Twin pregnancy: Overview

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Literature review current through: Sep 2021. | **This topic last updated:** Apr 09, 2021.

INTRODUCTION

Twin pregnancy is associated with higher rates of almost every potential complication of singleton pregnancy, with the exceptions of postterm pregnancy and macrosomia. The most serious risk is preterm delivery, which accounts for most of the increased perinatal mortality, neonatal morbidity, and long-term morbidity of twins. Higher rates of fetal growth restriction and congenital anomalies also contribute to adverse outcome in twin births. Monochorionic twins have intravascular anastomoses in the placenta and may have unequal placental sharing, which confers additional risk for serious complications unique to these pregnancies, such as twin-twin transfusion syndrome, twin anemia polycythemia sequence, and selective fetal growth restriction, while monoamniotic twins are also at risk for sequelae of cord entanglement.

This topic will provide an overview of twin pregnancy. Many specific issues related to twin pregnancy are reviewed in detail separately, including:

- (See "Twin pregnancy: Routine prenatal care".)
- (See "Twin pregnancy: Management of pregnancy complications".)
- (See "Twin pregnancy: Labor and delivery".)
- (See "Monoamniotic twin pregnancy (including conjoined twins)".)
- (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis" and "Twin-twin transfusion syndrome: Management and outcome".)
- (See "Selective fetal growth restriction in monochorionic twin pregnancies".)
- (See "Multifetal gestation: Role of delayed-interval delivery".)

EPIDEMIOLOGY

Prevalence — Twin births account for approximately 3 percent of live births and 97 percent of multiple births in the United States [1].

Dizygotic twins are more common than monozygotic twins: approximately 70 and 30 percent of twins, respectively (in the absence of the use of assisted reproductive technology [ART]) [2]. The prevalence of dizygotic twins varies among populations. By contrast, the prevalence of monozygotic twins is relatively stable worldwide at 3 to 5 per 1000 births and not affected by patient-specific factors, except for those undergoing in vitro fertilization (IVF).

Risk factors — The major factors influencing the prevalence of dizygotic twins are:

- **Use of fertility enhancing treatments** – Fertility enhancing treatments substantially increase the prevalence of twin pregnancy compared with natural conception. Over one-third of all twin infants born in the United States can be attributed to iatrogenic interventions (IVF, ovulation induction, superovulation plus intrauterine insemination) [3]. In the United States, twin births increased from 1 in 53 infants in 1980 (before widespread availability of IVF) to a peak of 1 in 29 infants in 2014 (after widespread availability of ART), then declined to 1 in 32 infants in 2019 (after guidance recommending a decrease in the number of embryos transferred per IVF cycle) [1]. (See "Strategies to control the rate of high order multiple gestation".)

  Dizygotic twins are more common in pregnancies conceived with IVF than in naturally conceived pregnancies (≥95 versus 70 percent) since some patients undergo double embryo transfer as part of IVF. However, IVF also appears to increase the risk of embryo cleavage, thus increasing the chance of monozygotic twins. IVF is the only risk factor for monozygotic twinning. (See "Pregnancy outcome after assisted reproductive technology", section on 'Monozygotic multiples'.)

  Dizygotic twins are also more common in pregnancies conceived with ovulation-inducing agents alone (without IVF) than in naturally conceived pregnancies since these drugs increase the likelihood of ovulation and fertilization of multiple oocytes.

- **Maternal age** – Approximately one-third of the increase in multiple births in recent decades can be attributed to increasing age at childbirth. The frequency of naturally conceived dizygotic twins increases two- to threefold between age 15 and age 35 [4]; this may be related to increases in follicle-stimulating hormone concentration with age [5]. Older individuals are also more likely to utilize fertility treatments.

  Although maternal age affects the prevalence of twins, it does not appear to affect twin pregnancy outcome significantly [6-12]. When matched for chorionicity and amnionicity, pregnant people ≥35 years appear to have the same or a lower risk of adverse perinatal outcome as younger pregnant people with twin pregnancies in observational studies [6,7,10,11].

- **Race/geographic area** – Significant variations in the prevalence of naturally conceived dizygotic twins occur worldwide. In one report, naturally conceived dizygotic twins accounted for 1.3 per 1000 births in Japan, 8 per 1000 births in the United States and Europe, and 50 per 1000 births in Nigeria [13]. Spontaneous twinning is more common in the Black population than in the White population [14].

- **Parity** – Increasing parity correlates with an increased likelihood of dizygotic twin birth, even after adjustment for maternal age [5].

- **Family history** – Dizygotic twinning appears to have a genetic component that is expressed in the mother but can be inherited from either her mother or father [15]. Thus, a mother is at increased risk of having twins if she has a family history of twin births. The family history of the biologic father appears to have little or no effect on his partner's risk of having twins; however, he could pass the familial trait to his daughters. This theory is supported by gene mapping studies in animals and humans that found that specific genetic variants expressed by oocytes or ovarian cells were at least partly responsible for twinning [15,16].

- **Maternal weight and height** – Pregnant patients with obesity (body mass index [BMI] ≥30 kg/m^2) and tall individuals (≥65 inches [164 cm]) are at greater risk for dizygotic twin birth than individuals who are underweight (BMI <20 kg/m^2) and who are short (<61 inches [155 cm]) [17-19].

- **Diet** – Diet may be an important factor affecting the dizygotic twinning rate in some geographic areas, among certain races, and in people of particular body habitus [5,20,21]. As an example, some studies have reported that folic acid supplementation increased the rate of twinning [22]. However, there were several limitations to these studies, which could have biased the results.

CLINICAL PRESENTATION

Twin pregnancies are usually first identified when an ultrasound examination is performed in early pregnancy for indications such as determining gestational age or viability, measuring nuchal translucency as part of Down syndrome screening, or performing a fetal anatomic survey.

Before an ultrasound is performed, there may be a heightened suspicion of twin pregnancy based on uterine size that is large for dates, family history of fraternal twins, use of assisted reproductive technology or ovulation induction to achieve pregnancy, or hyperemesis gravidarum.

DIAGNOSIS

Ultrasound examination is the best method for diagnosing twin gestation. Most pregnant patients in resource-abundant countries undergo one or more routine ultrasound examinations to provide detailed information about the developing pregnancy, including the number of fetuses. Randomized trials comparing routine ultrasound examination with ultrasound performed only for clinical indications have proven that a significant number of twin pregnancies are not recognized until the third trimester or even delivery in patients who do not undergo routine ultrasound examination [23,24]. For example:

- The Routine Antenatal Diagnostic Imaging with Ultrasound Study (RADIUS) of over 15,000 pregnancies found that when a routine second-trimester ultrasound examination was not performed, 38 percent of twin pregnancies were not diagnosed until after 26 weeks of gestation and 13 percent were not diagnosed until delivery [23].
- The Helsinki Ultrasound Trial reported similar findings: Approximately 25 percent of twin pregnancies were not diagnosed until after 21 weeks of gestation [24].

In both trials, no twin pregnancies were missed when an ultrasound examination was performed between 15 and 22 weeks of gestation.

Prenatal ultrasound screening guidelines vary worldwide. In the United States, the American College of Obstetricians and Gynecologists recommends ultrasound examination for all pregnant people, optimally at 18 to 22 weeks of gestation in the absence of specific indications (eg, size greater than dates, uterine bleeding, pelvic pain) [25]. (See "Overview of ultrasound examination in obstetrics and gynecology", section on 'Obstetric sonography'.)

SONOGRAPHIC DIAGNOSTIC EVALUATION

Determination of gestational age — Gestational age is determined by ultrasound examination, unless there is no known date of conception (eg, embryo transfer of pregnancy conceived by in vitro fertilization [IVF]). If there is a discrepancy between the twins in biometric measurements used for estimating gestational age, the general consensus is that the estimated delivery date (EDD) should be based on the measurements for the larger twin [26,27]. This will minimize the risk that a diagnosis of growth restriction, which is common in multiple gestations, will be missed due to underestimation of gestational age.

Ultrasound assessment before 22 weeks of gestation provides an accurate estimation of gestational age, which is important in all pregnancies but particularly important in management of twin pregnancies because of the higher frequency of complications. Accurate gestational age assessment is essential to accurately time the various screening and diagnostic tests performed in pregnancy, determine whether fetal growth is normal for gestational age, and accurately time planned late preterm or term delivery. (See "Prenatal assessment of gestational age, date of delivery, and fetal weight".)

Assessment of chorionicity and amnionicity — Determining amnionicity and chorionicity is critical because monochorionic twins have a shared fetoplacental circulation, which puts them at risk for specific serious pregnancy complications, such as twin-twin transfusion syndrome (TTTS), twin anemia polycythemia sequence (TAPS), selective

fetal growth restriction (sFGR), and twin reversed arterial perfusion (TRAP) sequence [28-32]. In addition to the complications associated with monochorionic twinning, monoamniotic twins are also at risk for cord entanglement and conjoined twins. Because these complications increase the risk for neurologic morbidity and perinatal mortality in monochorionic twins compared with dichorionic twins, monochorionic and monoamniotic twin pregnancies are monitored differently than dichorionic twin pregnancies [29,30,33-36].

Chorionicity and amnionicity are most accurately determined sonographically in the first trimester after seven weeks (sensitivity ≥98 percent [37]), but this may be before first recognition of twin pregnancy. Accuracy is lower but acceptable in the early second trimester (sensitivity ≥90 percent [37]) [38-44]. Sonographic assessment of the fetal membranes is more difficult and less accurate in the third trimester, especially in the setting of oligohydramnios.

Chorionicity and amnionicity are determined in the following ways:

- **Identification of two separate placentas is a highly reliable indicator of dichorionic twins** (image 1). This indicator is generally only useful in early pregnancy since separate placentas often appear fused later in gestation. Importantly, a single visible placental mass is not diagnostic of a monochorionic pregnancy as separate placentas can appear fused early in pregnancy. Rarely, a monochorionic placenta that is bilobed or has a succenturiate lobe gives the appearance of two separate placentas [45].

- The **presence/absence of the intertwin membrane and its sonographic characteristics early in pregnancy indicates chorionicity and amnionicity**. Care should be exercised when making the assessment of presence or absence of an intertwin membrane in the early first trimester (approximately seven to nine weeks) when the amnion may not be easily detectable and lead to incorrect diagnosis of monoamniotic twins. In this early assessment, two yolk sacs suggest diamniotic twins and one yolk sac suggests monoamniotic twins. Amnionicity should be confirmed on a later ultrasound as discrepancies have been reported in both cases of diamniotic twins with two yolk sacs and monoamniotic twins with a single yolk sac.

  In the case of suspected early co-twin demise in a monochorionic twin gestation, confirmation of the absence of vascular flow in the demised twin should be confirmed to exclude TRAP sequence. (See "Diagnosis and management of twin reversed arterial perfusion (TRAP) sequence".)

  - **Monochorionic/monoamniotic** – Visualization of intertwined umbilical cords (M-mode with two different heart rates in adjacent loops of cord) is diagnostic of monoamniotic twins (image 2), but cord entanglement is not always detected.

    Another finding is that the intertwin membrane is absent in a monochorionic/monoamniotic twin pregnancy. Visualizing the intertwin membrane becomes more difficult with advancing gestational age because of fetal crowding, progressive thinning of the membrane, and, in some cases, development of oligohydramnios in one or both sacs. These factors may lead to a false diagnosis of monochorionic/monoamniotic twins. On the other hand, monochorionic/monoamniotic twins may be misdiagnosed as monochorionic/diamniotic twins when separation of the amnion and chorion is mistaken for an intertwin membrane.

    In early gestation (prior to 10 weeks), the intertwin membrane may be missed and lead to an inaccurate diagnosis of monoamniotic twins. Assessment of the number of yolk sacs is helpful in these cases as monoamniotic twins will most often have only a single yolk sac.

  - **Dichorionic/diamniotic** – An intertwin membrane with the "twin peak" or "lambda (λ)" sign indicates dichorionic twins. This sign refers to a triangular projection of tissue that extends between layers of the intertwin membrane from a fused dichorionic placenta (image 3) [46]. It is best seen at 10 to 14 weeks, becomes less prominent after 20 weeks of gestation, and may disappear.

    An additional clue that twins are dichorionic is that the intertwin membrane is thicker with dichorionic than monochorionic twins since the dichorionic/diamniotic membrane consists of four layers (ie, two layers of

both amnion and chorion) (image 4), whereas the intertwin membrane in a monochorionic/diamniotic pregnancy only consists of two layers (only amnion) (image 5). There is no consensus about the cutoff between thin and thick membranes; thresholds of 1.5 to 2 mm in the first trimester have been suggested [42,47]. The difference in membrane thickness is less obvious later in pregnancy [48,49]. After the first trimester, identification of fetuses of different sex is a highly reliable means of confirming a dichorionic pregnancy, which is why guidelines for obstetric ultrasound include assessment of genitalia when twins are identified [50].

- **Monochorionic/diamniotic** – An intertwin membrane with the "T" sign indicates a monochorionic/diamniotic placenta. This sign refers to the appearance of the thin intertwin membrane composed of two amnions as it takes off from the placenta at a 90° angle.

- The number of chorion and amnion membrane layers in the intertwin membrane can be counted, but it is technically difficult; therefore, this method is not commonly employed. It is best accomplished between 16 and 24 weeks of gestation using high resolution, magnified images with the membrane perpendicular to the ultrasound beam.

In a study including over 600 twin pregnancies at 11 to 14 weeks of gestation at a tertiary referral center, use of the T sign, lambda sign, and number of placentas had sensitivity of 100 percent and specificity of 99.8 percent for determining monochorionicity, with only one dichorionic pregnancy incorrectly assigned as monochorionic [51]. A placental hematoma precluded diagnosis of the T or lambda sign in the incorrectly assigned pregnancy. Other smaller studies have reported sensitivity of 90 to 100 percent and specificity of 97.4 to 99.5 percent using these markers and fetal sex. In a systematic review of the accuracy of the lambda sign alone (2292 twins, nine studies), sensitivity for predicting dichorionicity was 99 percent (95% CI 98-100) and specificity was 95 percent (95% CI 92-97) [52]. Pooled sensitivity of the absence of the lambda sign for predicting monochorionicity was 96 percent (95% CI 92-98) and pooled specificity was 99 percent (95% CI 98-99).

Pitfalls in sonographic diagnosis — There are numerous reasons for imperfect accuracy of sonography, and clinicians should be mindful of the possibility of an exception to the usual rules for assigning chorionicity and amnionicity. For example, a monochorionic placenta may be bipartite and appear as two separate placentas (but careful imaging will reveal that vascular anastomoses between lobes and thus risk for TTTS are present) and rarely monozygotic twins have discordance in the phenotypic sex. An extensive review of the diagnosis of and pitfalls in assessing chorionicity and amnionicity is available elsewhere [53].

Relationship between chorionicity, amnionicity, and zygosity — Dizygotic or "fraternal" twins occur from ovulation and fertilization of two oocytes, which results in dichorionic/diamniotic placentation and two separate placentas (algorithm 1). Rare cases of dizygotic twins with monochorionic placentation after assisted reproductive technology (ART) have been reported, with unexplained etiology [54-58]. Rarely, dizygotic twins have also been reported after single embryo transfer.

Monozygotic or "identical" twins result from ovulation and fertilization of a single ovum, with subsequent division of the zygote (algorithm 1). Timing of egg division generally determines placentation. Monozygotic twins may have two separate placentas (dichorionic/diamniotic) or one placenta that is usually monochorionic/diamniotic but rarely monochorionic/monoamniotic. However, case reports of atypical twinning (eg, chimeric twins, mirror image twins, discordant monozygotic twins, polar body twins) have prompted hypotheses for other mechanisms of monozygotic twinning [59]. Sesquizygotic (Latin meaning "one and a half" zygotes) multiple pregnancy is the term used to describe a rare intermediate between monozygotic and dizygotic twinning thought to involve fertilization of one ovum by two sperm. In the fertilized ovum, independent (heterogoneic) assortment of the two paternal genomes and one maternal genome occurs, ultimately forming a chimeric blastomere that undergoes a twinning event [60]. The subsequent twins are genetically identical to each other with respect to maternal genes but differ with respect to paternal genes, sharing approximately 78 percent of paternal genomic information in one well documented case.

From an imaging perspective, approximately 80 to 90 percent of dichorionic placentas are associated with dizygotic twins and the remainder are associated with monozygotic twins. Determining the zygosity of same-sex twins is discussed below. (See 'Determining the zygostiy of same-sex twins' below.)

Use of NIPT to determine zygosity — It may be possible to determine zygosity with noninvasive prenatal testing (NIPT), and this could assist in the assessment of chorionicity when ultrasound findings are not clear. A small prospective blinded study to validate a single-nucleotide polymorphism-based NIPT reported 100 percent accuracy for zygosity for all 29 monozygotic and 64 dizygotic twin samples in which a result was reported; another two samples yielded no result [61]. While amnionicity and chorionicity in monozygotic twins will reflect the timing of zygotic split, dizygotic twins will be dichorionic in nearly all cases. However, because very rare cases of monochorionic dizygotic twins exist, dizygosity on NIPT alone very rarely does not confirm dichorionicity [62].

Other potentially significant sonographic findings — In addition to assessment of gestational age and chorionicity and amnionicity of twins, first trimester ultrasound examination may detect abnormalities associated with adverse outcome. These include crown-rump length discordance (which may be associated with aneuploidy or TTTS), enlarged nuchal translucency (which may be associated with aneuploidy, congenital anomalies, TRAP sequence, or TTTS), and some congenital anomalies. (See "Diagnosis and outcome of first-trimester growth delay", section on 'Discordant first-trimester fetal size in twin pregnancies' and "Increased nuchal translucency and cystic hygroma" and "Diagnosis and management of twin reversed arterial perfusion (TRAP) sequence".)

In the second and third trimesters, ultrasound is used to screen for congenital anomalies, Down syndrome, growth restriction, and disorders associated with monochorionic placentation. Screening for short cervical length is also performed by some providers, though evidence-based interventions are lacking among twin pregnancies with short cervical lengths. Proposed interventions have included vaginal progesterone or cerclage, which have mixed results in prospective studies. (See "Twin pregnancy: Routine prenatal care", section on 'Screening'.)

Labeling each twin — It is important to use a consistent strategy for identifying and labeling each twin over serial examinations in the second and third trimesters. In general, twin A is the presenting twin, and twin B is the nonpresenting twin. Since confusion can arise when the presenting twin seems to change positions, it is important to describe placental position and sex of each twin. In same-sex twins, each twin may be identified based on its orientation relative to the other twin: left or right lateral for twins positioned next to each other and top (fundal) or bottom (cervical) for twins positioned vertically. The presenting twin in laterally oriented twins may appear to change over time, but the bottom twin of vertically oriented twins is likely to remain the presenting twin throughout pregnancy [63]. Documentation of the sites of placental implantation (anterior, posterior, lateral) and of the sites and types of placental cord insertion (eg, marginal versus central, normal versus velamentous) is also useful.

Twins may not deliver in the order expected from antenatal ultrasound (termed perinatal switch), especially when delivered by cesarean.

PRENATAL CARE

The routine prenatal care of patients with twin pregnancies has some differences from the routine prenatal care of singleton pregnancies (eg, higher gestational weight gain, small differences in micronutrient supplementation, routine administration of preeclampsia prophylaxis, differences in choice of method for Down syndrome screening and the frequency and target of ultrasound monitoring). Prenatal care of twin pregnancies is reviewed in detail separately. (See "Twin pregnancy: Routine prenatal care".)

TYPES OF COMPLICATIONS

Vanishing twins — Early spontaneous reduction from twin to singleton pregnancy (ie, vanishing twin) is common, occurring in 7 to 36 percent of in vitro fertilization (IVF) twin pregnancies [64-66]. It is unclear if the rate is similar in

naturally conceived pregnancies, which are not routinely imaged from the earliest stages of pregnancy. Although some studies report that a vanishing twin increases the survivor's risk of low birth weight and a small for gestational age infant compared with pregnancies in which a singleton was conceived, others have reported equivalent risks of adverse outcome [64-73]. The discordance may be related to differences among studies in the gestational age range of the vanishing twin at demise and by differences in IVF techniques on perinatal outcomes. The demised twin can affect results of cell-free DNA testing when used to screen for the common fetal aneuploidies.

In general, the first trimester demise of a dichorionic twin has no negative affect on the surviving twin [74]. First trimester demise of a monochorionic twin may also have no effect on the co-twin; however, second and third trimester demise can have serious adverse effects. (See "Twin pregnancy: Management of pregnancy complications", section on 'Death of one twin'.)

Fetal complications

All twins — All twin pregnancies have higher rates of the following fetal complications than singleton pregnancies [75]:

- Growth restriction (see "Twin pregnancy: Routine prenatal care", section on 'Screening for fetal growth restriction and discordance' and "Twin pregnancy: Management of pregnancy complications", section on 'Growth restriction and discordance')
- Congenital anomalies (see "Twin pregnancy: Routine prenatal care", section on 'Screening for congenital anomalies' and "Twin pregnancy: Management of pregnancy complications", section on 'Growth restriction and discordance')
- Preterm birth (see "Twin pregnancy: Management of pregnancy complications", section on 'Preterm labor and delivery')

However, rates of postterm pregnancy and macrosomia are lower than in singleton gestations.

Monochorionic twins — The following fetal complications are of particular concern in monochorionic twin pregnancies and generally derive from the shared placental circulation [28-32]:

- **Twin-twin transfusion syndrome (TTTS)** – Unbalanced blood flow in anastomotic vessels along the equatorial plate of the shared placenta results in TTTS, which is characterized by oligohydramnios (including anhydramnios) in one amniotic sac and polyhydramnios in the other sac (table 1). First-trimester nuchal translucency >95th centile in one or both fetuses and crown-rump length discordance ≥10 percent in the first trimester appear to be modest predictors of future TTTS [76]. (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis" and "Twin-twin transfusion syndrome: Management and outcome".)
- **Twin anemia polycythemia sequence (TAPS)** – TAPS is a variant of TTTS in which one twin is anemic and the other twin is polycythemic. The prenatal diagnosis is based on the middle cerebral artery-peak systolic velocity (MCA-PSV) >1.5 multiples of the median (MoM) in one twin and <0.8 MoM in the other twin without amniotic fluid volume discordance (table 1). The disorder is caused by very small arteriovascular placental anastomoses that allow the slow unidirectional flow of blood from a donor (anemic) twin to a recipient (plethoric) twin. (See "Twin-twin transfusion syndrome and twin anemia polycythemia sequence: Screening, prevalence, pathophysiology, and diagnosis", section on 'Twin anemia polycythemia sequence'.)
- **Selective fetal growth restriction (sFGR)** – Selective growth restriction is variously defined as estimated weight of one twin below the 10th percentile or discordance in estimated twin weights greater than 25 percent:

Discordance = weight larger twin – weight smaller twin/weight larger twin

Selective growth restriction has been classified into three types (table 2). It is often due to unequal placental sharing (discordance in placental territory), but other factors can play a role (eg, umbilical cord insertion abnormalities, unequal splitting of the initial cell mass, imbalance in bidirectional flow between circulations) [77]. Selective growth restriction shares some features with TTTS and TAPS, but differential diagnosis is generally readily achieved (table 1). (See "Selective fetal growth restriction in monochorionic twin pregnancies".)

- **Twin reversed arterial perfusion sequence (TRAP)** – TRAP is a rare complication of monochorionic twins in which a living twin perfuses a nonliving (acardiac) twin through patent vascular channels. (See "Diagnosis and management of twin reversed arterial perfusion (TRAP) sequence".)

- **Single fetal demise** – The risk of a fetal death in monochorionic twins exceeds that in singletons and dichorionic twins. Of additional concern, a single fetal demise of one twin of a monochorionic pair can cause morbidity or mortality in the co-twin due to their shared placental circulation. In a retrospective series of 1000 consecutive twin pregnancies ≥24 weeks of gestation, the risk of single antepartum fetal death in monochorionic diamniotic twins was more than threefold higher than in dichorionic twins (3.6 versus 1.1 percent of twin pairs) and occurred in apparently normal twins monitored closely [78]. (See "Twin pregnancy: Management of pregnancy complications", section on 'Death of one twin'.)

- **Congenital anomalies** – Monochorionic twins have a higher rate of congenital anomalies than dichorionic twins and singletons. The anomalies have a high rate of concordance but can be discordant. (See "Twin pregnancy: Routine prenatal care", section on 'Screening for congenital anomalies' and "Twin pregnancy: Management of pregnancy complications", section on 'Discordant congenital anomalies'.)

Monoamniotic twins — In addition to the problems of monochorionic diamniotic placentation described above, the following fetal complications are of particular concern in monoamniotic twin pregnancies:

- **Intertwin cord entanglement** – Cord entanglement is common in monoamniotic twins and can lead to fetal death. (See "Monoamniotic twin pregnancy (including conjoined twins)", section on 'Cord entanglement'.)

- **Conjoined twins** – Conjoined twins are classified according to the anatomical site of union (eg, chest, head) with the suffix "pagus" (meaning fixed [eg, thoracopagus]). Findings on ultrasound include monoamnionicity, contiguous skin, shared organs, twins that stay in the same orientation to one another, fetal scoliosis, unusual limb positioning, and more than three vessels in the cord [79]. Associated congenital defects unrelated to the area of fusion are common, as is stillbirth. Detailed ultrasonography and echocardiography, possibly with additional magnetic resonance imaging, are essential to determine the extent of deformity, to counsel the parents about prognosis, and to prepare for possible postnatal surgical management [79-82]. Delivery of potentially viable infants is always by cesarean. (See "Monoamniotic twin pregnancy (including conjoined twins)", section on 'Conjoined twins'.)

Maternal complications — Although patients carrying twins are at higher risk for some adverse outcomes than those carrying singletons [83], chorionicity and amnionicity do not appear to impact this risk in most studies [84-87]. Some studies have reported a higher risk of pregnancy complications in twins conceived by in vitro fertilization, but data are inconsistent and the association may be due to infertility-related factors rather than assisted reproductive technology.

- **Maternal hemodynamic changes** – Twin pregnancy results in greater maternal hemodynamic changes than singleton pregnancy [88-91]. Individuals carrying twins have a 20 percent higher cardiac output and 10 to 20 percent greater increase in plasma volume than those with singleton pregnancy, which increases their risk of pulmonary edema when other risk factors are also present [88,89]. Physiologic anemia is common, even though red cell mass increases more in twin pregnancy than in singleton pregnancy. (See "Anemia in pregnancy".)

- **Gestational hypertension and preeclampsia** – Gestational hypertension and preeclampsia are more common in patients carrying twins (for each disorder: 13 percent in twins versus 5 to 6 percent in singletons) [86,92]. The

severe end of the spectrum (early severe preeclampsia and HELLP syndrome [Hemolysis, Elevated Liver enzymes, Low Platelets]) tends to occur more frequently in multiple than singleton gestations [92]. (See "Twin pregnancy: Routine prenatal care", section on 'Preeclampsia prevention' and "Twin pregnancy: Management of pregnancy complications", section on 'Preeclampsia'.)

- **Gestational diabetes** – Whether gestational diabetes is more common in twin pregnancies is unclear [93-97]. Screening, diagnosis, and management are similar to that in a singleton pregnancy. (See "Gestational diabetes mellitus: Screening, diagnosis, and prevention" and "Gestational diabetes mellitus: Glycemic control and maternal prognosis".)

- **Other** – Other maternal disorders observed more often in pregnant people with multiple gestations include pruritic urticarial papules and plaques of pregnancy (PUPPP), intrahepatic cholestasis of pregnancy, acute fatty liver of pregnancy, iron deficiency anemia, hyperemesis gravidarum, abruption, and thromboembolism [98-100]. The increased risk of thrombosis relates, at least in part, to the increased prevalence of antepartum hospitalization and cesarean delivery of these patients.

  - (See "Dermatoses of pregnancy".)
  - (See "Intrahepatic cholestasis of pregnancy".)
  - (See "Acute fatty liver of pregnancy".)
  - (See "Anemia in pregnancy".)
  - (See "Nausea and vomiting of pregnancy: Treatment and outcome".)
  - (See "Placental abruption: Pathophysiology, clinical features, diagnosis, and consequences" and "Placental abruption: Management and long-term prognosis".)
  - (See "Deep vein thrombosis in pregnancy: Epidemiology, pathogenesis, and diagnosis".)

MANAGEMENT OF COMPLICATIONS

(See "Twin pregnancy: Management of pregnancy complications".)

MANAGEMENT OF LABOR AND DELIVERY

In uncomplicated twin pregnancies, decision-making regarding the timing and route of delivery are based on chorionicity, amnionicity, and presentation of both twins. In complicated twin pregnancies, decision-making also considers the specific complication, as with singleton pregnancies. (See "Twin pregnancy: Labor and delivery", section on 'Timing of delivery' and "Twin pregnancy: Labor and delivery", section on 'Choosing the route of delivery'.)

Management of labor in twin pregnancies is generally similar to that in singleton gestations, but a prudent approach is to deliver all twin pregnancies in an operating room where cesarean delivery can be performed, if needed. Pediatric staff should be available for assisting the transition of each infant, including resuscitation if needed, and the facility should be able to provide the risk-appropriate level of care for the newborn infants. (See "Twin pregnancy: Labor and delivery", section on 'Management of labor' and "Management of normal labor and delivery".)

OUTCOME

Preterm birth rate

- Twin pregnancies have a higher preterm birth rate than singleton pregnancies and lower preterm birth rate than triplet pregnancies, as shown in the table (table 3).

- The risk of preterm birth (and death) in twins is affected by chorionicity and amnionicity, as shown in the table (table 4) [101].

Neonatal and infant morbidity and mortality

- Infant mortality in twins is significantly higher than that of singletons (table 5) [102].

- For a variety of reasons, neonatal morbidity and mortality tend to be lower in first-born than second-born twins, regardless of route of delivery. In a systematic review of observational studies, overall neonatal morbidity of first and second twins was 3.0 and 4.6 percent, respectively (odds ratio [OR] 0.53, 95% CI 0.39-0.70), and overall neonatal mortality was 0.3 and 0.6 percent, respectively (OR 0.55, 95% CI 0.38-0.81) [103].

  The higher risk of adverse neonatal outcome in second-born twins is likely related to lower birth weight; higher frequency of malpresentation, cord prolapse, and abruption; and a higher frequency of obstetric maneuvers at delivery [104-108]. These factors often lead to cesarean delivery of the second twin and explain, at least in part, the higher neonatal morbidity of the second twin following combined delivery (vaginal/cesarean; 19.8 percent) compared with vaginal delivery (9.5 percent; OR 0.55, 95% CI 0.41-0.74) or cesarean delivery (9.8 percent; OR 0.47, 95% CI 0.43-0.53) of both twins [103].

Additional information on newborn outcomes is available separately. (See "Neonatal complications, outcome, and management of multiple births" and "Neonatal complications, outcome, and management of multiple births", section on 'Outcome'.)

Maternal morbidity from delivery — Maternal complications at delivery are generally more common with twin than singleton pregnancies. In a large case-control study from France, the incidence of severe acute maternal morbidity in twins and singletons was 6.2 percent (197 of 3202, 95% CI 5.3-7.1) and 1.3 percent (2303 of 179,107, 95% CI 1.2-1.3), respectively, and the higher risk in twins remained after adjustment for confounders (adjusted OR 4.2, 95% CI 3.1-5.8) [109]. The increased risk was similar for both antepartum and intrapartum/postpartum complications and regardless of the underlying source of morbidity (severe hemorrhage, severe hypertensive complications, or other conditions).

In a pathology analysis, cesarean delivery itself was the attributable source of only 20.6 percent (95% CI 12.9-28.2) of the total risk of intrapartum/postpartum severe acute maternal morbidity associated with twin pregnancy. However, route of delivery did not appear to be an important risk factor for maternal morbidity in other studies. In the Twin Birth Study (n = 1398 pregnancies), the rate of death or serious maternal morbidity in patients randomly assigned to planned cesarean was similar to that of those assigned to planned vaginal delivery (7.3 versus 8.5 percent; OR 0.86, 95% CI 0.65-1.13) [110]. A large prospective study including over 8000 twin pregnancies also found that the rates of severe acute maternal morbidity were similar for patients who planned vaginal delivery and those who planned cesarean delivery (5.4 and 6.1 percent, respectively) [111]. Smaller, retrospective studies have reported inconsistent findings.

DETERMINING THE ZYGOSTIY OF SAME-SEX TWINS

Zygosity can be determined conclusively using detailed blood type or DNA markers [112].

It is of importance to parents and twins to know whether same-sex twins are monozygotic (in lay terms, "identical").

- If chorionicity is known, same-sex monochorionic twins are virtually always "identical," while same-sex, naturally conceived dichorionic twins are "identical" in 18 percent of cases. (See 'Relationship between chorionicity, amnionicity, and zygosity' above.)

- If chorionicity is not known, based upon a genotype and placental study of 668 consecutive twin pairs in Birmingham, England, parents of naturally conceived twins can be informed in the delivery room that 37 percent of all same-sex twins are "identical" [113].

These proportions do not apply to pregnancies conceived by in vitro fertilization (IVF), where twins usually result from double embryo transfer and implantation and are thus dizygotic. However, an embryo can divide after transfer, resulting in monozygotic twins. Interestingly, in IVF pregnancies, the rate of monozygotic twinning appears to be higher than in spontaneously conceived pregnancies (2.3 versus 0.4 percent of pregnancies) [114].

In addition, there are several reported cases of dizygotic twins with monochorionic placentation [54-56,115-117]. Blood studies in these twins demonstrate chimerism. The pathogenesis of monochorionic dizygotic twinning has not been explained but may be related to assisted reproductive technology (eg, in vitro culture environment, extended duration of culture, manipulation of the oocyte and sperm), although the occurrence has also been reported in naturally conceived pregnancies [116].

When counseling parents of monochorionic twins of discordant sex, the possibility of postzygotic loss of a Y chromosome in one 46,XY twin resulting in one 45,X and one 46,XY twin; rare cases of dizygotic twins with blood-chimerism; and a disorder of sexual differentiation in one of the twins should be addressed. Many cases of monochorionic dizygotic twins are probably unrecognized because the newborns have the same sex.

POSTPARTUM CARE

Postpartum care is similar to that for patients with singleton births. (See "Overview of the postpartum period: Normal physiology and routine maternal care" and "Overview of the postpartum period: Disorders and complications".)

Issues related to breastfeeding twins, newborn care, and family support are reviewed separately. (See "Neonatal complications, outcome, and management of multiple births".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Multiple gestation".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or email these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Having twins (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Diagnosis** – Routine ultrasound examination in the first or early second trimester is the best method to ensure early diagnosis of a twin pregnancy, establish an accurate gestational age, and determine chorionicity. (See 'Diagnosis' above and 'Sonographic diagnostic evaluation' above.)

- **Chorionicity** – The most reliable indicators of dichorionic twins are identification of two separate placentas and discordant fetal sex. If there is a single placental mass, chorionicity and amnionicity are determined by identification of an intertwin membrane and examination of this membrane for the twin peak or lambda sign (dichorionic twins), T sign (monochorionic/diamniotic twins), thickness (thick for dichorionic twins), and number of layers (four layers for dichorionic twins). (See 'Assessment of chorionicity and amnionicity' above.)

- Same-sex monochorionic twins are virtually always "identical," while same-sex dichorionic twins are "identical" in 18 percent of cases. If chorionicity is not known, parents of naturally conceived twins can be informed that 37 percent of all same-sex twins are "identical." (See 'Assessment of chorionicity and amnionicity' above and 'Determining the zygostiy of same-sex twins' above.)

- **Zygosity** – Dizygotic (fraternal) twins are more common than monozygotic (identical) twins (algorithm 1), approximately 70 and 30 percent of twins, respectively (in the absence of use of assisted reproductive technology). The prevalence of dizygotic twins varies among populations, whereas the prevalence of monozygotic twins is relatively stable worldwide at 3 to 5 per 1000 births. (See 'Prevalence' above and 'Relationship between chorionicity, amnionicity, and zygosity' above.)

- **Complications** – All twin pregnancies are at increased risk of preterm delivery, congenital anomalies, and growth restriction compared with singleton pregnancies, though twins are associated with lower rates of postterm pregnancy and macrosomia. Monochorionic twins are at significantly higher risk of adverse perinatal outcome than dichorionic twins (table 4). They are also at risk for unique pregnancy complications, such as twin-twin transfusion syndrome, twin anemia polycythemia sequence, twin reversed arterial perfusion sequence, and selective intrauterine growth restriction. Monoamniotic twins are at risk for cord entanglement and conjoined twins. (See 'Types of complications' above.)

- **Prenatal care** – The routine prenatal care of patients with twin pregnancies has some differences from the routine prenatal care of singleton pregnancies (eg, higher gestational weight gain, small differences in micronutrient supplementation, routine administration of preeclampsia prophylaxis, differences in choice of method for Down syndrome screening and the frequency and target of ultrasound monitoring). Prenatal care of twin pregnancies is reviewed in detail separately. (See "Twin pregnancy: Routine prenatal care".)

- **Delivery** – In uncomplicated twin pregnancies, decision-making regarding the timing and route of delivery are based on chorionicity, amnionicity, and presentation of both twins. In complicated twin pregnancies, decision-making also considers the specific complication, as with singleton pregnancies. (See "Twin pregnancy: Labor and delivery", section on 'Timing of delivery' and "Twin pregnancy: Labor and delivery", section on 'Choosing the route of delivery'.)

- **Outcome** – Early spontaneous reduction of one sac ("vanishing twin") has been reported in 15 to 36 percent of pregnancies conceived by in vitro fertilization. Rates of late fetal and infant death are shown in the table (table 4). Morbidity and mortality in twins is significantly higher than in singletons (table 5). (See 'Vanishing twins' above and 'Outcome' above.)

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Topic 6821 Version 151.0

GRAPHICS

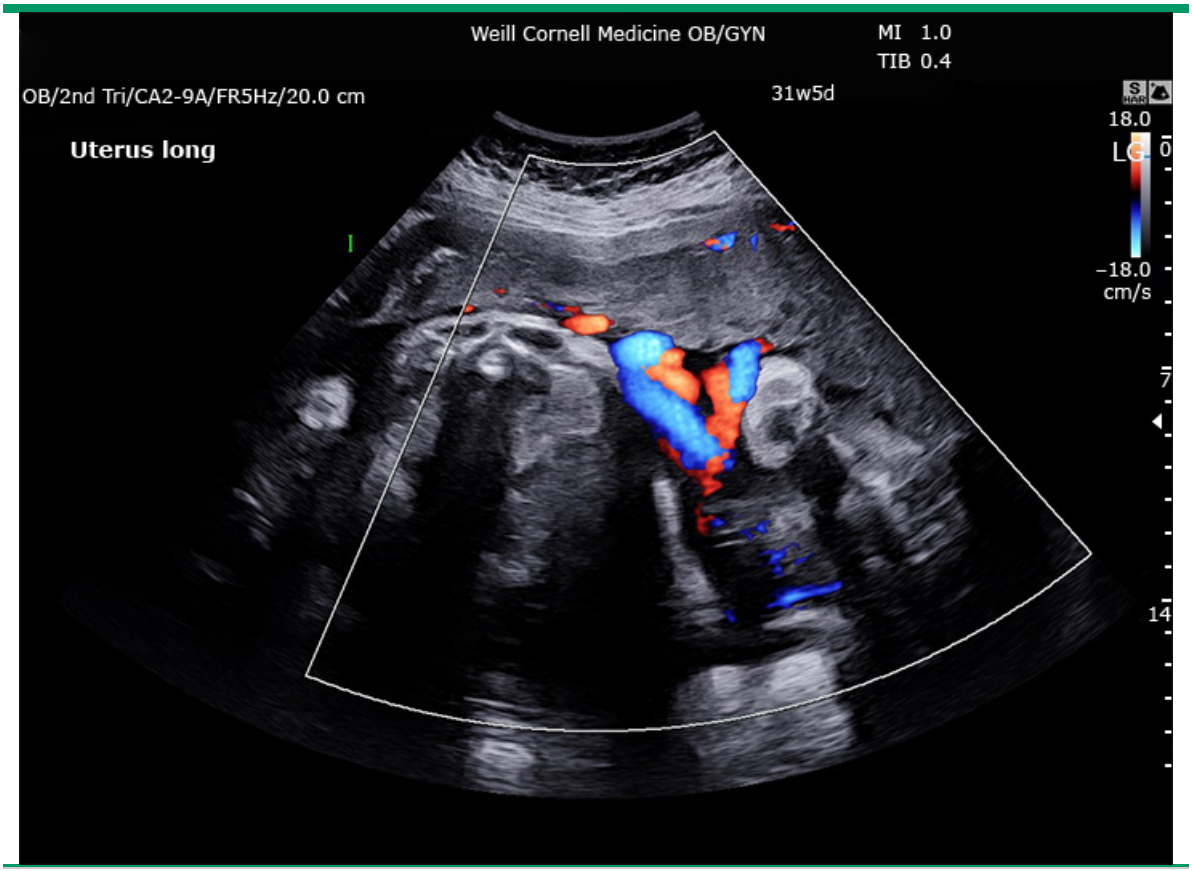
Dichorionic/diamniotic twin pregnancy with two separate placentas

Twin pregnancy at 18 weeks and 0 days gestation. The placenta of twin B (placenta B) is located anteriorly. The placenta of twin A (placenta A) is located posteriorly.

Courtesy of Stephen T Chasen, MD.

Graphic 131108 Version 2.0

Monochorionic/monoamniotic twins with cord entanglement

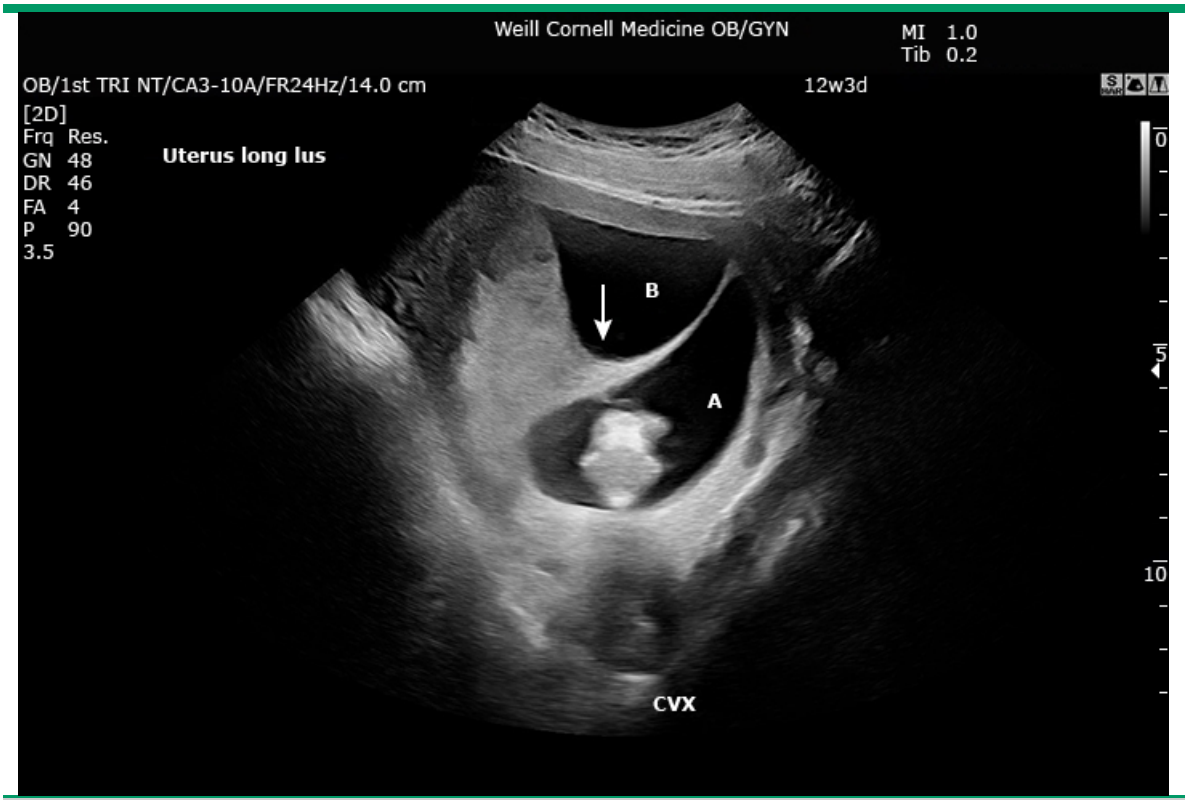


Longitudinal view of the uterus. Monochorionic/monoamniotic twins at 31 weeks and 5 days gestation with cord entanglement near the placental cord insertions demonstrated with color Doppler. Two different fetal heart rates (not shown) were identified in the adjacent loops of cord.

Courtesy of Stephen T Chasen, MD.

Graphic 131109 Version 2.0

Twin peak or lambda sign in twin pregnancy



The arrow points to a triangular projection of chorionic tissue emanating from fused dichorionic placentas and extending between layers of the intertwin membrane of a twin pregnancy at 12 weeks and 3 days gestation. This projection is characteristic of a dichorionic diamniotic twin pregnancy.

CVX: cervix.

Courtesy of Stephen T Chasen, MD.

Graphic 79928 Version 4.0

Thick intertwin membrane

The arrow points to a thick intertwin membrane separating the sac of twin A from the sac of twin B in a dichorionic/diamniotic twin pregnancy at 12 weeks and 6 days gestation.

Courtesy of Stephen T Chasen, MD.

Graphic 75595 Version 4.0

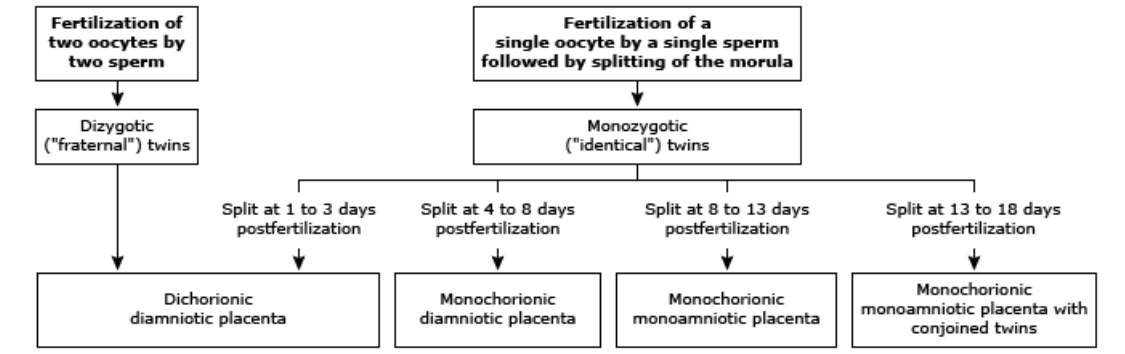
Monochorionic diamniotic pregnancy

Transverse view of the uterus. The arrow points to a thin intertwin membrane separating the sac of twin A from the sac of twin B in a monochorionic diamniotic twin pregnancy at 12 weeks and 0 days gestation.

Courtesy of Stephen T Chasen, MD.

Graphic 56124 Version 4.0

Relationship between zygosity and placentation in twins



Graphic 130827 Version 2.0

Similarities and differences among TTTS, TAPS, and sFGR on ultrasound examination of both twins

Ultrasound finding	TTTS	TAPS	sFGR
Fluid discordance	+++++ Oligohydramnios in one sac and polyhydramnios in the other sac	–	++ Oligohydramnios in the sac of the intrauterine growth restricted twin, normal amniotic fluid volume in the AGA twin
Growth discordance (>25% difference between twins)	++ 50% will have estimated fetal weight <10th percentile	+	+++++ 100% will have estimated fetal weight <10th percentile
MCA Doppler discordance (>1.5 MoM in donor/anemic **and** <0.8 MoM in recipient/plethoric)	++	+++++	+
Fetal bladder discordance	Small donor bladder and/or enlarged recipient bladder	–	–
Ductus venosus abnormalities	+++++	++	++
Fetal hydrops	+++++	+	–
Placental appearance: Donor side hyperechoic and thickened, recipient side normal	++	+++++	–

"+" signifies the prominence of the ultrasound finding. "–" signifies that the ultrasound finding is not associated with the diagnosis.

TTTS: twin-twin transfusion syndrome; TAPS: twin anemia polycythemia sequence; sFGR: selective fetal growth restriction; AGA: appropriate for gestational age; MCA: middle cerebral artery; MoM: multiples of the median.

Graphic 110205 Version 8.0

Diagnosis and classification of selective fetal growth restriction in monochorionic twins

Diagnosis: Estimated weight of one twin below the 10th percentile or discordance in estimated twin weights greater than 25%
Type 1: Normal/positive Doppler flow in the umbilical artery ▪ Mild intertwin weight discordance ▪ Usually favorable outcome for both twins: Very low risk of fetal demise of growth-restricted twin
Type 2: Absent/reversed end-diastolic flow in the umbilical artery ▪ Poorest prognosis: High risk of fetal demise of growth-restricted twin ▪ Mean gestational age at delivery: 29 weeks of gestation
Type 3: Intermittent absent/reversed end-diastolic flow in the umbilical artery ▪ Intermediate prognosis: 10 to 15% risk of fetal demise of growth-restricted twin ▪ Commonly survive to 32 weeks or more of gestation

Data from: Gratacos E, Ortiz JU, Martinez JM. A systematic approach to the differential diagnosis and management of the complications of monochorionic twin pregnancies. Fetal Diagn Ther 2012; 32:145.

Graphic 108170 Version 2.0

Gestational age and birth weight characteristics of United States singleton, twin, and triplet live births

	Singletons	Twins	Triplets
Number of births	3.6 million	120,291	3136
Average gestational age	38.51	35.04	31.66
Average birthweight	3286	2345	1681
Percent 34 weeks	2.1	19.96	62.9
Percent 37 weeks	8.47	60.87	98.5
Percent very low birth weight (<1500 grams)	1.09	9.40	34.10
Percent low birth weight (<2500 grams)	6.67	55.48	95.29

Adapted from: Martin JA, Hamilton BE, Osterman MJK, et al. Births: Final data for 2019. Natl Vital Stat Rep March 2021.

United States Department of Health and Human Services (US DHHS), Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS), Division of Vital Statistics, Natality public-use data 2016-2019, on CDC WONDER Online Database, October 2020. Accessed at http://wonder.cdc.gov/natality-expanded-current.html on May 27, 2021 3:33:16 PM

Graphic 60676 Version 7.0

Fetal and infant death rates in twin gestations (both fetuses alive at 20 weeks of gestation, n = 150,386)

Chorioamnionicity	Pregnancy loss <24 weeks (%)	Fetal or neonatal death ≥24 weeks (%)	Preterm birth <37 weeks with at least one live birth (%)	Preterm birth <32 weeks with at least one live birth (%)	Small for gestational age birth (%)
DC	2.3	1.0	48.6	7.4	31.2
MCDA*	7.7	2.5	88.5	14.2	37.8
MCMA	21.8	9.3	100	26.8	33.2

Pregnancy outcome data for 6225 twin pregnancies with two live fetuses at 11 to 13 weeks of gestation with no major abnormalities: 4896 DC pregnancies, 1274 MCDA pregnancies, and 55 MCMA pregnancies.

DC: dichorionic; MCDA: monochorionic diamniotic; MCMA: monochorionic monoamniotic

* 10% of these pregnancies underwent fetoscopic laser ablation for twin-twin transfusion syndrome or selective growth restriction; outcome data would have been poorer without this intervention.

Data from: Litwinska E, Syngelaki A, Cimpoca B. Outcome of twin pregnancy with two live fetuses at 11-13 weeks' gestation. Ultrasound Obstet Gynecol 2020; 55:32.

Graphic 66305 Version 5.0

Infant, neonatal, postnatal mortality per 1000 live births by plurality

	Infant deaths (birth to 1 year)	Neonatal deaths (birth to day 28)	Postneonatal (day 29 to 1 year)
Singletons	11.2	7.8	3.4
Twins	66.4	55.9	10.5
Triplets*	190.4	168.8	21.6

Calculated from US Vital Statistics, 1998 and from US Public Health Service. Healthy People 2000: National Health Promotion and Disease Prevention Objectives, DHHS Pub. No. (PHS)90-50212. Washington, DC: US Department of Health and Human Services, Public Health Service; 1990.

* Triplets and higher order multiple gestations.

Graphic 75320 Version 4.0

Contributor Disclosures

Stephen T Chasen, MD Nothing to disclose **Deborah Levine, MD** Nothing to disclose **Lynn L Simpson, MD** Nothing to disclose **Vanessa A Barss, MD, FACOG** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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