style-type: none"> Diamniotic Dichorionic (fused) Diamniotic Dichorionic (separated)

● Suggestive but not diagnostic :

- Historical factor
- Excessive weight gain
- excessive uterine fundal growth
- High levels of β - hCG and Maternal serum α -fetoprotein.
- Fetal heart auscultation in more than one quadrant.

Risk associated with Twins

Complication:

Multiple pregnancy will increase risk for :

- **Hyperemesis gravidarum** : severe nausea and vomiting during pregnancy
- **Anemia** due to :
 - increase demand for iron and folate
 - increase blood volume
 - increased risk for blood loss at delivery
- **Gestational diabetes**
- **Pregnancy induced HTN** : gestational HTN, pre-eclampsia and eclampsia
- **Compromised renal function** due to compression of the ureters.
- **Maternal respiratory embarrassment and orthostatic hypotension** due to compression of the vena cava,
- **Placenta abruption**
- **IUGR**
- **Congenital abnormalities and fetal malformation .**
- **Preterm labor / prematurity :**
 - Twins are delivered an average of 35 weeks
 - Triplets an average of 32 weeks
 - Quadruplets an average of 30 weeks
- **Postpartum depression**

BOX 13-1

COMPLICATIONS OF MULTIPLE GESTATIONS

Maternal

Anemia
Hydramnios
Hypertension
Premature labor
Postpartum uterine atony
Postpartum hemorrhage
Preeclampsia
Cesarean delivery

Fetal

Malpresentation
Placenta previa
Abruptio placentae
Premature rupture of the membranes
Prematurity
Umbilical cord prolapse
Intrauterine growth restriction
Congenital anomalies
Increased perinatal morbidity
Increased perinatal mortality

MoMo twins are an increased risk of cord entanglement and fetal death since the 2 fetuses are sharing the same space within the same amniotic sac without an intervening membrane



Or



Retained dead fetus syndrome:

One of the twin die and the other still viable.

- Fetus death <12 weeks will be reabsorbed.
- Fetus death >12 weeks will be shrink, dehydrated and flattened "Fetus papyraceus"
 - Over time (after 3 weeks or more in pregnancies that have progressed beyond 20 weeks), The retained dead fetus syndrome can develop, which involves disseminated intravascular coagulopathy in the mother as a result of the transfer of nonviable fetal material with thromboplastin-like activity into the maternal circulation. So check platelet & fibrinogen weekly in such case.

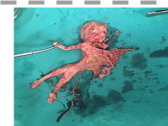


Fig.1: Fetus papyraceus.

ABNORMALITIES OF THE TWINNING PROCESS :

Among **monozygotic multiple gestations**, abnormalities in the twinning process are relatively common and include **conjoined twins**, **interplacental vascular anastomoses**, **twin-twin transfusion syndrome (TTTS)**, **fetal malformations**, and **umbilical cord abnormalities**.

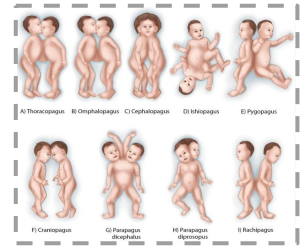
● **Conjoined Twins:**

Fortunately, this is a very rare event , it appear when separation of embryo occur after 12-13 days which embryonic disc is already formed cleavage of the embryo will be incomplete, resulting in **conjoined twins**.

● Conjoined Twins cont.

- Conjoined twins are classified according to the anatomic location of the incomplete splitting:

- Thoracopagus (anterior) **"most common"**
- Pyopagus (posterior)
- Craniopagus (cephalic)
- Ischiopagus (caudal)



● Umbilical cord abnormalities :

- **Absence of one umbilical artery** occurs in about 3-4% of twins, as opposed to 0.5-1% of singletons.
 - The absence of one umbilical artery is significant because in 30% of such cases, it is associated with other congenital anomalies (e.g., renal agenesis).
- **Marginal and velamentous umbilical cord insertion** also occur more frequently in twins and may cause growth abnormalities, particularly in the third trimester.

● Inter-placental vascular anastomosis

- It means there is vascular communications between the two fetuses via the placenta lead to shared circulation.
- Types : arterial-arterial (most common), arterial-venous, venous-venous.
- It may give rise to a number of problems including : abortion, hydramnios, **TTTS**, and **fetal malformations**.

● Fetal malformation :

- **Arterial-arterial placental anastomoses** can result in fetal structural malformations.
- In this situation, the **arterial blood from the donor twin enters the arterial circulation of the recipient twin**, and the reversed blood flow may cause thrombosis within critical organs or atresias due to trophoblastic embolization. In addition, **the recipient twin, being perfused (in a reverse direction) with poorly oxygenated blood, lead to fail to develop normally (acardiac twin)**
 - **Acardiac twin** has aplastic and/or dysmorphic anatomical development cephalad of the abdomen, but often has fully formed lower extremities.
- Overall, the incidence of both minor and major congenital malformations in twins is twice that of singletons, with the greater incidence of malformations occurring in monozygotic twins.

● **Twin- twin transfusion syndrome (TTTS) :** " most serious complications"

- This occurs when there is net flow from one twin to another, secondary to vascular anastomosis (typically arterial-venous connections) between the fetuses, , which means there is unbalanced anastomoses in the placenta.
- **More in Di-mo twins** than Mono-mono twins.
- In this syndrome, arterial blood from the "donor twin" enters the placenta (via the umbilical artery) and is taken up by the umbilical venous system belonging to the "recipient twin," which results in a net transfer of blood from the "donor" to the recipient twin.
- Both twins are at risk of demise from the circulatory derangement, and the pregnancy is predisposed to preterm delivery due to overdistention of the uterus with hydramnios

- **Twin- twin transfusion syndrome (TTTS) cont.**

The donor Twin :

- Hypovolemia
- Hypotension
- Anemia
- Oligohydramnios
- Growth restriction

- **Dx** by US, we can detect small and big fetuses
- **Rx** by endoscopic intrauterine laser ablation of vascular anastomosis is the 1st line therapy

The recipient Twin :

- Hypervolemia, edema
- Hypertension, thrombosis,
- Polycythemia, hyperviscosity
- Polyhydramnios
- Cardiomegaly, CHF

Management

Antepartum

- **Adequate nutrition**
 - Iron, **folate, vitamins** and Ca^{+2}
 - Extra 300 calories/day is needed.
- **Frequent BP monitoring** → because pregnancy induced HTN
- **Ultrasonic** examination

First and Second Trimesters :

- Every 1-2 weeks start in mid trimester (between 16-22 weeks) **for ultrasonic cervical length assessment.** → because incompetent cervix is more common with multiple gestations which can lead to preterm labor (Patient should be aware of labor signs)
→ A suture (cerclage) can be placed in the cervix if marked shortening is noted in the absence of contractions, though the benefit of a cervical cerclage has been under scrutiny recently.

Third Trimesters :

- **Every 4-6 wks at 24 wks** to assess fetal weight and if there is discordant fetal growth or no **(prevention of prematurity is of utmost importance)** . Also we looking for twin-twin transfusion (amniotic fluid discordance). **The high perinatal mortality rate in twin gestations is largely attributable to prematurity** and congenital anomalies.

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Intrapartum

Chorionicity	Time of delivery	Route of delivery
Conjoined twins		C-section
Uncomplicated Mo-mo	32-34 weeks	Always C-section Secondary to risk of Cord complication (cord entanglement)
Uncomplicated Di-mo	34-37+6 weeks	They can be / candidates for vaginal deliveries after 32 weeks.
Uncomplicated Di-di	38 weeks	HOWEVER fetal presentation will determine.

The **time of delivery** depends on **chorionicity**

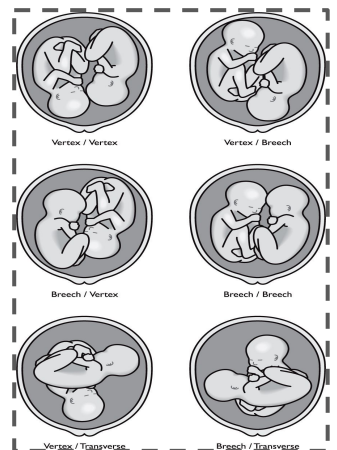
The **route of delivery** depends on:

- 1- **chorionicity**
- 2- **gestational age**
- 3- **fetal presentation**
- 4- **experience of the clinician** performing the delivery

Fetal Presentation : To choose the safest route of delivery for mother and babies, the presentations of the fetuses must be accurately known. By convention, the presenting twin is designated as twin A and the second twin as twin B.

Cephalic presentation / Vertex-vertex (most common)	<p>Vagina delivery (managed similarly to a singleton vertex presentation)</p> <p>After delivered first Twin, if second twin :</p> <ul style="list-style-type: none"> ● Remains cephalic = can be delivered also by vaginal delivery ● Flips to non-cephalic after delivery first twin or start out as non cephalic = <ul style="list-style-type: none"> ○ External cephalic then delivered by vaginal delivery ○ Or Delivered in breeched vaginal delivery <p>^ Because the second twin is at increased risk of cord prolapse, abruptio placentae, and malpresentation, careful attention to fetal heart monitoring is necessary.</p>
Vertex - breech	<p>When delivery of vertex-breech or vertex-transverse twins is contemplated, <u>informed consent by the mother</u> and the <u>skill of the obstetrician in non cephalic presentation twins</u> are determining factors in choosing between cesarean and vaginal delivery.</p> <p>Although there is presently no scientific evidence that cesarean delivery is superior for the vertex-breech presentation, difficulty in extracting the breech second twin can result in umbilical cord prolapse, head entrapment, neck injury, and asphyxia.</p>
Breech-Breech	<p>Increased risk of fetal injury exists with delivery of a breech fetus. For this reason they usually delivered by C-section</p>

HOWEVER, since all twin pregnancies are increase risk for cesarean delivery. Some patients and some clinicians may choose to proceed **cesarean delivery** with all twin gestations



Postpartum

- Watch for postpartum hemorrhage from uterine atony owing to an **overdistended uterus.**

Teaching Case

You are seeing a 28 year-old G2P1 now at 12 weeks. Her first pregnancy was full term and uncomplicated. At her first trimester screen she was noted to have a dichorionic diamniotic twin gestation with size equal to dates.

Q1: How is the diagnosis of chorionicity and zygosity made?

- 1st trimester or early 2nd trimester ultrasound is the most accurate time to identify chorionicity. It is difficult to determine chorionicity after that.
- In addition to the identification of 2 placentas, membrane thickness (thick) and evaluation of the membrane insertion site are also used to identify chorionicity. The presence of lambda sign, only in di di.
- Monozygous embryos dividing <72 hours after fertilization will be dichorionic (30% of monozygous twins).
- Ultrasound diagnosis of dichorionic twins cannot determine zygosity. Unless the twin fetus have different sex then it's a definitive dizygotic twin. And when the twin have monochorionic, it's a definitive monozygotic twins. (12 weeks it is too early to see the gender)
- Monochorionic embryos dividing >72 hours after fertilization are always monozygous.

Q2: What nutritional deficiencies is she at higher risk for in a twin gestation?

What recommendations will you make to her because of them, including weight gain?

- The increased circulating blood volume of multiple gestations accentuates the dilutional anemia of pregnancy.
- Each fetus will extract Fe from maternal circulation further exacerbating the physiologic anemia.
- Calcium depletion is also exacerbated in multiple gestations.
- Normal weight woman are recommended to gain an additional 10-15 lbs (total 35-40).
- **Calcium and iron supplementation** should be recommended even prior to anemia. We usually give five multivitamin & see if there is still Fe need, we give it right away.

Q3: You are counseling her about the increased maternal and fetal risks during the pregnancy, what specifically are you concerned about?

- Maternal risks include increased incidence of gestational diabetes, hypertension, anemia as well as ante and postpartum hemorrhage.
- There is an increased incidence of thrombosis, compounded by the increased risks of obesity, maternal age, bed rest and Cesarean deliveries in multiple gestations.
- Fetal risks include an increased chance of miscarriage, fetal growth restriction, preterm delivery, perinatal asphyxia and stillbirth (of one or both). All are more common in monochorionic gestations.
- The risk of fetal anomalies is more common in all multiple gestations, but each of a dichorionic twin set has the same risk of structural anomalies as a singleton. The risk to a fetus of a monochorionic gestation is double a singletons baseline risk.

Teaching Case

Q4: What additional management strategies are recommended in twin pregnancy?

- More frequent prenatal visits to screen for maternal hypertension.
- Periodic ultrasound surveillance to screen for fetal growth.
- Serial cervical ultrasound has been shown to be able to predict preterm delivery in twins to allow time for:
- Betamethasone use. *why? Accelerate lung maturity, reduce intracranial bleeding, reduce risk of necrotising enterocolitis "NEC" and reduce NICU stay "Improve survival".*
- Antenatal fetal testing is generally recommended in later pregnancy to evaluate increased fetal risk of continuing pregnancy.

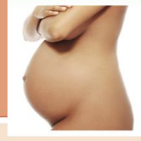
Q5: Your patient is now at 29 weeks without any complications. You are going to counsel her about delivery planning. What factors will determine the safest timing of delivery in a multiple gestation?

- 38 weeks has been shown to have the lowest risk of perinatal mortality in uncomplicated twin gestations.
- Maternal or fetal complications of pregnancy may warrant safest delivery at an earlier gestational age.

Q6: What are the risks of delivery in a multiple gestation and what are considerations for mode of delivery?

- Increased fetal risks include perinatal asphyxia, birth trauma; both primarily to the second twin.
- Discussion of mode of delivery needs to include fetal presentation, fetal and maternal status and time of delivery and ability to monitor both fetuses reliably.
- Maternal risks include increased risk of Cesarean delivery, postpartum hemorrhage, and anesthesia complications.

Reference



Multifetal Gestation and Malpresentation

CALVIN J. HOBEL

CLINICAL KEYS FOR THIS CHAPTER

- In the United States and other developed countries, multiple gestations have increased, and currently account for at least 3.5% of live births. The two major reasons for this increase have been the use of assisted reproductive technologies (ARTs) to treat infertility, and the increasing maternal age of women having children. Twins are twice as likely in women over the age of 35. Complications of pregnancy such as preeclampsia, preterm birth, poor fetal growth, and monochorionicity significantly increase the risk of perinatal morbidity and mortality in multifetal gestations.
- The prognosis and the risk for morbidity are dependent on zygosity (the genetic makeup of the zygote). Ultrasonographic evaluation of the pregnancy is helpful in determining zygosity. Monozygotic twins (monochorionic) are more likely to involve congenital anomalies, weight discordance, twin-twin transfusion syndrome (TTTS), and other morbidity. Discordant fetal gender confirms dizygotic (two chorions) gestations and visualization of a thick amnio-chorionic septum is suggestive of dizygotic twins. Confirmation of the zygosity may require detailed examination of the placenta at delivery.
- There are significant physiologic adaptations that must occur with multiple gestations. In a normal pregnancy,

the maternal blood volume is augmented by 40% (2 L) over the nonpregnant baseline, while in multiple gestations the blood volume increases by 3 L or more. These changes are associated with a significantly increased risk of iron and folate deficiency, and an increase in preeclampsia, hypertension, and maternal respiratory problems such as shortness of breath (dyspnea).

- Management of twin gestations during pregnancy and delivery depends upon the type of problems that develop during pregnancy such as preterm labor, poor fetal growth, hypertensive disorders, and how the fetuses present at the onset of labor. The key is to establish a plan of management that assures a safe delivery at or near term. Generally, if the first twin (twin A) is in a vertex position and the delivery is by the vaginal route, it is appropriate to plan to deliver twin B vaginally. When twin A is breech, the general consensus is that the birth of both twins should be by cesarean delivery.
- Common malpresentations include breech (the most common), face, and brow. Face and brow presentations occur in about 1 in 500 and 1 in 1400 deliveries, respectively. Compound and shoulder presentations are rare, and usually are associated with premature births. Persistent brow presentations almost always require cesarean delivery.

Multiple gestations are defined as any pregnancy in which two or more embryos or fetuses occupy the uterus simultaneously. It is of utmost importance to recognize multiple gestations as a complication of pregnancy. Because twins deliver at a mean gestational age of about 36 weeks, the perinatal mortality and morbidity for multiple gestations disproportionately exceed that of singleton pregnancies. Maternal morbidity is also increased, because of the additional physiologic stresses associated with two (or more) fetuses and placentas and a rapidly enlarging uterus.

The term **malpresentation** encompasses any fetal position other than vertex at delivery, and includes breech, face, brow, compound, and shoulder presentations. Both fetal and maternal factors contribute to the occurrence of a malpresentation. The most common malpresentation is breech.

Multiple Gestations

Multiple gestations include twins, identical and fraternal, and high-order multiple gestations that consist of three or more fetuses.

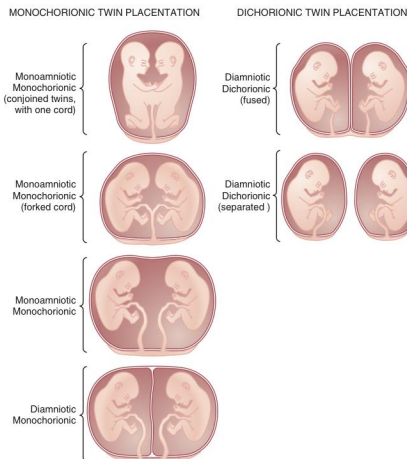


FIGURE 13-1 Diagrammatic representation of the major types of twin placentas found with monozygotic twins. (Redrawn from Benirschke K, Ditschell SG. Pathology of the human placenta. New York, 1974, Springer-Verlag, p 263.)

Conjoined Twins

If division of the embryo occurs very late (13 days, after the embryonic disc has completely formed), cleavage of the embryo will be incomplete, resulting in conjoined twins. Fortunately, this is a very rare event, occurring once in 70,000 deliveries. Conjoined twins are classified according to the anatomic location of the incomplete splitting: **thoracopagus** (anterior), **pygopagus** (posterior), **craniopagus** (cephalic), or **ischiopagus** (caudal). The majority of such twins are thoracopagus. Delivery of conjoined twins frequently requires cesarean delivery, but postnatally, these gestations have a surprisingly optimistic prognosis in many cases. More advanced contemporary imaging has allowed detailed mapping of the shared organs and more successful surgical separations.

Interplacental Vascular Anastomoses

Interplacental vascular anastomoses occur almost exclusively in monozygotic twins at a rate of 90% or

more. The most common type is arterial-arterial, followed by arterial-venous and then venous-venous. **Vascular communications between the two fetuses via the placenta may give rise to a number of problems, including abortion, hydramnios, TTTS, and fetal malformations.** Overall, the incidence of both minor and major congenital malformations in twins is twice that of singletons, with the greater incidence of malformations occurring in monozygotic twins.

Twin-Twin Transfusion Syndrome

The presence of unbalanced anastomoses in the placenta (typically arterial-venous connections) leads to a syndrome in which the circulation of one twin perfuses that of the other (i.e., TTTS) in approximately 10% of monozygotic twins. In this syndrome, arterial blood from the "donor twin" enters the placenta (via the umbilical artery) and is taken up by the umbilical venous system belonging to the "recipient twin," which results in a net transfer of blood from the "donor" to the recipient

TABLE 13-1
THE RELATIONSHIP BETWEEN THE TIMING OF CLEAVAGE AND THE NATURE OF THE MEMBRANES IN TWIN GESTATIONS

Time of Cleavage*	Nature of Membranes
0-72 hr	Diamniotic, dichorionic
4-8 days	Diamniotic, monochorionic
9-12 days	Monoamniotic, monochorionic

*Time interval between ovulation and cleavage of the egg.

ETIOLOGY AND CLASSIFICATION OF TWINNING

Multiple gestations occur either as the result of the splitting of an embryo (i.e., **identical or monozygotic twinning**) or the fertilization of two or more eggs produced in a single menstrual cycle (i.e., **fraternal or dizygotic twinning**). Because dizygotic twins arise from separate eggs, they are structurally distinct pregnancies coexisting in a single uterus, each with its own amnion, chorion, and placenta. **Monozygotic twins** arise from cleavage of a single fertilized egg at various stages during embryogenesis, and thus the arrangement of the fetal membranes and placentas will depend on the time at which the embryo divides (Table 13-1). The earlier the embryo splits, the more separate the membranes and placentas will be. If division occurs within the first 72 hours of fertilization, the membranes will be **diamniotic, dichorionic** with a thick, four-layered intervening membrane. If division occurs after 4 to 8 days of development, when the chorion has already formed, **monochorionic, diamniotic** twins will evolve with a thin, two-layered septum. If splitting occurs after 8 days, when both amnion and chorion have already formed, the result will be **monochorionic, monoamniotic**, twins residing in a single sac with no septum. Of all monozygotic twins, 30% are dichorionic, diamniotic, and 69% are monochorionic, diamniotic. Only 1% of twins are monoamniotic. Because twins share a sac in this type, without an intervening membrane, the risk of umbilical cord entanglement is high, resulting in a net mortality in these twins of almost 50% (Figure 13-1).

INCIDENCE AND EPIDEMIOLOGY

Twins account for approximately 3.5% of all births in the United States. The frequency of **monozygotic twinning**, which depends on a very infrequent biologic event (embryo splitting), is constant in all populations studied at about 1 in 250 births. However, the frequency of **dizygotic twinning**, which arises from multiple ovulations in the mother, is strongly influenced by family history, ethnicity, and maternal age. A family history of dizygotic but not monozygotic twins in the maternal pedigree increases the likelihood of dizygotic twinning in subsequent generations. In western

Nigeria, twinning occurs in 1 of 22 gestations, whereas in the Native American and Inuit populations, twinning is less than one-fifth of that rate. Twins are twice as common in women over 35 as in women at 25 years of age. Given these statistics, approximately two-thirds of spontaneously conceived twins are fraternal and one-third are identical (monozygotic). However, in recent years, the incidence of multizygotic multifetal gestation has increased markedly with the more widespread use of ovulation induction agents and the practice of transferring multiple embryos after in vitro fertilization. The incidence of multiple gestations following the use of clomiphene is about 6-8% and about 20-30% following gonadotropin therapy.

DETERMINATION OF ZYGOSITY

The prognosis and expected morbidity of twins is strongly dependent on zygosity: **monozygotic twins are more likely to have congenital anomalies, weight discordance, twin-twin transfusion syndrome, neurologic morbidity, premature delivery, and fetal death.** Thus, **determination of zygosity is the most important next step after multifetal pregnancy has been first diagnosed.**

Ultrasonographic evaluation of the pregnancy is frequently very helpful in determining zygosity. Imaging of discordant fetal gender confirms a dizygotic gestation. Visualization of a thick amnio-chorionic septum is suggestive of dizygotic twins, as is the presence of a "peak" or inverted "V" at the base of the membrane septum (Figure 13-2, A). Conversely, in a monochorionic gestation, the dividing membrane is fairly thin (see Figure 13-2, B). Because an early embryonic split can infrequently result in dichorionic, diamniotic twins with separate placentas, these findings are not definitive. Similarly, in rare cases of postzygotic genetic events, monochorionic twins may be gender discordant. Thus, **definitive diagnosis of zygosity may require detailed examination of the placenta after delivery.** Thirty percent of twins will be of different sex and are, therefore, dizygotic. Twenty-three percent have monochorionic placentas and are, therefore, monozygotic. Twenty-seven percent will have the same sex, dichorionic placentas, but different blood groupings, and must be, therefore, dizygotic. **Twenty percent will have the same sex, dichorionic placentas, and identical blood groupings.** For the latter group, further studies, such as human leukocyte antigen (HLA) typing or DNA analysis, will be required to allow determination of zygosity.

ABNORMALITIES OF THE TWINNING PROCESS

Among monozygotic multiple gestations, abnormalities in the twinning process are relatively common and include conjoined twins, interplacental vascular anastomoses, twin-twin transfusion syndrome (TTTS), fetal malformations, and umbilical cord abnormalities.

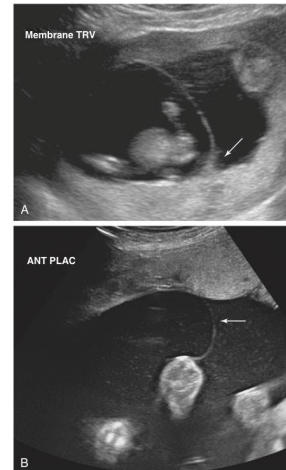


FIGURE 13-2 A, Real-time ultrasound with a thick vertical amnio-chorionic septum (membrane) separating one twin (left side) from the second twin on the right. The arrow (right) points to a "peak" or "inverted V" suggesting dizygotic twins. B, Ultrasound of a thin vertical membrane separating one twin on the left side from the second twin on the right suggesting a monochorionic gestational sac. ANT PLAC, Anterior placenta; TRV, transverse view of membrane.

twin. **Fetal complications include hypovolemia, hypertension, anemia, oligohydramnios, and growth restriction in the donor twin, and hypervolemia, hydramnios, hyperviscosity, thrombosis, hypertension, cardiomegaly, polycythemia, edema, and congestive heart failure in the recipient twin.** Both twins are at risk of demise from the circulatory derangement, and the pregnancy is predisposed to preterm delivery due to overdistention of the uterus with hydramnios.

Twin to twin transfusion is diagnosed using ultrasound. Typically, the donor twin is smaller and may have oligohydramnios, absent bladder, and anemia. The recipient twin, on the other hand, is larger with possible polyhydramnios, cardiomegaly, and ascites or hydrops (Figure 13-3).

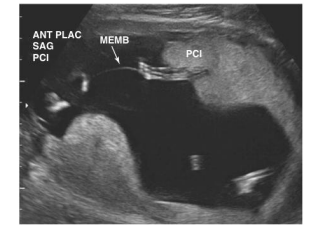


FIGURE 13-3 Ultrasound of a twin-twin transfusion syndrome with one twin (upper left) in an amniotic cavity with a reduced fluid volume and a membrane separating this fetus from the second twin in an amniotic cavity with an excessive amount of fluid (right and lower half of scan image). ANT PLAC, Anterior placenta; MEMB, membrane (amion); PCI, placental cord insertion; SAC, sagittal view.

Given the poor prognosis of untreated TTTS (approximately 50% survival of any twin), **treatment with either serial amniocenteses with fluid reduction from the recipient twin's sac, or laser photocoagulation of the anastomotic vessels on the surface of the placenta, are performed in specialized centers.**

Fetal Malformations

Arterial-arterial placental anastomoses can result in fetal structural malformations. In this situation, the arterial blood from the donor twin enters the arterial circulation of the recipient twin, and the reversed blood flow may cause thrombosis within critical organs or atresias due to trophoblastic embolization. The recipient twin, being perfused in a reverse direction with relatively poorly oxygenated blood, fails to develop normally. This so-called **acardiac** twin typically has aplastic and/or dysmorphic anatomical development cephalad of the abdomen, but often has fully formed lower extremities.

Umbilical Cord Abnormalities

Abnormalities of the umbilical cord occur with a higher frequency in twins and are primarily associated with monochorionic twins. Absence of one umbilical artery occurs in about 3-4% of twins, as opposed to 0.5-1% of singletons. **The absence of one umbilical artery is significant because in 30% of such cases, it is associated with other congenital anomalies (e.g., renal agenesis).** Marginal and velamentous umbilical cord insertions also occur more frequently in twins and may cause growth abnormalities, particularly in the third trimester.

Reference

Retained Dead Fetus Syndrome

It is not unusual for one twin to die in utero remote from term, whereas the remaining twin and the pregnancy continue to be viable. Over time (after 3 weeks or more in pregnancies that have progressed beyond 20 weeks), the retained dead fetus syndrome can develop, which involves disseminated intravascular coagulopathy in the mother as a result of the transfer of nonviable fetal material with thromboplastin-like activity into the maternal circulation. In such cases, the maternal platelet count and fibrinogen levels should be checked once a week to identify possible coagulation abnormalities. The dead fetus will be reabsorbed if the demise occurs before 12 weeks' gestation. Beyond this time, the fetus will shrink and become dehydrated and flattened (fetus papyraceus).

ALTERED MATERNAL PHYSIOLOGIC ADAPTATION WITH MULTIPLE FETUSES

A number of normal maternal physiologic responses to pregnancy are exaggerated with multiple gestations. Whereas in normal pregnancy, maternal blood volume is augmented by 40% (2 L over the nonpregnant baseline), in twins this increase may be 3 L or more. The increased blood volume and demand for iron and folate increase the risk of anemia in the mother and make the patient less able to tolerate the stresses of infection, labor, and premature labor. Preeclampsia and gestational hypertension are almost doubled in multifetal gestation. The increased uterine size associated with multiple fetuses can cause maternal respiratory embarrassment, orthostatic hypotension due to compression of the vena cava, and compromised renal function due to compression of the ureters.

DIAGNOSIS

Historical factors such as a maternal family history of dizygotic twinning, the use of fertility drugs, a maternal sensation of feeling larger than with previous pregnancies, or a sensation of excessive fetal movements should raise the suspicion of twins. Physical signs, including excessive weight gain, excessive uterine fundal growth, and auscultation of fetal hearts in separate quadrants of the uterus are suggestive but not diagnostic. An obstetric ultrasound should be performed when a multiple gestation is suspected. The diagnosis of multiple gestations requires a sonographic examination demonstrating two separate fetuses and heart activities, and can be made as early as 6 weeks' gestation.

ANTEPARTUM MANAGEMENT

Because of the high risk of preterm birth, intensive antepartum management schemes should be directed at prolonging gestation and increasing birth weight, in order to decrease perinatal morbidity and mortality. The complications of multiple gestations are shown in Box 13-1.

BOX 13-1

COMPLICATIONS OF MULTIPLE GESTATIONS

Maternal
Anemia
Hydramnios
Hypertension
Premature labor
Postpartum uterine atony
Postpartum hemorrhage
Preeclampsia
Cesarean delivery
Fetal
Malpresentation
Placenta previa
Abruptio placentae
Premature rupture of the membranes
Prematurity
Umbilical cord prolapse
Intrauterine growth restriction
Congenital anomalies
Increased perinatal morbidity
Increased perinatal mortality

First and Second Trimesters

Between 16 and 22 weeks, the patient is seen every 2 weeks for ultrasonic cervical length assessment, because incompetent cervix is more common with multiple gestations. A suture (cerclage) can be placed in the cervix if marked shortening is noted in the absence of contractions, though the benefit of a cervical cerclage has been under scrutiny recently and is the subject of multiple clinical studies with conflicting findings. Adequacy of maternal diet is assessed due to the increased need for overall calories, iron, vitamins, and folate. The Institute of Medicine (IOM) recommends women with twins gain a total of 16.0 to 20.5 kg (35 to 45 lb) during the pregnancy. However, optimal weight gain is somewhat dependent on prepregnancy maternal body mass index (BMI), because obese women (BMI > 30) have better outcomes with less weight gain than women who are of normal weight before pregnancy.

Third Trimester

During the third trimester, prevention of prematurity is of utmost importance. The cervix is monitored closely with ultrasonic measurements for early effacement and dilation that may precede frank premature labor. A cervical length less than 25 mm at 24 to 28 weeks is associated with a doubling of the risk of preterm birth. Interventions to prolong the length of twin pregnancy, such as bed rest, serial uterine activity monitoring, hospitalization, and prophylactic vaginal progesterone, have been carried out but have not been

consistently shown to prolong gestation. Nevertheless, most experts utilize a combination of these therapies, individualized for the patient's circumstances.

Discordant fetal growth, which is signified by one fetus flattening its growth rate, is a cause of morbidity and mortality. Fetal growth is monitored by ultrasound every 4 to 6 weeks beginning at 24 weeks, with additional fetal surveillance (e.g., biophysical testing, nonstress fetal heart rate assessment) when fetal growth falls below the normal curve. The patient should be monitored closely for signs of preeclampsia, including the development of nondependent edema, urinary protein, and rising arterial blood pressure.

Because twins experience higher rates of stillbirth and growth restriction than singletons, fetal well-being should be confirmed at least weekly by nonstress testing (NST) or biophysical profile (BPP) assessment from 36 weeks onward, and earlier in the presence of complications such as intrauterine growth restriction (IUGR), discordant growth, hypertension, or polyhydramnios. Umbilical artery Doppler assessment of fetal well-being is helpful to help determine the timing of delivery to prevent fetal demise if the fetus has IUGR (see Chapter 7). The contraction stress test (CST) should not be used, because these pregnancies are already predisposed to preterm labor.

Intrapartum Management

TREATMENT OF PRETERM LABOR

The treatment of preterm labor is discussed elsewhere (see Chapter 12), but multiple gestations present special challenges. Relative contraindications to tocolysis in these pregnancies include a gestational age of 34 weeks or more, growth failure of one or more fetuses, concerning fetal status on biophysical monitoring, and preeclampsia. Aggressive tocolysis typically involves use of agents with adverse cardiovascular effects in the mother, such as β -mimetics, magnesium sulfate, and calcium channel blockers. These agents, particularly when combined with antenatal corticosteroid therapy, have been associated with maternal volume overload and congestive heart failure. Box 13-2 provides a list of necessary prerequisites for the management of labor in pregnancies complicated by multiple gestations.

In the special case of monoamniotic twins, birth by cesarean delivery is usually accomplished by 34 to 36 weeks because of the increased risk of lethal cord entanglement. For diamniotic twin pregnancies, delivery management is outlined below.

VERTEX-VERTEX PRESENTATIONS

To choose the safest route of delivery for mother and babies, the presentations of the fetuses must be accurately known. By convention, the presenting twin is designated as twin A and the second twin as twin B.

BOX 13-2

PREREQUISITES FOR THE INTRAPARTUM MANAGEMENT OF MULTIPLE GESTATIONS

- A secondary or tertiary care center
- A delivery room equipped for immediate cesarean delivery, if necessary
- A well-functioning large-bore intravenous line (e.g., 16-gauge) for rapid administration of fluids and blood
- Blood available for transfusion
- The capability to continuously monitor the fetal heart rates simultaneously
- An anesthesiologist who is immediately available to administer general anesthesia should intrauterine manipulation or cesarean delivery be necessary for delivery of the second twin
- Two obstetricians scrubbed and gowned for the delivery, one of whom is skilled in intrauterine manipulation and delivery of the second twin
- Imaging techniques (i.e., sonography) for determining the precise presentations of the twins
- Two pediatricians, one of whom is skilled in the immediate resuscitation of the newborn
- An appropriate number of nurses to assist in the delivery and care of the newborn infants

Vertex (twin A)-vertex (twin B) occurs 50% of the time, followed by vertex-breech, breech-vertex, and breech-breech.

Vertex-vertex twins are managed similarly to a single vertex presentation. Both fetal heart rates should be monitored continuously during labor (Figure 13-4). Oxytocin (Pitocin) can be used to manage hypotonic contractions. After delivery of the first twin, the cord is clamped (identified as twin A) and cut, but cord blood samples are not obtained until the second fetus has been delivered to prevent potential hemorrhage from the undelivered fetus through placental vascular anastomoses. A vaginal examination is then performed to assess the presentation and station of the second twin. If the second twin is still in a vertex presentation, spontaneous delivery is expected. If necessary, forceps or vacuum can be used to assist delivery of a vertex second twin. Because the second twin is at increased risk of cord prolapse, abruptio placentae, and malpresentation, careful attention to fetal heart monitoring is necessary.

After delivery of the second fetus, the cord blood samples can be obtained and the placenta delivered. Care should be taken not to disrupt the fetal membranes, as these will often reveal the zygosity of the twins. Following delivery of the placenta, uterine tone should be closely monitored, as the incidence of postpartum atony and hemorrhage is increased in multiple gestations. See Chapter 10 for the prevention of postpartum hemorrhage.

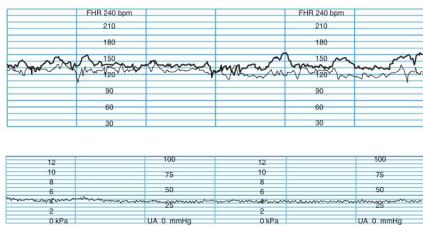


FIGURE 13-4 A fetal heart rate (FHR) tracing of a twin gestation. One twin (dark tracing) has accelerations of FHR more marked than those of the second twin (lighter tracing). Both degrees of accelerations indicate a state of "fetal well-being" for both twins.

BOX 13-3

CAUSES OF PERINATAL MORBIDITY AND MORTALITY IN TWINS

- Respiratory distress syndrome
- Birth trauma
- Cerebral hemorrhage
- Birth asphyxia
- Birth anoxia
- Congenital anomalies
- Stillbirths
- Prematurity

MANAGEMENT OF OTHER PRESENTATIONS

Increased risk of fetal injury exists with delivery of a breech fetus. For this reason, breech-breech and breech-vertex twins are usually delivered by cesarean delivery. When delivery of vertex-breech or vertex-transverse twins is contemplated, informed consent by the mother and the skill of the obstetrician are determining factors in choosing between cesarean and vaginal delivery. Although there is presently no scientific evidence that cesarean delivery is superior for the vertex-breech presentation, difficulty in extracting the breech second twin can result in umbilical cord prolapse, head entrapment, neck injury, and asphyxia. Unless the obstetrician is comfortable with managing these problems, planned cesarean is the only reasonable choice.

PERINATAL OUTCOME

The high perinatal mortality rate in twin gestations (30 to 50 per 1000 births), approximately five times that in singleton gestations, is largely attributable to prematurity and congenital anomalies (Box 13-3). Birth asphyxia is also a significant factor, and thus it is not

surprising that second twins have twice the perinatal mortality of first-born twins. Compared with singletons, death from complications of birth trauma (with both cesarean and vaginal routes) is four times more frequent with second-born twins and twice as frequent with first-born twins. Congenital anomalies and stillbirths account for about a third of the perinatal mortality rate. Stillbirths occur twice as frequently in twins as in singletons. Cerebral hemorrhage, asphyxia, and anoxia account for one-tenth of the overall perinatal mortality rate.

Twin gestations experience a fourfold increase in cerebral palsy. The increased morbidity in multiple gestations is related to placental and anatomic abnormalities, and trauma associated with the delivery. Low birth weight (mean birth weight in twins is 2395 vs. 3377 g for singletons), prematurity, and IUGR may predispose to permanent brain injury. Postnatally, twins on average are shorter and lighter than singletons of similar birth weight until 4 years of age.

MULTIPLE GESTATIONS WITH MORE THAN TWO FETUSES

Although higher order multiple gestations (triplets and higher) can result from embryo splitting and polyovulation, the most frequent cause today is iatrogenic from the use of ovulation induction agents. The incidence of spontaneous triplets is 1 in 8000 and that of spontaneous quadruplets 1 in 700,000 births. However, because of the widespread use of assisted reproductive technologies, the current estimate of the incidence of triplets is 1 in 3000 births. This rate has tripled in the last two decades. Recently advanced treatment for infertility, such as in vitro fertilization (IVF) has been focused on a reduction in multiple births. There has been a significant decrease in twins and higher order multiple births from IVF as a result of embryo freezing

at the blastocyst stage (day 5) and elective single embryo transfer.

Prematurity increases as the number of fetuses increases. The average length of gestation is 33 weeks for triplets but only 29 weeks for quadruplets, with mean birth weights 1818 and 1395 g, respectively. Theoretically, delivery of higher order multiples can follow the principles outlined above for twins. However, in contemporary practice, almost all high order multiples are delivered by cesarean delivery to decrease the risk of morbidity in these very premature pregnancies. The perinatal mortality rate for triplets and quadruplets is 50 to 100 per 1000 births, a rate that is twice that of twins.

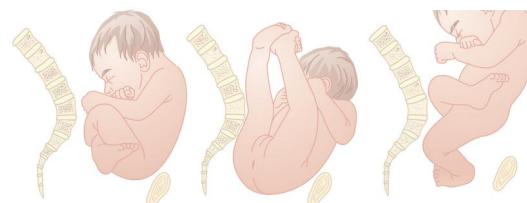


FIGURE 13-5 Types of breech presentation.



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Good Luck!



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