CHAPTER 30

Multiple Gestations

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KEY ABBREVIATIONS

Dichorionic	DC
Disseminated Intravascular Coagulation	DIC
Dizygotic	DZ
Estimated Fetal Weight	EFW
Fetal Fibronectin	FFN
Intrauterine Fetal Death	IUFD
Intrauterine Growth Restriction	IUGR
In Vitro Fertilization	IVF
Low Birthweight	LBW
Monochorionic	MC
Monozygotic	MZ
Multifetal Pregnancy Reduction	MPR
Necrotizing Enterocolitis	NEC
Neonatal Intensive Care Unit	NICU
Preterm Birth	PTB
Respiratory Distress Syndrome	RDS
Retinopathy of Prematurity	ROP
Selective Termination	ST
Transvaginal Cervical Length	TVCL
Twin–twin Transfusion Syndrome	TTTS
Twin Reversed Arterial Perfusion	TRAP
Very Low Birthweight	VLBW

The increase in multiple births during the past 30 years has been well documented, making multiple gestations one of the most common high-risk conditions encountered by obstetricians. The increase in multiples is due primarily to assisted reproduction technology but also in part to older maternal age at childbirth, which is a known risk factor for spontaneous dizygotic twinning. After years of rapidly increasing twin birth rates, the rates now seem to show signs of stabilizing. The twin birth rate rose 70% from 1980 to 2004. According to the most recent National Vital Statistics data, however, the twin rate remained stable between 2004 and 2006 at 32.1 per 1000. Likewise, rates of triplets and higher-order multiples increased by more than 400% during the 1980s and 1990s, reaching an all-time high in 1998 at a rate of 193.5 per 100,000. Since that peak, triplets and higher-order multiples have decreased by 20% to 30%, with the most recent available triplet rate at 143.4 per 100,000 and the quadruplet and higher-order birth rate at 9.89 per 100,000.[1] The apparent plateau of the twin birth rate and the decline of triplet and higher-order multiple births are likely due to refinements in assisted reproduction techniques and recommendations from the American Society for Reproductive Medicine to limit the number of embryos transferred during in vitro fertilization (IVF) procedures. Issues remain with the current use of ovulation-induction drugs.

ZYGOSITY AND CHORIONICITY

Twins can be either monozygotic (MZ) or dizygotic (DZ). Zygosity refers to the genetic makeup of the twin pregnancy, and chorionicity indicates the pregnancy's placental composition (Figure 30-1). **Chorionicity is determined by the mechanism of twinning and, in MZ twins, by the timing of embryo division. Early determination of chorionicity is vital because it is a major factor in determining obstetrical**

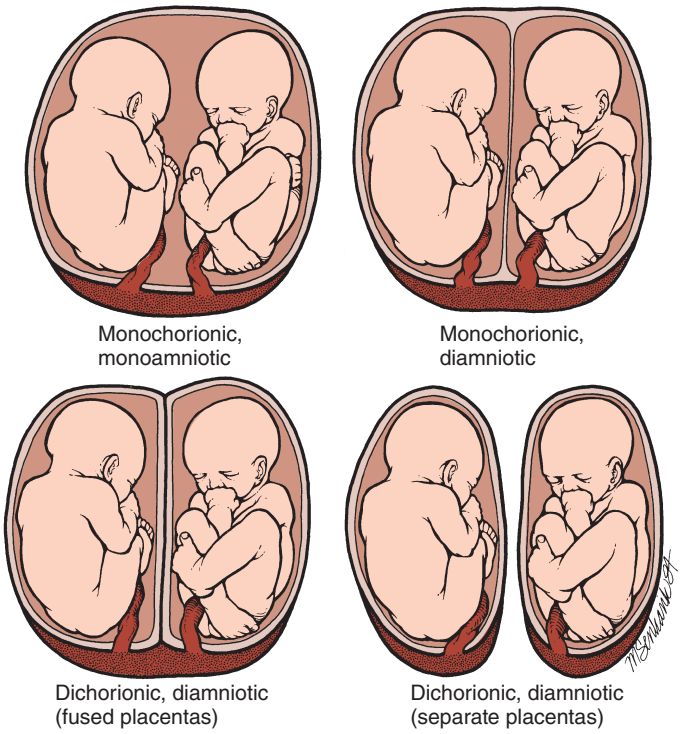

FIGURE 30-1. Placentation in twin pregnancies.

risks, management and outcomes. DZ twins, because they result from the fertilization of two different ova by two separate sperm, always develop a dichorionic, diamniotic placentation because each blastocyst generates its own placenta. An MZ twin pregnancy is created by the fertilization of one egg by one sperm and then subsequent spontaneous cleavage of the fertilized ovum. Thus, the type of placentation that develops is determined by the timing of this cleavage (Table 30-1).

MZ twins are at higher risk for adverse outcomes than are DZ twins. Not only do MZ twins have higher rates of anomalies than DZ twins, but they also deliver earlier, have a lower birthweight, and have higher rates of intrauterine and neonatal death. **However, several studies, including one by Carroll and colleagues using DNA analysis to confirm zygosity, have shown that monochorionicity, rather than monozygosity per se, is the determining factor.**[2] Since MZ dichorionic twins result from an earlier embryonic split, it is logical that they would have more complete separation, and thus fewer fetal anomalies and placental abnormalities, than twins in whom the embryonic split occurs later.

DISTRIBUTION AND CAUSES OF DIZYGOTIC VERSUS MONOZYGOTIC TWINNING

Among natural conceptions, DZ twins arise in about 1% to 1.5% of pregnancies and MZ twins occur in 1 in 250 pregnancies. Rates of spontaneous DZ twinning are greatly affected by maternal age, family history, and race. The risk for DZ twinning increases with maternal age, peaking at 37 years of age.[3] Maternal family history, particularly in first-degree relatives, also increases the chance of spontaneous DZ twinning; paternal family history contributes little or nothing to this risk. Finally, women of African descent have higher rates of DZ twinning than white women, who in turn have higher rates than women of Asian descent. For instance, in Japan, 1 in 250 newborns is a twin, whereas in Nigeria, 1 in 11 babies is a product of a twin gestation.[3]

TABLE 30-1 Determination of Monozygotic Twin Placentation

TIMING OF CLEAVAGE OF FERTILIZED OVUM	RESULTING PLACENTATION	PERCENTAGE OF MONOZYGOTIC TWINS
<72 hr	Diamniotic, dichorionic	25%-30%
Days 4-7	Diamniotic, monochorionic	70%-75%
Days 8-12	Monoamniotic, monochorionic	1%-2%
≥Day 13	Conjoined	Very rare

The causes of DZ twinning are much better understood than the causes of MZ twinning. DZ twins result from multiple ovulation, which is associated with higher maternal follicle-stimulating hormone (FSH) levels. FSH levels, and thus rates of DZ twinning, vary with season, geography, maternal age, and body habitus. Increases in DZ twins have been reported in summer months, locations with more daylight hours, and taller, heavier, and older mothers.[3]

The causes of MZ twinning are less clear. There are no naturally occurring animal models for MZ twinning, with the exception of armadillos, which produce MZ quadruplets or octuplets. However, MZ twinning has been induced by delayed fertilization in rabbits and by iatrogenic hypoxia in mice.[3] It has been proposed that MZ twinning in humans is a teratogenic event. Theories for MZ twinning in humans include fertilization of an "old" ovum with a more fragile zona pellucida or inadequate cytoplasm and with damage to the inner cell mass leading to two separate points of regrowth and splitting of the fertilized ovum.[3] **MZ twinning rates are constant across all variables, with the exception of assisted reproduction.** IVF and ovulation induction have been shown to produce higher rates of MZ twins. Against a spontaneous rate of 0.4% in the general population, studies have reported that the rate of MZ twinning may be more than 10-fold higher in pregnancies conceived by assisted fertility. One theory to explain these increased rates of MZ twinning is that injury to the zona pellucida may be responsible for the increased tendency toward iatrogenic zygote splitting.

DIAGNOSIS OF MULTIPLE GESTATIONS

Prenatal ultrasound is invaluable in the early diagnosis of a multiple gestation. Before the advent of routine prenatal ultrasound, many twins were not diagnosed until late in gestation or at delivery. **Using transvaginal ultrasound, separate gestational sacs with individual yolk sacs can be identified as early as 5 weeks from the first day of the last menstrual period and embryos with cardiac activity can**

TABLE 30-2 DETERMINATION OF CHORIONICITY AND AMNIONICITY IN FIRST-TRIMESTER PREGNANCIES

PLACENTATION	NO. OF GESTATIONAL SACS	NO. OF YOLK SACS	NO. OF AMNIOTIC CAVITIES
Dichorionic, diamniotic	2	2	2 (thick dividing membrane)
Monochorionic, diamniotic	1	2	2 (thin dividing membrane)
Monochorionic, monoamniotic	1	1*	1

*Although this is nearly always true, there have been case reports of two yolk sacs in early pregnancy in twins later confirmed to be monoamniotic.

usually be seen by 6 weeks. Retromembranous collections of blood or fluid or a prominent fetal yolk sac should not be confused with a twin gestation. Another entity that could be confused with a multiple gestation would be a singleton pregnancy with a separate pseudosac in a bicornuate uterus (or other anomaly with a second uterine horn, such as a unicornuate uterus with a rudimentary horn or a uterine didelphys). The sonographer must be compulsive in examining the entire uterine cavity in order to avoid underdiagnosing or overdiagnosing a multiple gestation.

Determination of Chorionicity

Accurate determination of chorionicity and amnionicity early in pregnancy is vital to optimal obstetrical care. A recent editorial argued that "there is no diagnosis of twins" but rather any twin gestation must be further described as either monochorionic or dichorionic.[4] **Knowledge of chorionicity is essential in counseling patients on obstetrical and neonatal risks because chorionicity is a major determinant of pregnancy outcome.** Furthermore, in some cases, precise knowledge of chorionicity is paramount. For instance, when contemplating selective reduction of a multiple gestation, incorrectly assuming dichorionicity when the pregnancy is in fact monochorionic could have tragic consequences.

Determination of chorionicity is easiest and most reliable when assessed in the first trimester. Between 6 and 10 weeks, counting the number of gestational sacs and evaluating the thickness of the dividing membrane is the most reliable method of determining chorionicity (Table 30-2). Two separate gestational sacs, each containing a fetus, and a thick dividing membrane strongly suggest a dichorionic diamniotic pregnancy, whereas one gestational sac with a thin dividing membrane and two fetuses suggests a monochorionic diamniotic pregnancy (Figure 30-2). For monochorionic gestations, the dividing amniotic membrane may be very difficult to visualize in the first trimester. However, with rare exceptions, the number of amniotic sacs will be the same as the number of yolk sacs, which are relatively easy to count in early gestation.

After 9 weeks, the dividing membranes become progressively thinner, but in dichorionic pregnancies, they remain thicker and easy to identify. At 11 to 14 weeks' gestation, sonographic examination of the base of the intertwin membrane for the presence or absence of the lambda or twin peak sign provides reliable distinction between a fused dichorionic and a monochorionic pregnancy. The twin peak sign is a triangular projection of tissue extending beyond the chorionic surface of the placenta (Figure 30-3). This tissue is insinuated between the layers of the intertwin membrane, wider at the chorionic surface, and tapering to a point at some distance inward from that surface. This finding is produced by extension of chorionic villi into the potential interchorionic space of the twin membrane at the place where it encounters the chorion and placenta of the co-twin. This space exists only in dichorionic pregnancies. The twin peak sign cannot occur in monochorionic placentation because the single continuous chorion does not extend into the potential interamniotic space of the monochorionic, diamniotic twin membrane.

After the early second trimester, determination of chorionicity and amnionicity becomes less accurate, and different techniques are used (Figure 30-4). The sonographic prediction of chorionicity and amnionicity should be systematically approached by determining the number of placentas and the sex of each fetus, and then by assessing the membranes that divide the sacs. Scardo and associates[5] found that, using these criteria, dichorionicity could be determined with 97.3% sensitivity and 91.7% specificity and monochorionicity with 91.7% sensitivity and 97.3% specificity in twin gestations first scanned at 22.6 ± 6.9 weeks. In some pregnancies with monochorionic, diamniotic placentation, the dividing membranes may not be sonographically visualized because they are very thin. In other cases, they may not be seen because severe oligohydramnios causes them to be closely opposed to the fetus in that sac. This results in a "stuck twin" appearance, in which the trapped fetus remains firmly held against the uterine wall despite changes in maternal position. In many cases, a small portion of the dividing membrane can be seen extending from a fetal edge to the uterine wall (Figure 30-5). Diagnosis of this condition confirms the presence of a monochorionic, diamniotic gestation, which should be distinguished from a monoamniotic gestation, in which dividing membranes are absent. In the latter situation, free movement of both twins, and entanglement of their umbilical cords, can be demonstrated.

Determination of Zygosity

If a twin set is monochorionic, monozygosity can be inferred. If twins are different genders, then with very rare anecdotal exceptions, they can be assumed to be DZ. **It is estimated that based on these two findings, about 55% of all twins' zygosity can be determined by examination of the babies and placentas.** Conversely, 45% of all twins (same sex, dichorionic twins) would need further genetic testing to determine zygosity.

MATERNAL AND FETAL RISKS OF MULTIPLE GESTATION

Maternal Adaptation to Multifetal Gestation

The degree of maternal physiologic adaptation to pregnancy is exaggerated with multiple gestation.[6] Levels of maternal progesterone, estriol, and human placental

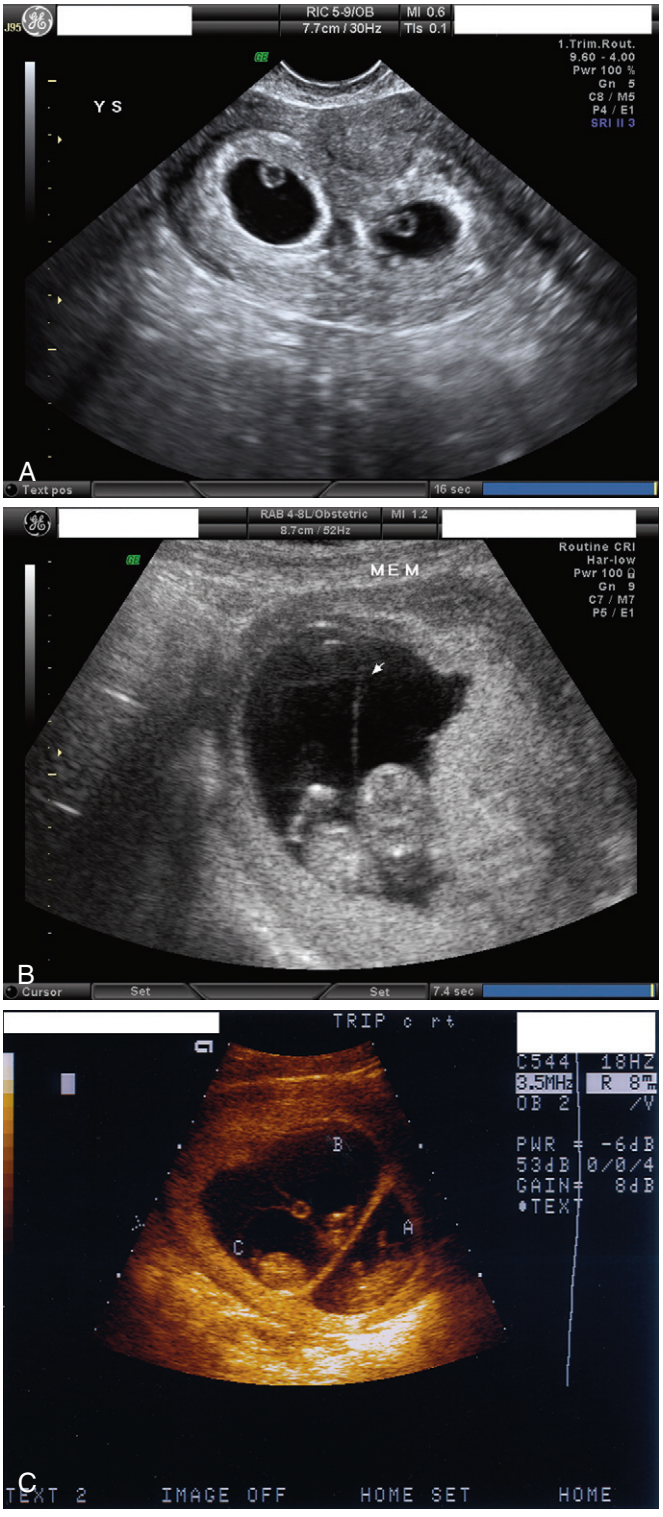

FIGURE 30-2. **A,** An early first-trimester dichorionic twin gestation. Note the clearly separate gestational sacs, each surrounded by a thick echogenic ring. **B,** A mid–first-trimester monochorionic, diamniotic twin pregnancy with a very thin, hairlike dividing membrane *(arrow)*. **C,** An early first-trimester image of a dichorionic, triamniotic triplet pregnancy. Note that monochorionic triplets B and C are separated by a very thin membrane, whereas triplet A, with its own placenta, is separated from B and C by a thick membrane.

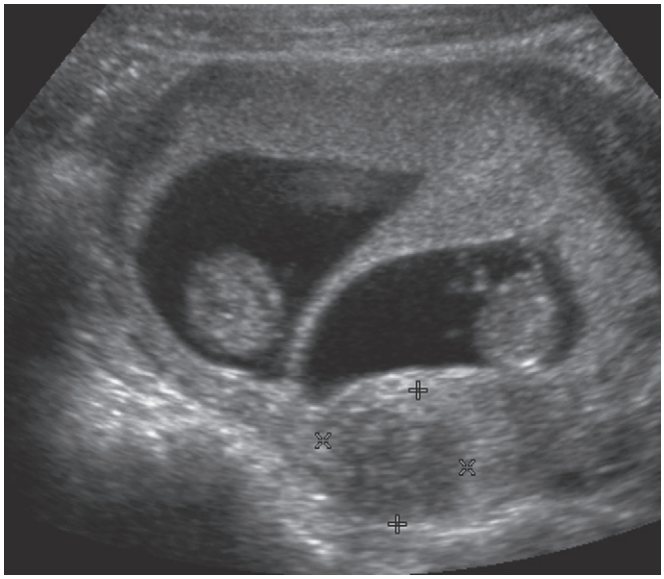

FIGURE 30-3. Twin peak sign in a dichorionic twin pregnancy with a fused anterior placenta.

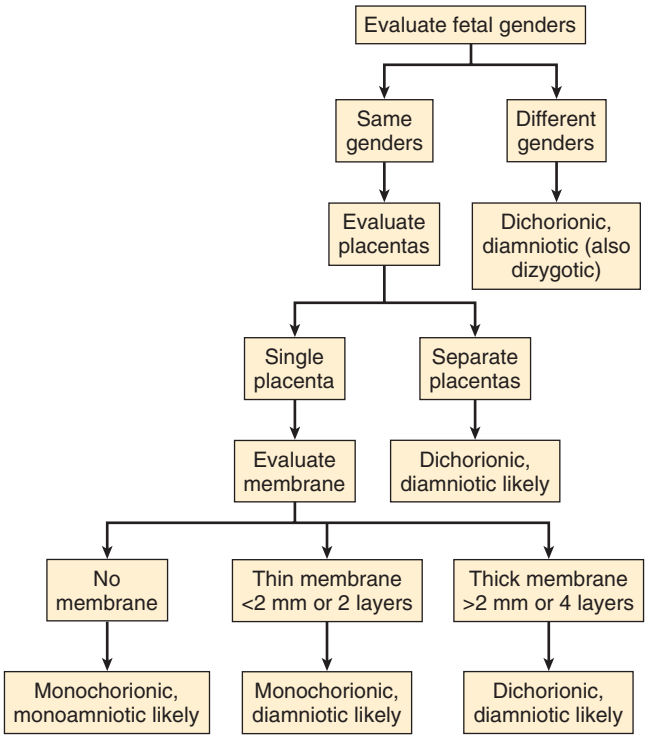

FIGURE 30-4. Algorithm for determination of chorionicity and amnionicity in the second and third trimesters.

lactogen are higher in multiple gestations than in singletons. This increase in human placental lactogen is thought to be the cause of the increased risk for gestational diabetes seen in multifetal pregnancies. Increased production of multiple placental proteins such as human chorionic gonadotropin may contribute to clinical conditions such as a greater risk for hyperemesis and complicates the interpretation of both first- and second-trimester maternal serum screening tests. Cardiovascular adaptations are also greater; both heart rate and stroke volume are increased

compared with singleton gestations, resulting in increased cardiac output. In addition to these cardiac changes, plasma volume expansion and total body water are increased in twin gestations. Partially as a consequence of increased total body water, colloid osmotic pressure is reduced. Clinical effects of the decreased colloid osmotic pressure are increased dependent edema as well as a heightened sensitivity to pulmonary edema, a risk that must be considered when tocolysis of a multiple gestation is contemplated.

Studies using dye excretion have suggested that hepatic clearance capacity is reduced in pregnancy in general, and more so in twin gestation.[6] As described previously, serum protein concentrations are decreased during pregnancy. Although this is partially due to increased total body water, there is likely some degree of reduced hepatic contribution of serum proteins, again more exaggerated in multifetal gestation compared with singleton pregnancy. Most obvious to patients, marked uterine changes also occur. By 25 weeks' gestation, the average twin gestation uterine size is equal to a term singleton pregnancy. By term, the total uterine volume is often 10,000 mL, and the weight of the uterus and its contents can exceed 8 kg.

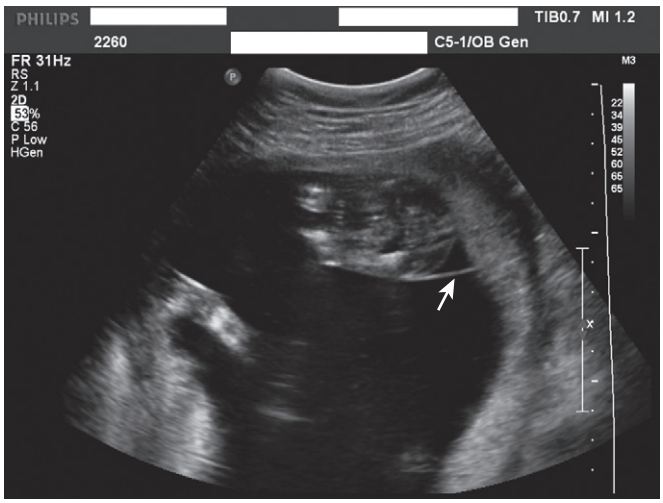

FIGURE 30-5. The donor twin "stuck" against the anterior uterine wall in a case of twin-twin transfusion syndrome. Note the small portion of membrane visible *(arrow)* extending from the edge of the fetus to the uterine wall.

Maternal Morbidity and Mortality

Rates of essentially every obstetrical complication, with the exception of macrosomia, are elevated with multiple gestations and in general rise proportionally to increasing plurality. Table 30-3 provides the relative risks for obstetrical complications in twin gestations compared with singletons.[7] In addition to the conditions listed in the table, multiples are associated with higher rates of gestational diabetes and rare but life-threatening conditions such as acute fatty liver and peripartum cardiomyopathy. **Additionally, women pregnant with multiples not only have higher risks for developing certain conditions but also are more likely to have more severe manifestations of those conditions.** For instance, Sibai and associates showed that not only are twin mothers more likely to develop preeclampsia (relative risk [RR], 2.62; 95% confidence interval [CI], 2.03 to 3.38), but also twin mothers with preeclampsia have higher rates of delivery before 37 weeks and before 35 weeks, as well as higher rates of placental abruption and small-for-gestational-age infants than singleton mothers with preeclampsia.[8] A large retrospective analysis of 24,781 singleton, 6859 twin, 2545 triplet, and 189 quadruplet pregnancies found an incidence of pregnancy-related hypertensive conditions of 6.5% in singletons, 12.7% in twins, and 20% in triplets and quadruplets. The risk for interventional delivery due to hypertensive complications also increased by plurality: about twofold higher in twins and threefold higher in triplets compared with singletons.[9] Atypical presentations of preeclampsia are also more common in multifetal gestations, especially higher-order multiples. One retrospective review of 21 triplet and 8 quadruplet pregnancies found that only half of the women who were delivered for preeclampsia had elevated blood pressures before delivery. Furthermore, proteinuria was present in only 3 of 16 women before delivery. Predominant presentations of preeclampsia in this series were laboratory abnormalities (chiefly elevated liver enzymes) and maternal symptoms.[10]

TABLE 30-3 MATERNAL COMPLICATIONS IN MULTIPLE GESTATIONS

	SINGLETON (*n* = 71,851) (%)	TWIN (*n* = 1694) (%)	RELATIVE RISK	95% CONFIDENCE INTERVAL
Hyperemesis	1.7	5.1	3.0	2.1-4.1
Threatened SAB	18.6	26.5	1.4	1.3-1.6
Anemia	16.2	27.5	1.7	1.5-1.9
Abruption	0.5	0.9	2.0	1.2-3.3
GHTN	17.8	23.8	1.3	1.2-1.5
Preeclampsia	3.4	12.5	3.7	3.3-4.3
Eclampsia	0.1	0.2	3.4	1.2-9.4
Antepartum thromboembolism	0.1	0.5	3.3	1.3-8.1
Manual placental extraction	2.5	6.7	2.7	2.2-3.2
Evacuation of retained products	0.6	2.0	3.1	2.0-4.8
Primary PPH (>1000 mL)	0.9	3.1	3.4	2.9-4.1
Secondary PPH	0.6	1.7	2.6	1.8-4.6
Postpartum thromboembolism	0.2	0.6	2.6	1.1-5.9

From Campbell DM, Templeton A: Maternal complications of twin pregnancy. Int J Gynecol Obstet 84:71, 2004.
GHTN, Gestational hypertension; *PPH*, postpartum hemorrhage; *SAB*, spontaneous abortion.

TABLE 30-4 BIRTH OUTCOMES FOR MULTIPLE GESTATIONS

	MEAN BIRTHWEIGHT (g)	GESTATIONAL AGE AT DELIVERY (wk)	DELIVERY <32 WEEKS (%)	LBW: <2500 g (%)	VLBW: <1500 g (%)
Singleton	3298	38.7	1.6	6.5	1.1
Twin	2323	35.2	12.1	57.2	10.2
Triplet	1655	32.0	36.3	95.4	34.8
Quad	1225	29.3	79.2	98	73.4

From Martin JA, Hamilton BE, Sutton PD, et al: Births: Final Data for 2006. National Vital Statistics Reports; Vol 57, No 7. Hyattsville, MD, National Center for Health Statistics, 2009.

One theory for the higher incidence of atypical preeclampsia in women with triplet and higher-order multiples is that the exaggerated hemodynamic changes found in higher-order multiples do not allow for the "typical" maternal manifestations of preeclampsia.

These increased maternal risks extend to life-threatening morbidity and even mortality. Multiple gestation has been found to be an independent risk factor for intensive care unit admission.[11] Finally, although fortunately still a very rare event, maternal death is also increased in multifetal gestations. A relative risk of 2.9 (95% CI, 1.4 to 6.1) for maternal death in women pregnant with multiples has been reported.[12]

Perinatal Morbidity and Mortality

Multifetal gestations carry significant perinatal risks. **Babies who are products of multiple gestations have higher rates of low birthweight, earlier gestational age at delivery, and higher rates of neonatal and infant death and cerebral palsy** (Table 30-4). One in eight twins and one in three triplets is born before 32 weeks' gestation, compared with only 2 in 100 singletons. Additionally, the risk for infant death is higher: 29.8 per 1000 for twins and 59.6 per 1000 for triplets, compared with 6 per 1000 for singletons.[1] Rates of cerebral palsy have been estimated as 4 to 8 times higher in twins than singletons and as much as 47 times higher in triplets.[13] Much of this increased risk is likely attributable to higher rates of preterm delivery and low birthweight in multiple gestations. Of note, although the overall rates of cerebral palsy are higher in twins than singletons, low-birthweight preterm twins do not have higher rates than like-weight, gestational age–matched singletons. Interestingly, however, most studies have demonstrated higher rates of cerebral palsy for twins born at term weighing more than 2500 g than for comparable singletons. This difference is mostly a reflection of the effect of monochorionicity on twin growth and development.

Fetal Anomalies

Fetuses in multiple gestations are known to be at increased risk for anatomic abnormalities, although the exact degree of risk is debated. The largest series available, an international study of more than 260,000 twins, found a relative risk for major anomalies of 1.25 (95% CI, 1.21 to 1.28). Anomalies were found in all organ systems.[14] This study, however, was not informed on zygosity or chorionicity, and most experts believe that much of the increased risk for structural anomalies in multiple gestation is associated with MZ twinning.

A 2009 population-based study from England found that rates of congenital anomalies were 1.7 times more frequent in twins compared with singletons (95% CI, 1.5 to 2.0) and that the relative risk for monochorionic twins was nearly twice that of dichorionic twins (RR, 1.8; 95% CI, 1.3 to 2.5).[15] A Taiwanese series of 844 twin sets compared with 4573 control singletons found a doubling of the relative risk of major congenital malformations in twins compared with singletons. When broken down by zygosity, the relative risks were 1.7 for DZ twins and 4.6 for MZ twins, with an anomaly prevalence of 0.6% for singletons, 1% for DZ twins, and 2.7% for MZ twins. Anomalies were concordant in 18% of the MZ twins but in none of the DZ twins.[16] Older studies have shown somewhat higher overall anomaly rates (both for singletons and twins) but found similar distributions. **Thus, the overall evidence supports an approximately twofold increased risk for congenital anomalies in twins versus singletons, with most of this risk occurring in MZ twins.**

There is a strong association between MZ twinning and midline defects. Nance[17] presents evidence to suggest that a group of birth defects involving midline structures, including symmelia, exstrophy of the cloaca, and midline neural tube defects, may be associated with the twinning process. Symmelia is a severe, rare defect that results from fusion of the preaxial halves of the developing hind limb buds, producing a single lower extremity with a knee that flexes in the opposite direction from normal. The incidence of this condition is 100 times higher in MZ births than in singletons. MZ twins have also been shown to have a higher frequency of neural tube defects than singletons, and they are usually discordant for the abnormality. Nance suggests that the MZ twinning process, with its attendant opportunities for asymmetry, cytoplasmic deficiency, and competition in utero, may favor the discordant expression of midline defects in these gestations.

ISSUES AND COMPLICATIONS UNIQUE TO MULTIPLE GESTATIONS

"Vanishing Twin"

The "vanishing twin" is a well-known obstetrical phenomenon. This term refers to the loss of one member of a twin (or other higher-order multiple) gestation early in pregnancy. This is typically either asymptomatic or associated with spotting or mild bleeding. Landy and colleagues reported on a series of 1000 first-trimester ultrasounds, with an incidence of twinning of just over 3%.[18] After confirming a twin gestation (two embryos with heartbeats), 21.2% ultimately delivered singletons. In general, if two gestational sacs are confirmed by the first-trimester ultrasound, the chance of delivering twins is 63% for women younger than 30 years and 52% for women 30 years or

older. If two embryos with cardiac activity are seen in the first trimester, the chance of a twin birth rises to 90% for women younger than 30 years and 84% for women 30 years or older.[19] Other investigators have shown that, not unexpectedly, the earlier the initial ultrasound, the greater the chance of a vanishing twin phenomenon. Additionally, monochorionic twin gestations are at a higher risk for either a vanishing twin or a complete pregnancy loss than are dichorionic twins. Again, it is important for sonographers to identify the presence of embryonic structures before making the diagnosis of a vanishing twin.

"Appearing Twin"

Another interesting entity is that of the "appearing twin." **An appreciable percentage of cases of multiple gestations may be missed between 5 and 6 weeks' gestation.** Doubilet and Benson reported on their experiences with appearing twins in pregnancies initially diagnosed as singletons.[20] They found that 14% of pregnancies later diagnosed as multiple gestation had been initially undercounted. Monochorionic twin gestations were far more likely than dichorionic to have been undercounted (86% vs. 11%). **The authors noted that pregnancy outcomes were no different for initially undercounted pregnancies than for those pregnancies correctly diagnosed on their initial ultrasound.** The entity of an appearing twin underlines once again the importance of a thorough ultrasonographic survey of the entire uterine cavity before diagnosing any pregnancy.

First-Trimester Multifetal Pregnancy Reduction

The increasing use of ovulation induction and assisted reproduction has resulted in a growing number of multifetal pregnancies with three or more fetuses. **Because the risk for pregnancy loss, preterm delivery, and long-term morbidity for children who are products of multiple gestations is directly proportional to the number of fetuses being carried, first-trimester multifetal pregnancy reduction has been advocated as a method to reduce the risk for prematurity and associated morbidity and mortality.** Currently, the method of choice is injection of a small dose of potassium chloride into the thorax of one or more of the fetuses, either transabdominally or transvaginally, under real-time sonographic guidance. The latter approach is used less frequently because it is associated with a greater infection risk and a higher loss rate than the former. In monochorionic pregnancies, the use of these techniques is contraindicated because of the vascular communications within the placenta.

Multifetal pregnancy reduction (MPR) is an outpatient procedure. It is usually performed between 11 and 13 weeks, and chorionic villus sampling (CVS) can safely be performed on some or all of the fetuses before the procedure to confirm karyotype if desired. Ultrasound is used to map the location of each fetus, nuchal translucencies should be measured, and prophylactic antibiotics are often administered. Any fetus appearing to be anatomically abnormal or small for gestational age, or known to have a karyotypic abnormality, is included among those that are reduced. If no abnormalities can be detected, generally the fetus or fetuses that are technically most accessible are chosen for reduction. Whenever possible, the fetus whose sac overlies the cervical os is not electively reduced, in order to minimize the risk for premature rupture of the membranes. Follow-up ultrasound examinations should be performed to confirm the success of the procedure and to monitor the growth of the remaining fetuses.

Evans and colleagues[21] published a series of 3513 completed first-trimester MPR procedures from 11 centers in five countries. The overall loss rate was 9.6%, but each of the participating centers showed significant improvement in this parameter as the operators developed more experience over time. Additionally, loss rates increased steadily from 4.5% to 15.4% as the number of starting fetuses rose from three to six or more. The rate of loss for those who reduced to twins was 6%, compared with 18.4% for those who were left with triplets.

Stone and colleagues[22] reported the outcome of 1000 consecutive patients undergoing MPR at a single institution. Similar to the Evans study, these investigators also demonstrated a learning curve with fewer complications with increasing experience. The unintended pregnancy loss with the first 200 patients was 9.5% but fell to 5.4% after 1000 patients. An updated 2008 report[23] of the most recent 1000 multifetal reductions at the authors' institution found that the overall unintended pregnancy loss rate had dropped to 4.7%. This loss rate is unlikely to drop further because it approximates the baseline risk for pregnancy loss with twins in general. The rates of loss in the original report were 2.5% for those who reduced from twins to a singleton and 12.9% for those who presented with six or more fetuses, but the rate was stable at 4.7% to 5.4% for women who started with either three, four, or five fetuses. The rates of loss were 16.7%, 5.5%, and 3.5% for those who reduced to triplets, twins, and singletons, respectively. Significantly, the mean gestational ages for surviving fetuses were 35.3 weeks and 33.5 weeks for twins and triplets, respectively, which is what would be expected if these women had naturally conceived that number of fetuses.

Although perinatal morbidity and mortality are clearly improved when pregnancies with quadruplets or greater are reduced to smaller numbers, the medical advantages of reducing triplets to twins remain debatable. A 2006 meta-analysis attempted to answer this question.[24] The authors analyzed data from 893 pregnancies beginning as triplets, of which 411 were expectantly managed and 482 underwent MPR to twins. The rate of pregnancy loss before 24 weeks was higher in the MPR group (8.1% vs. 4.4%; $P = .036$). However, this risk was offset by a lower risk for delivery between 24 and 32 weeks in the MPR group (10.4% vs. 26.7%; $P < .0001$). The authors calculated that 7 reductions are needed to prevent one delivery before 32 weeks, and the number of reductions that would cause one loss before 24 weeks was 26. Thus, reducing triplets to twins may be associated with overall improvements in outcome.

Because the majority of losses occur several weeks after the procedure, the period from 18 to 24 weeks should be one of heightened surveillance. It is also recommended that these patients not undergo second-trimester aneuploidy serum screening because maternal serum α-fetoprotein (AFP) levels are often significantly elevated as a result of the retained dead fetus. Because the

incidence of intrauterine growth restriction (IUGR) may be increased in the surviving fetuses after MPR procedures, serial sonographic growth assessment has been suggested. Additionally, women who have undergone MPR can have significant grief reactions, and their emotional status should be monitored carefully.

Discordance for Anomalies

When an anomaly is detected in a twin gestation, even in an MZ set, the co-twin is usually normal. The diagnosis of discordance for a major anatomic abnormality places the parents in an extremely difficult position. Management choices include the following:

1. Expectant management
2. Termination of the entire pregnancy
3. Selective termination of the anomalous fetus

Several issues should be considered when counseling patients about the management of a multiple pregnancy complicated by discordant anomalies. These include (1) severity of the anomaly, (2) chorionicity, (3) effect of the anomalous fetus on the remaining fetus or fetuses, and (4) the parents' ethical beliefs. It is important to counsel patients if conservative management could result in adverse outcomes for the healthy twin. Although not all study results are consistent, most show that in a twin pregnancy discordant for major fetal anomalies, the normal fetus is at increased risk for preterm delivery and low birthweight. Some studies have also shown a higher risk for mortality in normal co-twins of an anomalous fetus. The most recent paper, a population-based retrospective study of more than 3000 normal co-twins of fetuses with nonchromosomal structural anomalies compared with more than 12,000 control twins unaffected by structural anomalies, showed higher rates of preterm birth (both <37 and <32 weeks), low birthweight, and perinatal mortality in normal co-twins of an affected pregnancy.[25] Reasons for higher rates of preterm birth are unclear, but polyhydramnios associated with anomalies and maternal psychosocial stress from the diagnosis of a fetal anomaly are possible explanations.

Selective Termination of an Anomalous Fetus

Although multiple techniques have been used to effect selective termination (ST) of a single fetus in a multiple gestation, the most common approach in dichorionic gestations is intracardiac injection of potassium chloride.

Evans and collegues[26] reported the outcomes of 402 ST procedures from eight centers in four countries using ultrasound-guided intracardiac injection of potassium chloride. They reported successful delivery of one or more viable infants in greater than 90% of cases. There were no cases of disseminated intravascular coagulation (DIC) or serious maternal complication. Similarly, Eddleman and associates[27] reported favorable outcomes in 200 ST cases performed at one institution on 164 twins, 32 triplets, and 4 quadruplets. The median gestational age at the time of the procedure was 19 weeks, 6 days, with a range of 12 weeks to 23 weeks, 6 days. The indications included chromosomal abnormalities, structural anomalies, mendelian disorders, placental insufficiency, and cervical incompetence. The unintended pregnancy loss rate was 4%, but the losses were fivefold higher in triplets than in twins. The average gestational age at delivery was 37 weeks, 1 day, and 84% delivered after 32 weeks' gestation. Only 3.7% delivered at less than 28 weeks' gestation.

In monochorionic twins, ST is far more challenging. Ablation of the umbilical cord of the anomalous fetus is needed to avoid back-bleeding through communicating vessels, which may precipitate death or neurologic injury in the remaining normal co-twin. Furthermore, in this situation, a lethal agent injected into the anomalous twin could enter the circulation of its normal sibling. Most reported attempts at ST in monochorionic pregnancies without occlusion of all vessels in the abnormal twin's cord have resulted in the death of the second twin within a short time. The indications and technique for cord occlusion are reviewed later.

Immediate complications associated with ST procedures include selection of the wrong fetus, technical inability to accomplish the procedure, premature rupture of membranes, and infection with loss of the entire pregnancy. When the indication for ST is an abnormal karyotype diagnosed by amniocentesis or CVS, a sonographically identifiable marker may or may not be present. If the gender of the twins is different, or the affected fetus has a gross morphologic anomaly, the abnormal twin can be easily identified by sonography. However, in the absence of such visible signs, one must rely on information provided from the original diagnostic procedure, which frequently has been performed elsewhere and several days or weeks before the patient presents for ST. If accurate localizing information is lacking, fetal blood sampling with rapid karyotype determination should be performed to identify the abnormal fetus before ST is attempted. Furthermore, in all cases, a sample of aspirated fetal blood or amniotic fluid should be obtained from the terminated twin at the time of the procedure to confirm that the correct fetus has been terminated. Intracardiac potassium chloride injection without concomitant cord occlusion is contraindicated if dichorionicity cannot be confirmed.

Cord Occlusion for Selective Termination in Monochorionic Twins

Selective termination by cord occlusion can be considered in several circumstances involving monochorionic multiple gestations. **These include:**

1. **Severely discordant anomalies**
2. **Severely discordant growth with high risk for intrauterine fetal death (IUFD) at a previable or periviable gestational age**
3. **Twin reversed arterial perfusion (TRAP) sequence**
4. **Severe twin–twin transfusion syndrome (TTTS) with associated discordant anomaly or in cases in which laser ablation was precluded by position of the fetus and placenta**

Each of the above indications is discussed in more detail in corresponding sections of this chapter.

Bipolar coagulation is probably the most commonly used technique, although radiofrequency ablation, laser coagulation, and ligation of the cord have also been successful. The site for port insertion is chosen according to the position of the placenta, the amniotic sac of the target fetus, and its umbilical cord. Preferentially, the other sac is avoided. Sometimes amnioinfusion is necessary to expand

the target sac. Bipolar coagulation can be accomplished with either 3-mm or 2.4-mm forceps, according to the cord diameter. Under ultrasound guidance, a portion of the umbilical cord is grasped while avoiding direct contact with the placenta, fetus, or membranes. Usually coagulation is effective at 25 watts, as demonstrated by the appearance of turbulence and steam bubbles. Limiting energy avoids tissue carbonization and cord perforation. Doppler studies can confirm arrest of flow, but many operators nonetheless coagulate three sections. In monoamniotic twins, the umbilical cord is often transected to avoid cord entanglement.

Pregnancy outcomes for the surviving co-twin are relatively favorable after selective cord occlusion. Rossi and D'Addario recently published a review of the literature regarding umbilical cord occlusion in complicated monochorionic twin pregnancies.[28] They evaluated 12 studies totaling 345 cases of cord occlusion at median gestational ages between 18 and 24 weeks. PPROM complicated 22% of pregnancies (59% of which occurred within 4 weeks), and co-twin fetal demise was a complication in 15% of cases (79% within 2 weeks of surgery). The overall survival rate for the remaining twin was 79% and was higher for cases after 18 weeks (89%) than for those undergoing the procedure earlier than 18 weeks (69%), regardless of the indication. Survival rates were 86% after radiofrequency ablation, 82% after bipolar cord coagulation, 72% after laser, and 70% after cord ligation. Long-term follow-up was not available for most studies, but in one series, the incidence of developmental delay was 8% in 67 infants older than 1 year who underwent evaluation by a pediatrician.[29]

Intrauterine Fetal Death of One Twin

IUFD of one twin occurs most commonly during the first trimester. This phenomenon is known as a vanishing twin and was discussed earlier in this chapter. Although it may be associated with vaginal spotting, the loss of one conceptus in the first trimester is often not clinically recognized, and the prognosis for the surviving twin is generally excellent. Single IUFD of one fetus in a multiple gestation in the second or third trimesters is much less common, complicating about 0.5% to 6.8% of twin pregnancies, but it can have more severe sequelae for the surviving fetus.[30] Monochorionic twins are at increased risk for a single fetal death, as are twins with a structural anomaly. In triplet pregnancies, studies have reported single IUFD rates between 4.3% and 17%.[30] In higher-order multiples, demise of a single fetus may be even more common.

The etiology of IUFD in a multiple pregnancy may be similar to that for singletons or be unique to the twinning process. Death in utero may be caused by genetic and anatomic anomalies, abruption, placental insufficiency, cord abnormalities such as a velamentous insertion, infection, and maternal diseases, including diabetes and hypertension. In diamniotic monochorionic pregnancies, IUFD may result from complications of TTTS. In addition, monoamniotic twins are at increased risk for cord entanglement and subsequent IUFD. Just as in singletons, however, the etiology of many IUFDs remains elusive.

Single IUFD in a multiple gestation can adversely affect the surviving fetus or fetuses in two ways: (1) risk for multicystic encephalomalacia and multiorgan damage in monochorionic pregnancies, and (2) preterm labor and delivery in both dichorionic and monochorionic twins.

Multicystic encephalomalacia results in cystic lesions within the cerebral white matter distributed in areas supplied by the anterior and middle cerebral arteries and is associated with profound neurologic handicap (Figure 30-6). The risk for this following single IUFD in a monochorionic pregnancy may be greater than 20% for the surviving co-twin.[31]

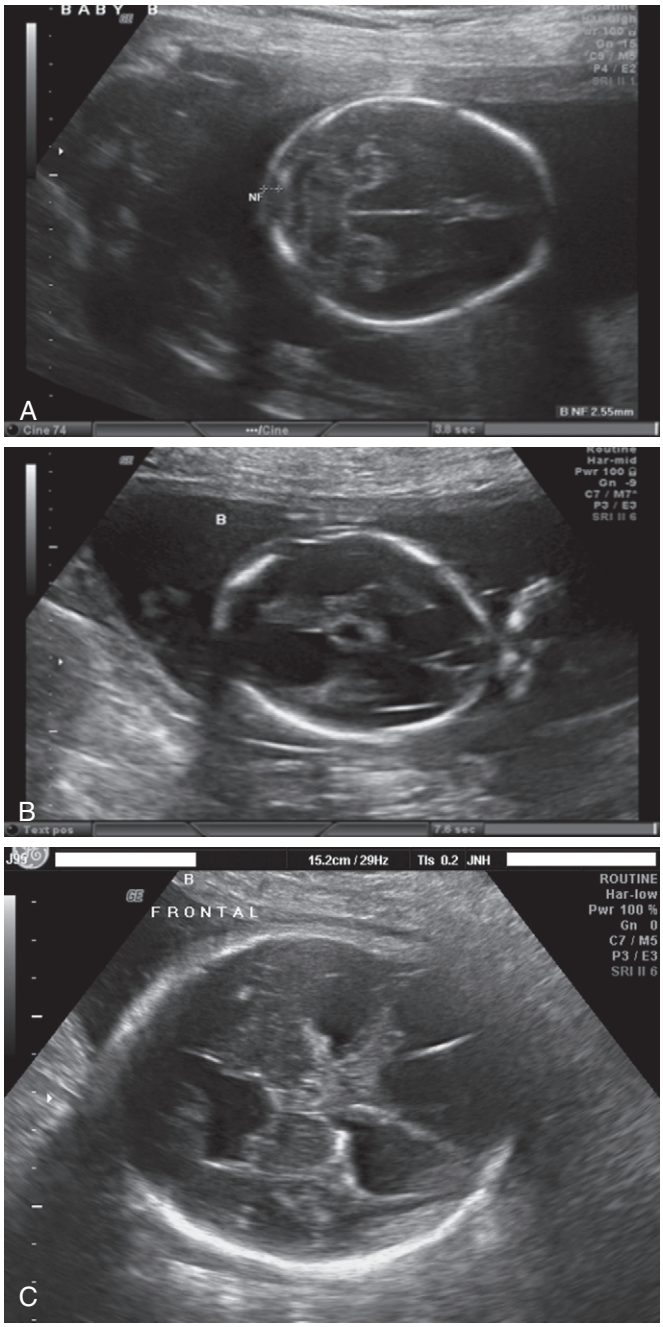

FIGURE 30-6. Ultrasound of the fetal brain of a monochorionic twin before **(A)** and after **(B, C)** intrauterine fetal death of the co-twin at 20 weeks' gestation. Note the normal brain anatomy in **A,** the dilation and cystic changes shortly after the co-twin's demise in **B,** and finally the residual irregular hydrocephalus and parenchymal loss 12 weeks later in **C.**

Two theories exist to explain this neurologic injury in the surviving co-twin in a monochorionic pregnancy. The first theory is that the deceased fetus produces thromboplastic substances, which traverse the vascular communications between the twins and cause infarcts and a DIC-like picture. The second and more widely accepted hypothesis is that significant hypotension at the time of demise of the co-twin causes neurologic injury in the surviving fetus. After death of the first twin, the resulting low pressure in that twin's circuit causes blood from the survivor to back-bleed rapidly into the demised twin through placental anastomoses. This can be thought of as an acute form of TTTS. If the resulting hypotension is severe, the surviving twin is at risk for ischemic damage to vital organs. Because the injury is coincident with the IUFD, rapid delivery of the co-twin following single IUFD in a monochorionic pregnancy will not improve the outcome.

It is unclear how early in gestation the death of one fetus in a monochorionic pregnancy can cause adverse sequelae for the surviving co-twin. Until relatively recently, it was thought that intrauterine demise in a monochorionic twin gestation could not cause neurologic injury to a co-twin until at least the mid-second trimester. However, in 2003 Weiss and coworkers reported a case of injury to a fetus after IUFD of the co-twin at about 13 weeks. Multicystic encephalomalacia was diagnosed by ultrasound and magnetic resonance imaging (MRI) in the co-twin at about 20 weeks.[32] The patient was counseled regarding the poor prognosis and opted for termination. Multicystic encephalomalacia was confirmed pathologically, although the exact timing could not be determined.

In addition, the IUFD of one twin can result in preterm delivery in both monochorionic and dichorionic pregnancies. Carlson and Towers[33] reported that 76% of 17 twin pregnancies complicated by IUFD of one fetus were delivered before 36 weeks and 41% were delivered at less than 32 weeks. The most common reason for early delivery was spontaneous labor, followed by abnormal fetal testing. The average interval from diagnosis to delivery was 16 days. Another series of 32 twin pregnancies complicated by single IUFD after 20 weeks followed by expectant management found strikingly similar numbers; the rate of delivery before 37 weeks was 81.3%, and delivery before 32 weeks occurred in 41.6% of the patients.[34] The median interval between diagnosis and delivery was 11 days. Of note, mothers with a single IUFD do not appear to be at increased risk for infection due to a retained twin demise. Cesarean delivery rates appear to be increased in these patients, often because of non-reassuring fetal status of the living twin. Dystocia caused by the dead fetus may also occasionally occur.

The determination of chorionicity is important for the counseling and management of patients with a single IUFD. Optimally, this has been established early in pregnancy. If, however, it has not been done before the IUFD, an attempt should be made to determine the chorionicity by ultrasound examination when the demise is discovered. Sonographic evaluation may not establish chorionicity with absolute certainty in some of these cases, and when the diagnosis is in doubt, DNA studies of amniocytes may be considered.

The optimal treatment for IUFD in multiples is not well established owing to the paucity of reported cases. To date, recommendations have been based on case reports, case series, and expert opinion. Referral to a tertiary care perinatal unit is advised when one fetus in a multifetal gestation has died in utero. In some of these cases, labor will already have started, and in others, coexisting maternal illness or placental abruption may make it necessary to expeditiously deliver the surviving fetus or fetuses. Clinical management depends on the gestational age, fetal lung maturity, or detection of in utero compromise of the surviving fetus or fetuses. The goal is to optimize outcome for the survivor while avoiding unnecessary or extreme prematurity and its potential adverse sequelae. It should be emphasized that close surveillance, even with reassuring antenatal testing, after the diagnosis of single IUFD in a monochorionic twin gestation cannot guarantee a good outcome for the surviving fetus.

Patients with monochorionic placentation should be counseled about the risk for multicystic encephalomalacia if an IUFD of one twin occurs after viability has been reached. It is difficult to predict which surviving monochorionic twins will develop cerebral injury. The nonstress test and biophysical profile give insight into the fetus' physiologic status but may not reflect subtle central nervous system changes. Ultrasound examination of the fetal brain may be suggestive of multicystic encephalomalacia but cannot definitively rule it out. Antenatal MRI of the fetal brain is investigational at this time but appears to be useful in detecting multicystic encephalomalacia in utero. As a consequence, we currently offer fetal MRI to all patients with monochorionic placentas approximately 2 to 3 weeks after the demise of one fetus has been detected. Although it is uncertain if normal MRI definitively rules out brain abnormalities, it is a reassuring sign. A single course of antenatal corticosteroids is recommended if premature delivery is anticipated and the gestational age is between 24 and 34 completed weeks. Surviving offspring are monitored with weekly biophysical profiles and nonstress tests.

The 2011 NICHD and SMFM workshop on timing of indicated late-preterm and early-term birth addressed the issue of single IUFD in a twin pregnancy. If the IUFD occurs at 34 weeks or beyond, delivery can be considered.[34a] Vaginal delivery is not contraindicated, and cesarean delivery is reserved for routine obstetric indications. At delivery, umbilical cord gas measurements should be performed. Autopsy should be offered for the stillborn fetus but may not be helpful if the demise has occurred several weeks earlier. Pathologic examination of the placenta is recommended. In addition, the pregnancy history should be communicated to the pediatricians caring for the neonate.

If IUFD occurs prior to 34 weeks, timing of delivery should be individualized based on other fetal or maternal issues.[34a] If, for instance, IUFD occurs at 18 weeks, delivery at term is likely the best option in the absence of any other complications, whereas a 33-week IUFD may warrant delivery between 34 and 37 weeks. Fetal surveillance should be considered once viability has been achieved. Monochorionic pregnancies complicated by IUFD before viability are more challenging. It is recommended that these patients be counseled regarding the

risk of multiorgan injury, including multicystic encephalomalacia. Ultrasound imaging and fetal MRI can be helpful in making the diagnosis. Some patients may opt to terminate the entire pregnancy, whereas others will choose expectant management. Once the surviving co-twin reaches viability, these women should be managed according to the recommendations described earlier.

Besides fetal risks, there may be maternal risks associated with IUFD in a multiple pregnancy. For example, there is a theoretical possibility of maternal consumptive coagulopathy in twin pregnancies complicated by a single IUFD. It was originally estimated that there was a 25% incidence of maternal DIC when a dead fetus was retained in a multiple gestation. However, only a few isolated cases of laboratory changes consistent with a subclinical coagulopathy have been reported under these circumstances, and this 25% incidence is certainly an overestimation.[30] It is also reassuring to note that no cases of clinically significant coagulopathy have been reported in the extensive literature on ST and MPR. When IUFD occurs in a multiple pregnancy, we recommend baseline maternal hematologic studies including a prothrombin time, partial thromboplastin time, fibrinogen level, and platelet count. If these values are within normal limits, many experts do not perform serial laboratory surveillance, given the very low risk for coagulopathy.

The occurrence of IUFD causes feelings of loss, sadness, anxiety, and guilt. In women with twins and an IUFD of one of the fetuses, bereavement may be underestimated by physicians because there is a shift in focus to the living offspring. As a result, we suggest that patients with a multiple pregnancy complicated by IUFD of one fetus be offered psychological or bereavement counseling, or both.

Twin–Twin Transfusion Syndrome

Etiology

TTTS is exclusively a complication of diamniotic monochorionic pregnancies. **It occurs in about 15% of monochorionic gestations and is thus the most common severe complication specific to this type of twinning.** TTTS is characterized by an imbalance of fetal blood flow through communicating vessels across a shared placenta, leading to underperfusion of the donor twin and overperfusion of the recipient (Figure 30-7). The donor twin develops IUGR and oligohydramnios, whereas the recipient experiences volume overload with polyhydramnios and potentially cardiac failure and hydrops. On echocardiography, the recipient demonstrates decreased ventricular function, tricuspid regurgitation, and cardiomegaly.[35] These cardiac abnormalities often progress during pregnancy and persist into the neonatal period. In response to the increased blood volume, the recipient also becomes hypertensive and produces increasing amounts of atrial and brain natriuretic peptides. Resulting polyhydramnios leads to uterine overdistention and increased uterine pressure, both of which may contribute to an increased risk for preterm labor and preterm premature rupture of membranes.

The syndrome can present at any gestational age. However, earlier onset is associated with a much poorer prognosis. The transfer of blood can occur in small increments chronically over the course of the pregnancy, or it can be acute. If untreated, the reported mortality rates range from 80% to 100% (Figure 30-8). Furthermore, if one fetus dies in utero, the surviving twin is at risk for death or multiorgan damage from acute exsanguination due to back-bleeding into the demised co-twin. This organ damage frequently includes severe neurologic compromise. Even if both twins survive, the pathophysiology of TTTS can still result in adverse neurologic sequelae in one or both twins.

Although all monochorionic twins share vascular anastomoses and thus exist in a state of constant intertwin transfusion, as noted earlier, only a minority develop TTTS. The following mechanism has been proposed to explain this observation. In monochorionic placentas, there can be three types of vascular communications: arteriovenous (AV), arterioarterial (AA), and venovenous (VV). AA and VV anastomoses are typically superficial, bidirectional anastomoses on the surface of the chorionic plate. AV anastomoses, usually referred to as deep anastomoses, involve a shared cotyledon, receiving arterial supply from one twin and draining on the venous side to the other twin. All these anastomoses are identifiable at the chorionic surface, a feature that allows laser ablation of these anastomoses as a treatment of TTTS. Superficial anastomoses, especially those that are AA, are crucial for maintaining bidirectional flow. **According to this hypothesis, the absence of adequate superficial AA and VV anastomoses, which help maintain balanced blood flow, is the mechanism underlying TTTS.**

Diagnosis and Staging

The diagnosis of TTTS is made antenatally by ultrasound. Many experts recommend ultrasound examinations every 2 weeks beginning at 16 weeks' gestation in monochorionic twins in order to allow early detection of TTTS. The four requirements, none of which is pathognomonic, include (1) the presence of a single placenta, (2) same-gender fetuses, (3) significant weight discordance, and (4) significant amniotic fluid discordance, often with a "stuck twin." The most important criterion in diagnosing TTTS is disparity in the amniotic fluid volume. The maximal vertical pocket should be less than 2 cm for the donor twin and greater than 8 cm for the recipient twin. The differential diagnosis of a stuck twin includes selective uteroplacental insufficiency, structural or chromosomal abnormality (i.e., renal agenesis), abnormal placental cord insertion, intrauterine infection, and rupture of the amniotic membranes for one twin.

A staging system for TTTS was developed in 1999 by Quintero and colleagues to categorize disease severity and to standardize comparison of different treatment results.[36] The Quintero staging system is depicted in Table 30-5.

Although Quintero staging is widely used and has proved enormously useful in our evolving understanding of TTTS, many experts have noted its limitations. Stage does not always progress; nor do patients, when they do worsen, always progress sequentially through the stages. For instance, a pregnancy can become stage 5 (fetal death) without progressing through stage 4 (hydrops). Several investigators have commented on the relatively frequent

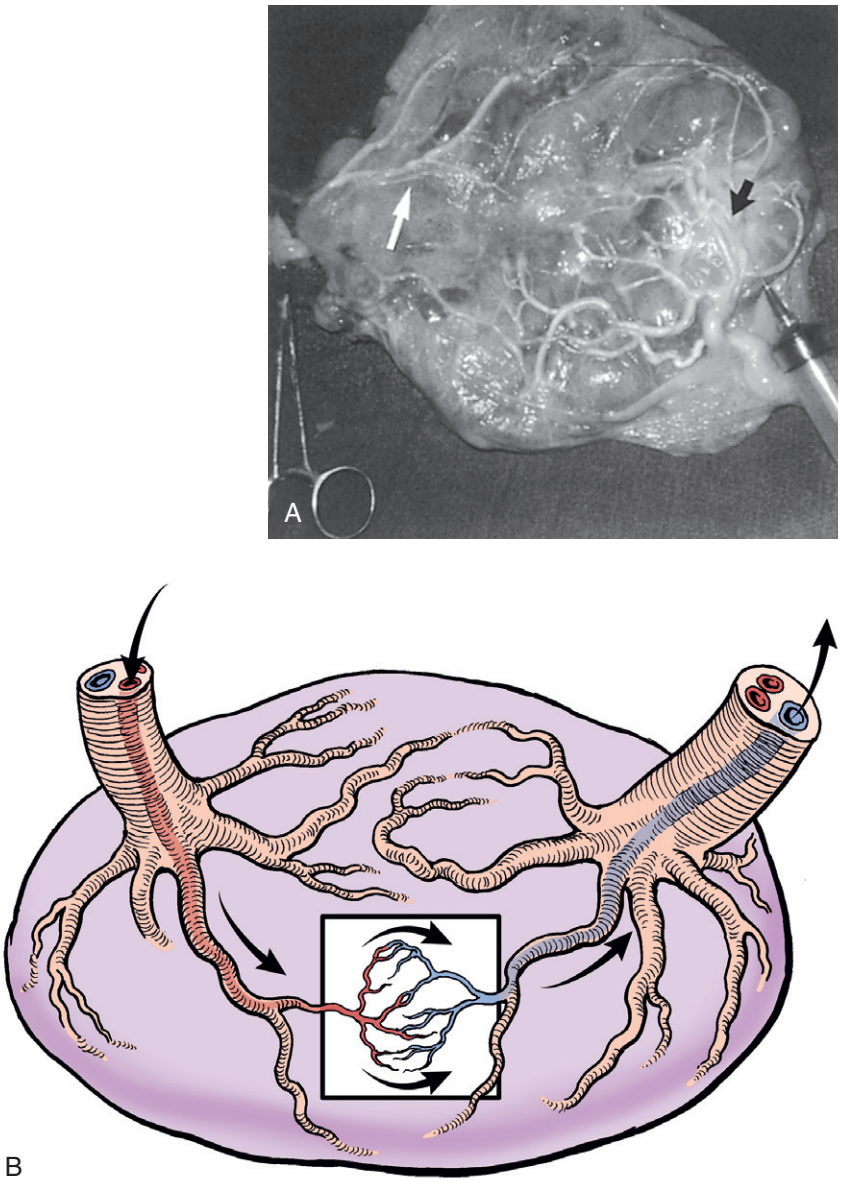

FIGURE 30-7. A, The placenta of a pregnancy complicated by twin-twin transfusion syndrome. Milk has been injected into an artery on the donor side of the placenta *(black arrow)*. It can be seen returning through the venous circulation on that side but is also evident in the venous circulation of the recipient *(white arrow)*. **B,** The arteriovenous shunt shown in **A.**

TABLE 30-5 QUINTERO STAGING FOR TWIN-TWIN TRANSFUSION SYNDROME

Stage I	Oligohydramnios, polyhydramnios sequence. Donor twin bladder visible.
Stage II	Oligohydramnios, polyhydramnios sequence. Donor twin bladder not visible. Doppler scan normal.
Stage III	Oligohydramnios, polyhydramnios sequence. Donor twin bladder not visible, and Doppler scans abnormal (absent or reversed end-diastolic velocity in the umbilical artery, reversed flow in the ductus venosus, or pulsatile flow in the umbilical vein).
Stage IV	One or both fetuses have hydrops.
Stage V	One or both fetuses have died.

occurrence of TTTS fetuses with Doppler abnormalities but a still visible fetal bladder in the donor. This has been referred to as an atypical stage III. Taylor and associates conducted a prospective observational study to validate the Quintero staging system's ability to predict perinatal outcomes. The study included 52 consecutive cases of TTTS that were either managed expectantly or treated with methods other than laser ablation. They found that only 45% of pregnancies progressed to a more advanced Quintero stage, and stage at presentation did not have a significant influence on survival. However, a progressive worsening of Quintero stage did predict worse outcomes. The authors concluded that Quintero staging does have a role in charting disease progress, but the stage at presentation does not accurately predict ultimate outcome.[37]

Several modifications of Quintero staging have been proposed, incorporating the differences in cardiovascular pathophysiology between donors and recipients, which is not accounted for in the Quintero staging system. None of these proposed staging alternatives, however, has been validated in prospective studies. The Cincinnati Modification categorizes all pregnancies in which the recipient exhibits cardiomyopathy (as assessed by AV valvular incompetence, ventricular wall thickness, and

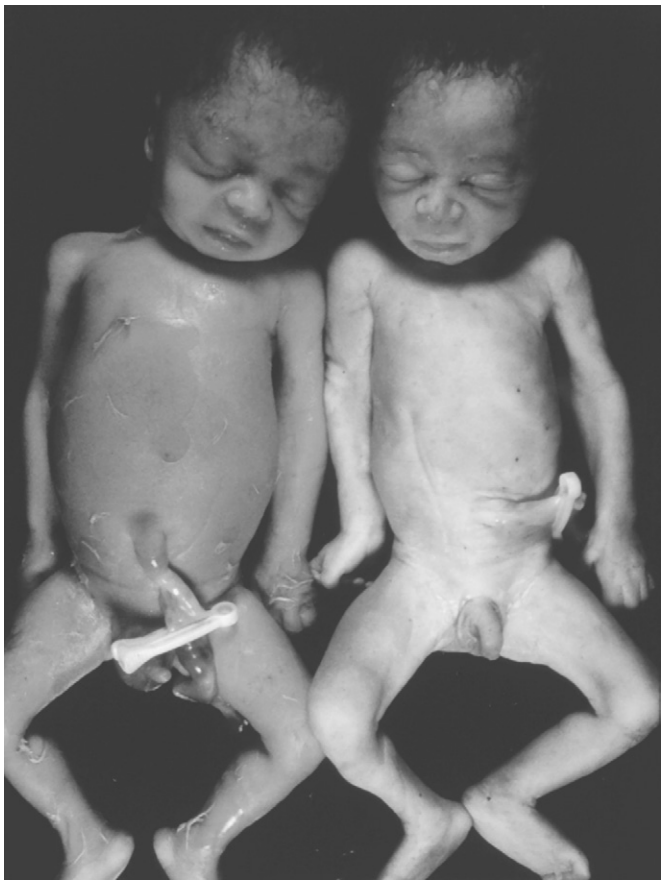

FIGURE 30-8. Stillborn male twins at 31 weeks' gestation, secondary to twin-twin transfusion syndrome. The plethoric twin on the left weighed 1670 g, and the anemic growth-restricted twin on the right weighed 1300 g.

ventricular function) as stage III. Furthermore, this modification stratifies stage III into those with abnormal Doppler scans, those with mild to moderate cardiomyopathy, and finally those with moderate to severe cardiomyopathy.[38] A 2009 meta-analysis designed to determine the efficacy of Quintero staging in patients treated with laser ablation did not find a statistically significant difference in survival by initial Quintero stage, but there was a consistent, although nonsignificant, trend toward lower survival as the stage increased. The authors proposed a new "double" staging system, one for donors and one for recipients, focused on the different pathophysiology of TTTS in donors and recipients.[39] Other parameters that have received attention as potential criteria in predicting severity and prognosis in TTTS are first-trimester discrepancy in twin nuchal translucencies (thicker in the future recipient), intertwin hemoglobin discordance (as determined by middle cerebral artery Doppler scans), amniotic fluid markers of renal and cardiac function, and presence or absence of AA anastomoses.[40]

Management

Expectant management is generally not recommended in TTTS because of the poor perinatal outcomes associated with the disorder. **However, management depends on the gestational age at diagnosis and, despite the previously mentioned limitations, on the severity of the clinical findings.** When TTTS is diagnosed after 26 to 28 weeks, conservative management may be the appropriate decision. This would include serial fetal assessment and control of polyhydramnios as needed. On the other hand, when the diagnosis is made in the early to mid-second trimester, aggressive management is generally advised. However, in patients with apparent mild stage I disease, a 1- to 2-week trial of conservative management may be warranted, mainly to confirm the correct diagnosis and assess for progression. Although medical management with digoxin and indomethacin has been attempted, there is limited evidence for success, and current treatment for severe TTTS requires physical intervention. There are three main management options: (1) serial amnioreduction, (2) amniotic septostomy, and (3) laser ablation of the anastomoses. All three options are discussed separately next.

Serial Amnioreduction

In serial reduction amniocentesis, an 18-gauge spinal needle is placed into the polyhydramniotic sac under ultrasound guidance. Amniotic fluid is withdrawn until the fluid volume returns to normal (i.e., deepest vertical pocket <8 cm). Because of the large amount of fluid to be removed, attaching the needle to a closed-system vacuum container is more practical than withdrawing fluid manually. Amnioreduction is repeated as often as necessary to maintain a near-normal amniotic fluid volume. The mechanism by which this procedure restores the amniotic fluid balance is unknown. Removing excessive fluid from the sac with polyhydramnios may result in decreased pressure on the sac with oligohydramnios. This, in turn, may result in increased placental perfusion to the stuck twin, especially through thin-walled superficial venous anastomoses with secondary improvement in its amniotic fluid volume. Additionally, normalizing the amniotic fluid may help prolong pregnancy by relieving uterine overdistention and pressure on the cervix.

Although there are no prospective studies comparing serial amnioreduction to conservative management, based on observational data amnioreduction does appear to offer a twofold to threefold increase in overall survival compared with no intervention. The exception may be late-onset (third-trimester) stage I TTTS that remains stable over a 1- to 2-week observation period. A large retrospective study using the International Amnioreduction Registry to analyze 223 sets of twins with TTTS diagnosed before 28 weeks' gestation and treated with serial amnioreduction found a live birth rate of 78%. Sixty percent of the original 446 babies were alive 4 weeks after birth. IUFD of at least one twin occurred in 31% of the pregnancies, and in 14% of cases, IUFD of both babies occurred. Of those babies alive 4 weeks after birth, 24% of the recipients and 25% of the donors had abnormal findings on cranial imaging. Poor prognostic factors for survival were earlier gestational age at diagnosis, presence of absent end-diastolic flow in the umbilical arteries, hydrops, low birthweight, and earlier gestational age at delivery. Complications within 48 hours (spontaneous rupture of the membranes, spontaneous delivery, fetal distress, fetal death, and placental abruption) occurred in 15% of patients.[41]

Septostomy

Amniotic septostomy is another management option. In this procedure, a 20-gauge spinal needle is inserted through the dividing membrane under ultrasound guidance. Amnioreduction of the polyhydramniotic sac is generally performed concomitantly. The amniotic fluid then sometimes equilibrates across the disrupted membrane. Similar to serial amnioreduction, the mechanism of action of this technique is unclear. It is possible that the defect in the membranes and reaccumulation of fluid in the donor sac allow the donor to swallow a sufficient volume of fluid to augment its circulating blood volume, secondarily increasing its urine output. The only randomized trial of amnioreduction versus septostomy for the treatment of TTTS was terminated early after enrollment of 73 women because the rate of survival of at least one infant was similar in both groups (78% vs. 80%; $P = .82$). The major advantage seen with septostomy was that women randomized to the septostomy group were more likely to require only a single procedure for treatment (64% vs. 46%; $P = .04$).[42] Because septostomy could functionally create an iatrogenic monoamniotic pregnancy with its own inherent complications and risks, the procedure has been criticized. Likewise, comparing amnioreduction to septostomy is challenging because both procedures use amnioreduction, and, alternatively, serial amnioreduction can be complicated by inadvertent septostomy.

Laser Therapy

Laser ablation of placental anastomoses is a third invasive treatment option that has been used to treat TTTS (Figure 30-9). In the United States, the use of laser therapy to treat TTTS is restricted to gestations earlier than 26 weeks. **Unlike both serial amnioreduction and septostomy, which would be considered palliative procedures, laser ablation is the only therapeutic option that aims to correct the underlying pathophysiologic aberration causing TTTS. Additionally, because laser ablation interrupts the vascular anastomoses between the fetuses, it has the advantage of being protective of the surviving twin should one twin succumb in utero.** In this procedure, first described by De Lia, the strategy is to ablate all anastomosing vessels that might connect the fetuses using either Nd:YAG, KTP, or diode laser and 400- to 600-mm fibers in a nontouch technique. The procedure is performed percutaneously under local or regional anesthesia. An endoscopic cannula is inserted into the amniotic cavity of the recipient fetus under ultrasound guidance at an angle perpendicular to the presumed vascular equator. The positions of the fetuses, umbilical cord insertions, and placenta are mapped. Initial landmarks include both umbilical cord insertions and the intertwin membrane. The operator visualizes the entire vascular equator and coagulates all visible anastomoses. Sections of about 1 to 2 cm are coagulated with pulses of 3 to 4 seconds, the duration judged by tissue response. Arteries are distinguishable from veins because they have a darker color and pass over the veins. Reduction amniocentesis is simultaneously performed. When the placenta is anterior, operative conditions are more difficult. Special instruments have been proposed, including curved sheaths, flexible endoscopes, and a double insertion technique. Most centers hospitalize patients for 1 or 2 postoperative days, and many experts use periprocedure tocolytics and antibiotics.

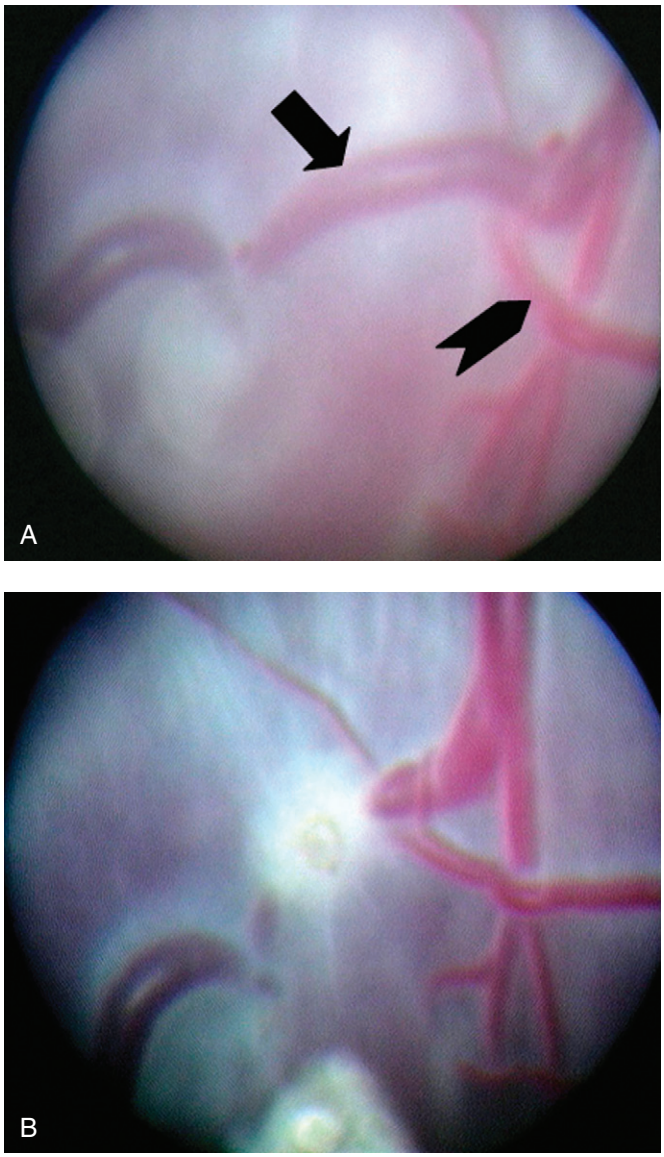

Figure 30-9. **A,** An artery from one twin going to a cotyledon, which is drained by a vein returning to the co-twin *(arrow)*. The cotyledon is also perfused by a small artery from the co-twin *(arrowhead)* and drained by a large vein going also to the co-twin. To preserve this cotyledon for the co-twin, the arterial perfusion to the cotyledon from the other twin is interrupted by laser photocoagulating the other artery. **B,** The effect of photocoagulation. (Courtesy Timothy M Crombleholme, MD, University of Cincinnati College of Medicine.)

Outcomes after Laser Therapy

In general, laser ablation has been shown to be a more effective technique than serial amnioreduction. In 2004, Senat and colleagues published the results of the European prospective multicenter randomized controlled trial of endoscopic laser (semiselective technique) versus serial amnioreduction for the treatment of severe TTTS between 15 and 26 weeks' gestation.[43] As the result of an interim analysis demonstrating a significant benefit for the laser group, the study was stopped after 142 patients had been

treated. Compared with the amnioreduction group, the laser group had a higher likelihood of survival of at least one twin to 28 days of life (76% vs. 56%; $P = .009$) and 6 months of age (76% vs. 51%; $P = .002$). The median gestational age at delivery was significantly more advanced in the laser group than in the amnioreduction group (33.3 vs. 29.0 weeks; $P = .004$). Neonates from the laser group also had a lower incidence of periventricular leukomalacia and were more likely to be free of neurologic deficits at 6 months of age (52% vs. 31%; $P = .003$). The authors concluded that endoscopic laser coagulation of anastomoses is a more effective first-line treatment than serial amnioreduction for severe TTTS diagnosed before 26 weeks' gestation. Although this study did include patients in Quintero stages I to IV, most (90% of the laser group and 91% of the amnioreduction group) were stage II or III.

A National Institute of Child Health and Human Development (NICHD)-sponsored prospective randomized multicenter trial is the only other randomized clinical trial comparing amnioreduction to fetoscopic laser photocoagulation.[44] That trial, in which all patients were Quintero stages II to IV, was stopped early after only 40 patients, mainly because of recruitment difficulties but also because of concern about a trend toward adverse fetal outcomes affecting the recipient twin in the laser arm. Analysis of the 40 patients treated before termination of the study showed no difference, either for donors or recipients, in the primary outcome of 30-day neonatal survival (55% in both arms for donors, and 45% vs. 30% in the amnioreduction vs. laser arms for recipients; $P > .5$). There was an increased *fetal* mortality rate for recipients in the laser group, and this was more pronounced in Quintero stages III and IV disease. The overall conclusion of these investigators was that the trial had not conclusively demonstrated the superiority of either treatment modality, although the results were limited by the small sample size.

Subsequently, both a Cochrane review and another meta-analysis comparing laser therapy with serial amnioreduction supported the role of laser therapy in the treatment of severe TTTS. The Cochrane review found a decreased risk for perinatal and neonatal death (odds ratio [OR], 0.59; 96% CI, 0.4 to 0.87, and OR, 0.29; 95% CI, 0.14 to 0.61, respectively) as well as a higher incidence of survival without neurologic handicap at 6 months of age (OR, 1.66; 95% CI, 1.17 to 2.35) with laser therapy compared with amnioreduction. The review concluded that laser therapy should be considered in all stages, although further research is needed in stages I and II.[45] The meta-analysis by Rossi and colleagues[46] found an advantage of laser therapy in improving overall survival (OR, 2.04; 95% CI, 1.52 to 2.76), decreasing neonatal death (OR, 0.24; 95% CI, 0.15 to 0.4), and decreasing neurologic morbidity (OR, 0.2; 95% CI, 0.12 to 0.33) compared with serial amnioreduction.

Short-term complications of laser ablation include abruption, rupture of membranes, IUFD, and labor. In Senat's trial, there was a 1% to 12% risk for each of these complications in both the laser and amnioreduction groups. Rates of IUFD, pregnancy loss, and preterm premature rupture of the membranes (PPROM) within 7 days of the procedure were 1.5- to 5-fold higher in the laser group, although these differences did not reach statistical significance.[43] In the NICHD trial,[44] incidence of PPROM before 28 weeks was 4.8% in the laser arm and 0% in the amnioreduction arm. Maternal complications are not consistently reported in the literature. However, no maternal deaths have been reported in all of the TTTS laser therapy literature, and serious complications such as pulmonary edema or blood transfusion appear to be very rare.

A few papers have studied the long-term neurologic outcomes of babies treated in utero with laser ablation for TTTS. Banek and associates studied all 89 surviving infants of pregnancies treated with laser surgery at their institution between 1995 and 1997. The children underwent neurodevelopmental testing at a median age of 21 months. Normal development was seen in 78%, minor deficiencies in 11%, and major deficiencies in 11%. There was a nonsignificant trend toward normal outcome for those infants who were born as both surviving twins, as opposed to babies born following the intrauterine death of their co-twin.[47] In a more recent report, Lopriore and colleagues followed up 278 surviving babies from 212 pregnancies treated with laser ablation at three European centers between 2000 and 2005. The children underwent neurologic, mental, and psychomotor development testing at age 2 years. The overall incidence of neurodevelopmental impairment at 2 years of age was 18%, and cerebral palsy was diagnosed in 6% of the children. Risk factors associated with neurodevelopmental impairment were greater gestational age at laser surgery, lower gestational age at birth, lower birthweight, and higher Quintero stage.[48]

The current consensus is that laser ablation of vascular anastomoses is the optimal therapy for Quintero stages II to IV disease before 26 weeks' gestation. Controversy, however, exists as to the optimal management of stage I disease. This controversy is based on several observations. First, the prognosis for stage I patients can be quite good without laser surgery. In a series by Taylor and colleagues, 70% of stage I patients treated with either expectant management, amnioreduction, or septostomy remained stable or regressed.[37] O'Donoghue and colleagues reviewed all cases of TTTS at their institution between 2000 and 2006 and identified 46 cases presenting with stage I TTTS, all of which were treated either expectantly or with amnioreduction. They found that 70% either remained stable or regressed.[49] On the other hand, recent studies have shown that even in stages I and II TTTS, the recipient can suffer cardiac dysfunction, something not taken into account by the commonly used Quintero staging system. Michelfelder and associates examined echocardiographic parameters of 42 TTTS patients, of whom 14 were stage I.[50] Of the stage I patients, 57% had ventricular hypertrophy, and 14% had AV valve dysfunction. Because it has been shown that cardiac dysfunction in the recipient improves after laser therapy but not after amnioreduction, this suggests that laser therapy may be the better choice in select patients presenting with Quintero stage I TTTS.[51] A single retrospective study published in 2009 directly compared outcomes in stage I patients treated with laser surgery versus conservative management. Of 50 women presenting with stage I TTTS, 40% underwent laser surgery, and 60% were managed either expectantly, or, if maternal symptoms were present, with amnioreduction. Although short-term outcomes (gestational age at delivery and perinatal

survival) were not significantly different between the two treatment groups, long-term neurodevelopmental impairment (as determined by neurologic examination and neuropsychological developmental testing at a minimum of 2 years of age) was decreased in the laser group (0/21 vs. 7/30; $P = .03$).[52] The improvement in long-term neurologic outcome in the laser-treated pregnancies in this study raises the question as to whether there is ongoing neurologic damage from mild TTTS even if the disease does not progress, and whether this damage could be prevented by interrupting the underlying cause of TTTS by laser ablation. **Synthesis of all the above information leads one to conclude that further study is needed in stage I disease, particularly focusing on echocardiographic parameters and long-term neurodevelopmental outcomes.** This sentiment was recently echoed in an excellent publication summarizing the current literature on TTTS and outlining recommendations of a scientific consensus panel convened to develop recommendations for TTTS diagnosis, therapy, and research.[40]

A wise overall approach to managing TTTS was aptly summarized in a 2005 review by Harkness and Crombleholme: "A thoughtful approach to the management of TTTS requires consideration of every aspect of the presentation, including gestational age, stage, Doppler findings, echocardiographic findings, concomitant placental insufficiency, and maternal risk factors. Until we have an effective medical therapy for TTTS, a judicious application of invasive procedures should be employed to optimize risk-to-benefit ratios for the mother and fetuses."[38]

Monoamniotic Twins

Monoamniotic twinning is an uncommon form of twinning in which both fetuses occupy a single amniotic sac. **Monoamniotic twins account for only 1% of all MZ twin pregnancies**. Historically, perinatal morbidity and mortality rates have been reported to be in excess of 50%. This has been attributed to premature delivery, growth restriction, congenital anomalies, and vascular anastomoses between twins, but mostly to umbilical cord entanglement and cord accidents (Figure 30-10). More recent reviews of prenatally diagnosed cases suggest improved perinatal outcomes, with mortality rates in the range of 10% to 20%.[53-55] This decrease is likely due to early prenatal diagnosis, the use of antenatal corticosteroids, increased fetal surveillance, and early elective delivery.

Because cord accidents are the primary cause of fetal death, most management protocols emphasize intense fetal surveillance to identify umbilical cord constriction before fetal loss. Fetal surveillance should be initiated after fetal viability has been achieved because IUFD has been documented to occur in monoamniotic twins throughout gestation.[54,56] Furthermore, this surveillance must be repeated frequently because fetal compromise and death can happen without much warning.

Many older reports on monoamniotic twins are not optimal for counseling patients because in most of those cases, the diagnosis of monoamnionicity was made postnatally. There have been several more recent series that are helpful. Rodis and coworkers reviewed 13 cases of monoamnionicity at one tertiary care center over a 10-year period.[53] All patients underwent serial ultrasound examinations and antenatal fetal surveillance two to seven times per week starting between 24 and 26 weeks' gestation. The mean gestational age at delivery was 32.9 weeks' gestation, with a mean birthweight of 1669 g. All pregnancies exhibited cord entanglement at the time of delivery, with 62% having knotted cords. Sixty-two percent of the pregnancies were delivered for abnormal fetal testing. If undelivered earlier, all patients had cesarean delivery by 35 weeks' gestation, and there were no fetal deaths. Two neonates died during the perinatal period: one from a congenital heart defect, and the other from asphyxia and sepsis. Compared with 77 sets of monoamniotic twins from the literature that had not been diagnosed prenatally, these patients had a 71% reduction in the relative risk for perinatal mortality.

A more recent study evaluated the impact of routine hospitalization for fetal monitoring on perinatal survival and neonatal morbidity in a multicenter retrospective cohort study of 96 monoamniotic twin gestations.[55] Of 87 women with both twins surviving at 24 weeks, 43 patients were admitted electively at a median gestational age of 26.5 weeks for inpatient surveillance and fetal testing two to three times daily. The remaining 44 women were followed as outpatients with fetal testing one to three times weekly. IUFD did not occur in any hospitalized patient, but 14.8% (13 of 88) of the fetuses were stillborn among those women followed as outpatients. Statistically significant improvements in birthweight, gestational age at delivery, and neonatal morbidity were also noted for the hospitalized women. This study suggests that improved neonatal survival and decreased perinatal morbidity are achievable in patients with monoamniotic twins admitted electively for daily fetal monitoring after viability.

Although the good outcomes obtained in the previously mentioned studies could be due to chance, we recommend fetal testing two to three times per day in the hospital for all patients with monoamniotic twins starting between 24 and 26 weeks' gestation. Although cord accidents cannot be predicted, daily fetal heart rate monitoring may reveal an increasing frequency of variable decelerations. If these are identified, continuous monitoring is recommended, with emergency delivery if worsening non-reassuring fetal status is encountered. Antenatal corticosteroids should be administered early because of the near certain chance of delivery at or before 34 weeks' gestation.

In the absence of non-reassuring fetal testing, the timing of elective delivery is not well established. Some authors have advocated delivery of all monoamniotic twin pregnancies as soon as fetal lung maturity has been demonstrated, whereas others have recommended elective delivery at 32 weeks' gestation.[56] Still others suggest that it is unnecessary to deliver monoamniotic twins before term. A retrospective evaluation of 24 sets of histologically confirmed monoamniotic twin pregnancies revealed no perinatal deaths after 30 weeks of gestation.[57] The authors suggested that there is no advantage to elective premature delivery of these pregnancies. Tessen and Zlatnik reviewed 20 monoamniotic twin pregnancies. In their retrospective series, there were no perinatal deaths after 32 weeks of gestation, and the authors suggested that prophylactic premature delivery of these women might not be indicated. However, in a subsequent addendum to the original paper,

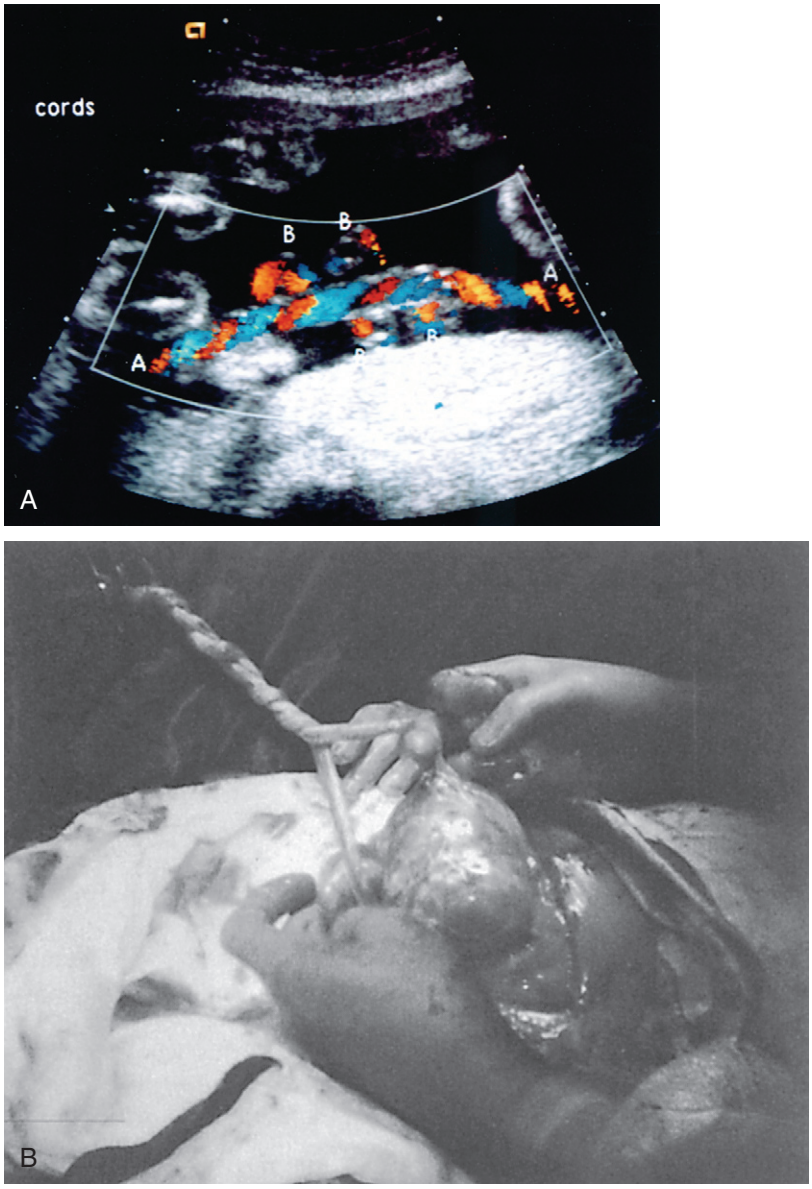

FIGURE 30-10. **A,** Cord entanglement detected by Doppler ultrasound in a monoamniotic twin gestation. **B,** Entangled cords found during cesarean delivery in a case of monochorionic monoamniotic twins.

they reported a double fetal death at 35 weeks just after publication of their report.[58] Despite these two reports suggesting a negligible risk for fetal death after 32 weeks, subsequent papers, including a 2009 study of 98 patients managed from 2000 to 2007, have confirmed the occurrence of a significant number of fetal deaths even after 32 weeks.[54,56,59]

Because of the continuing risk of fetal death, many experts perform elective delivery following the administration of antenatal corticosteroid therapy between 32 and 34 weeks' gestation. The recent 2011 NICHD and SMFM workshop addressing timing of indicated late-preterm and early-term birth also cites this gestational age interval as their recommendation.[34a] Delivery at this time is associated with a low risk of serious neonatal morbidity when weighed against the uncertain risk of continuing the pregnancy. However, it may be reasonable to manage selected cases of monoamniotic twins expectantly beyond 34 weeks' gestation, with careful ongoing fetal surveillance.

Cesarean delivery has been recommended to eliminate the risk for intrapartum cord accidents, but vaginal delivery of these patients is not entirely contraindicated if careful fetal monitoring is performed. In one series, no fetal deaths and only one case of non-reassuring fetal testing requiring emergency cesarean delivery occurred during labor in 15 monoamniotic twin pregnancies delivered vaginally.[58] On the other hand, there have been case reports of a nuchal cord affecting the first twin being cut to facilitate delivery, only to discover that the cut cord actually belonged to the second twin. Given these issues and a high incidence of intrapartum non-reassuring fetal testing, most experts recommend cesarean delivery of all monoamniotic twin pregnancies.

Twin Reversed Arterial Perfusion Sequence

The TRAP sequence, also known as acardiac twinning, is a malformation that occurs only in monochorionic

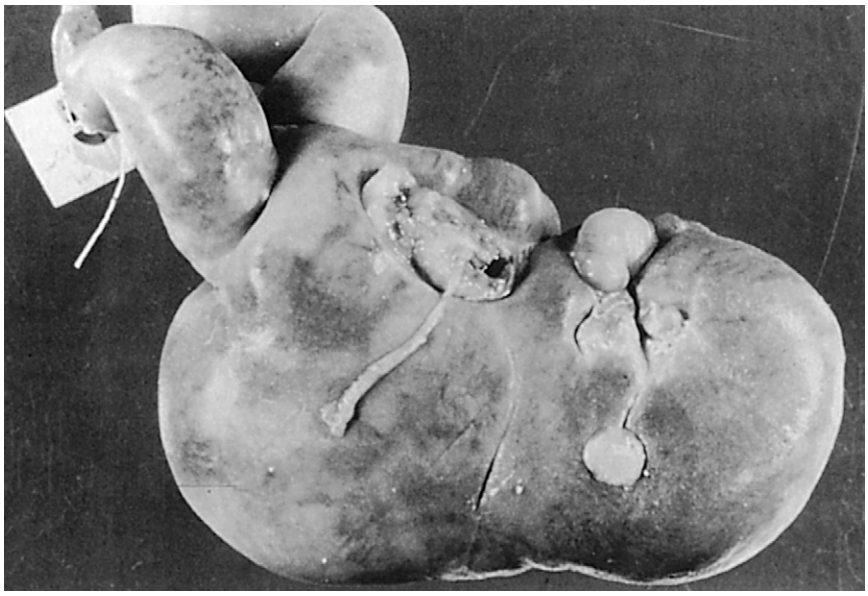

FIGURE 30-11. Acardiac twin. (Courtesy Dr. James Wheeler, Department of Surgical Pathology, Hospital of the University of Pennsylvania, Philadelphia.)

pregnancies with a frequency of about 1 per 30,000 deliveries. These extremely malformed fetuses have no heart at all (holoacardia) or only rudimentary cardiac tissue (pseudoacardia) in association with multiple other developmental abnormalities (Figure 30-11). Acardiac twins are sometimes classified by the degree of gross morphologic malformation: (1) acardius acephalus (absent head with relatively well-developed trunk and lower extremities), (2) acardius amorphous (amorphous mass of tissue, unrecognizable as a fetus), (3) acardius anceps (poorly formed head with well-developed trunk and lower extremities), and (4) acardius acormus (presence of a fetal head only, connected to the placenta by a cord). These classifications are used only as a descriptive tool because they have no clinical prognostic value.

Patients with TRAP sequence always have a monochorionic placenta with vascular anastomoses that sustain the life of the acardiac twin. Two theories exist as to the etiology of this condition. One theory holds that the TRAP anomaly is caused by an abnormal twinning event. The alternative hypothesis is that the acardia is a primary defect in cardiac development, and the acardiac twin, otherwise destined to end in an early spontaneous abortion, continues to grow because of monochorionic vascular anastomoses to a normal co-twin.

Antenatal diagnosis by ultrasound of an acardiac fetus coexisting with a normal co-twin is fairly straightforward. The only other entity in the differential diagnosis is an intrauterine fetal demise of one twin. However, continued growth of the abnormal, presumed dead twin rules this out, as can demonstration of blood flow in the presumed dead twin by color Doppler. Additionally, a retrograde pattern of fetal perfusion can be demonstrated to occur through the umbilical arteries.[60]

The acardiac twin clearly has no chance of survival, but its presence is not innocuous for the normal pump twin. The pump twin, although structurally normal, is at increased risk for in utero cardiac failure, and mortality rates of 50% or higher have been reported.[61] The estimated weight of the acardiac twin relative to the normal twin is an important prognostic factor. In the largest series of pregnancies complicated by TRAP sequence (N = 49), Moore and coworkers reported 90% preterm delivery, 40% polyhydramnios, and 30% cardiac failure of the normal twin when the weight ratio of acardiac to normal pump twin was more than 70%, compared with 70% preterm delivery, 30% polyhydramnios, and 10% cardiac failure for the normal pump twin when the weight ratio was less than 70%.[61]

Management of patients with pregnancies complicated by TRAP is controversial. Expectant management with serial ultrasound surveillance, including fetal echocardiography, is reasonable in the absence of the poor prognostic features outlined previously. Delivery may be indicated if signs of cardiac decompensation are noted at a viable gestational age. Maternal administration of digoxin and indomethacin have been attempted but with little evidence of benefit. In the face of previable or periviable cardiac failure in the normal pump twin or if poor prognostic features are present, another treatment option is interruption of the vascular communication between the twins. Methods of vascular interruption have included ultrasound-guided injection of thrombogenic materials into the umbilical circulation of the acardiac twin, ligation of the umbilical cord of the acardiac twin under fetoscopic guidance, and radiofrequency cord ablation.[60]

Conjoined Twins

Conjoined twins are another extremely rare complication of monochorionic twinning. They are believed to arise when an embryo incompletely divides between 13 and 15 days after fertilization. This event occurs with a frequency of about 1 per 50,000 deliveries. Most conjoined twins are female, with a reported female-to-male ratio of 2:1 or 3:1. The mortality rate is very high, as evidenced by a retrospective case series from the Children's Hospital of Philadelphia, which found an incidence of 28% intrauterine death, 54% death shortly after birth, and 18% overall survival among 14 sets of conjoined twins treated at their institution between 1996 and 2002.[62]

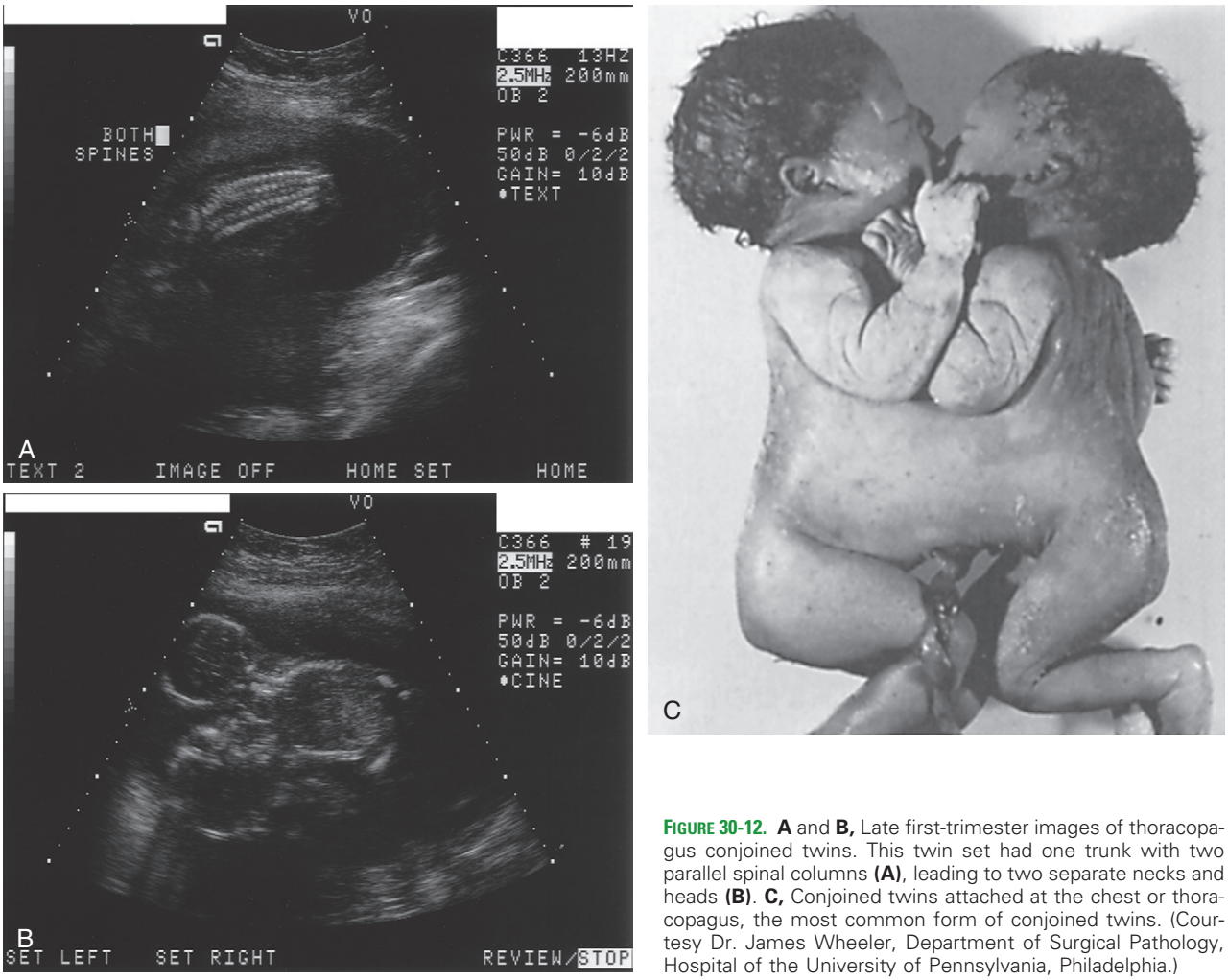

FIGURE 30-12. **A** and **B,** Late first-trimester images of thoracopagus conjoined twins. This twin set had one trunk with two parallel spinal columns **(A)**, leading to two separate necks and heads **(B)**. **C,** Conjoined twins attached at the chest or thoracopagus, the most common form of conjoined twins. (Courtesy Dr. James Wheeler, Department of Surgical Pathology, Hospital of the University of Pennsylvania, Philadelphia.)

Conjoined twins are classified according to their site of union. The most common location is the chest (thoracopagus: Figure 30-12), followed by the anterior abdominal wall (omphalopagus), the buttocks (pygopagus), the ischium (ischiopagus), and the head (craniopagus). Organs are shared to varying degrees. Major congenital anomalies of one or both twins are common, and polyhydramnios is present in almost half of the reported cases of conjoined twins.

Ultrasound can establish this diagnosis in utero, as early as the first trimester, based on visualization of a bifid fetal pole. Three-dimensional ultrasound, color Doppler, fetal echocardiography, and MRI can be used to complement two-dimensional ultrasound imaging to confirm the diagnosis, determine the extent of organ sharing, and definitively classify the type of conjoined twinning.[62,63] Once the diagnosis of conjoined twins is made, management options should be discussed with the patient. If the diagnosis is confirmed before viability, pregnancy termination should be offered. **If the patient desires expectant management, she should be counseled that the prognosis for survival and successful separation depends on the degree of organ and vascular sharing between the two fetuses, especially the heart.** Multimodality fetal evaluation as described previously should be used prenatally to carefully survey fetal anatomy. To optimize postnatal management, patients with conjoined twins should be cared for by a multidisciplinary team during the antenatal period. This team should include maternal-fetal medicine specialists, neonatologists, pediatric anesthesiologists, pediatric surgeons, and appropriate pediatric subspecialists.

Patients with conjoined twins should deliver at a tertiary care facility where neonatal and pediatric specialists are available. Cesarean delivery near term will be necessary to minimize maternal and fetal injury. If the twins are thought to have a poor chance of surviving and are believed to be small enough to pass through the birth canal without traumatizing the mother, vaginal delivery might be considered.

Of conjoined twins who undergo elective separation, survival rates approach 80%. Of conjoined twin sets who require emergent separation, however, survival rates are much lower, around 25%.[63] Although the long-term follow-up of conjoined twins who have undergone successful surgical separation is limited, the data seem favorable. Although survivors frequently require additional surgeries following the initial separation to correct urologic, orthopedic, and neurosurgical issues, many achieve educational levels similar to their singleton peers.

ANTEPARTUM MANAGEMENT OF MULTIFETAL PREGNANCY

Maternal Nutrition and Weight Gain

The two factors that most influence pregnancy outcome are gestational age at delivery and the adequacy of fetal growth. Nutritional status during gestation is linked to both these outcomes. Poor weight gain and deficient nutritional status are associated with low birthweight, preterm delivery, and higher rates of neonatal complications. **The higher baseline risk for these adverse outcomes in twin pregnancies creates a situation in which enhancement of nutrition and weight gain has the potential to provide tremendous positive impact.**

As discussed earlier in the chapter, multifetal gestation requires an exaggerated physiologic adaptation compared with singleton pregnancy. Because of these increased physiologic demands, mothers pregnant with twins have a 10% higher resting energy expenditure. Consequently, to meet the heightened metabolic expenditure, multiple gestations require modification of the current weight gain, caloric intake, and vitamin supplementation recommendations for singleton pregnancies. A recent review of nutrition in twin pregnancy outlined four goals for optimizing maternal nutrition in multifetal gestation[64]:

1. Optimize fetal growth and development
2. Reduce the incidence of obstetrical complications
3. Increase gestational age at delivery
4. Avoid excess maternal weight gain, which could result in unnecessary postpartum weight retention

Evidence demonstrates a positive relationship between maternal weight gain and infant birthweight. It also shows that poor maternal weight gain adversely affects birthweight and preterm delivery rates, mostly in women with an underweight prepregnancy body mass index (BMI). Correspondingly, poor weight gain has a lower impact on overweight and obese women, although an effect is still seen.

Both total maternal weight gain and the timing of that weight gain are critical to optimizing twin birthweight and obstetrical outcomes. Pederson and colleagues found that optimal pregnancy outcome, defined as gestational age at delivery of more than 37 weeks and both babies weighing more than 2500 g, was associated with a total weight gain of 44 lb. Furthermore, worse outcomes in general were seen with weight gain less than 37 lb.[65] Luke and colleagues have shown that weight gain before 28 weeks accounts for 80% of the maternal weight gain effect on infant birthweights.[66] Underscoring this point, Luke and colleagues demonstrated that even when there is appropriate weight gain after 24 weeks, suboptimal gain before 24 weeks is still associated with earlier delivery and poor intrauterine growth. Ideal maternal weight gain is also associated with a 1- to 2-week longer gestational period and a more than three times shorter infant length of hospital stay.[67] BMI-specific weight gain patterns associated with ideal twin birthweight, defined as 2850 to 2950 g at 36 weeks or later, are summarized in Table 30-6. Although the BMI categories used differ slightly from current BMI categories, the differences by weight status can easily be appreciated. Compared with singleton gestations, these recommended rates of weight gain are more than double early in pregnancy (0 to 20 weeks), about 50% higher during midpregnancy (20 to 28 weeks), and about 25% higher late in gestation (28 to 38 weeks).[68]

The crucial role of early weight gain and the more pronounced benefits of appropriate weight gain in underweight women suggest that early weight gain provides improved maternal nutrient stores for use later in pregnancy when fetal demands increase. Additionally, optimal maternal nutrition and weight gain early in pregnancy may enhance placental growth, thus providing a better nutrient supply to the babies. Both of these theories may explain why adequate weight gain in late pregnancy after inadequate gain in early pregnancy does not provide complete catch-up in fetal growth or outcomes.

Partially in response to evidence such as that cited previously, the Institute of Medicine issued new BMI-specific weight gain recommendations for pregnancy in 2009. These recommendations are summarized in Table 30-7. After these guidelines were published, Fox and coworkers

TABLE 30-6 RECOMMENDED RATES OF MATERNAL WEIGHT GAIN IN TWIN PREGNANCIES

GESTATIONAL AGE PERIOD	UNDERWEIGHT (BMI <19.8)	NORMAL WEIGHT (BMI = 19.8-26)	OVERWEIGHT (BMI = 26.1-29)	OBESE (BMI >29)
Early (<20 wk)	1.25-1.75 lb/wk	1-1.5 lb/wk	1-1.25 lb/wk	0.75-1 lb/wk
Mid (21-28 wk)	1.5-1.75 lb/wk	1.25-1.75 lb/wk	1-1.5 lb/wk	0.75-1.25 lb/wk
Late (≥29 wk)	1.25 lb/wk	1 lb/wk	1 lb/wk	0.75 lb/wk

From Luke B, Hediger ML, Nugent C, et al: Body mass index-specific weight gains associated with optimal birth weights in twin pregnancies. J Reprod Med 48:217, 2003.

TABLE 30-7 2009 INSTITUTE OF MEDICINE RECOMMENDATIONS FOR WEIGHT GAIN IN PREGNANCY

PREPREGNANCY BMI	BODY MASS INDEX (kg/m^2) WHO CRITERIA	TOTAL WEIGHT GAIN SINGLETON (lb)	TOTAL WEIGHT GAIN TWIN (lb)
Underweight	<18.5	28-40	No recommendations made
Normal weight	18.5-24.9	25-35	37-54
Overweight	25.0-29.9	15-25	31-50
Obese	≥30.0	11-20	25-42

From Rasmussen KM, Yaktine AL (eds): Institute of Medicine (Committee to Reexamine IOM Pregnancy Weight Guidelines, Food and Nutrition Board and Board on Children, Youth, and Families). Weight Gain During Pregnancy: Reexamining the Guidelines. Washington, DC, National Academy Press, 2009.

retrospectively studied a cohort of 297 twin pregnancies from a private Maternal-Fetal Medicine practice, applying the 2009 Institute of Medicine (IOM) guidelines in order to compare pregnancy outcomes between those women who met or exceeded the weight gain guidelines and those who did not meet the recommendations.[69] They found that women with a prepregnancy BMI placing them in the normal or overweight categories who met the weight gain recommendations demonstrated improvement in outcomes. Normal-weight women who met or exceeded the weight gain recommendations had significantly larger babies and a greater likelihood of both babies weighing more than 2500 g. Overweight women meeting the weight gain recommendations had more advanced gestational ages at delivery as well as heavier weight of the larger twin. Both normal-weight and overweight women who met weight gain goals had some reduction in overall preterm birth and spontaneous preterm birth. In the obese gravidas, there were no statistically significant differences, although this group was small ($n = 29$). This study, along with the previous work cited, supports optimizing maternal weight gain in twin pregnancy in order to improve outcomes. Notably, underweight women were excluded from the study because the IOM guidelines do not provide a specific weight gain recommendation for women with an underweight prepregnancy BMI who are pregnant with twins. However, because other literature clearly demonstrates that underweight women benefit even more from optimal gestational weight gain, special attention should be given to nutritional counseling and weight gain recommendations in this population. Incorporation of formal nutritional consultation into the care of women with multiples is clinically recommended and should be cost-effective.

Although increased maternal weight gain in pregnancy is associated with improved outcomes, maternal weight retention and its long-term health effects remain of concern. There are no long-term prospective studies of weight retention in twin mothers; however, a recent abstract (using BMI-specific weight gain goals established by Luke and colleagues, which are very similar to the 2009 IOM recommendations) demonstrated higher weight retention 6 weeks postpartum in women who exceeded the recommendations compared with women who met the recommended weight gain (6 kg vs. 2 kg; $P < .001$).[70] Therefore, in the setting of multiple gestations, emphasis should be placed on appropriate weight gain, while avoiding gains exceeding the recommendations.

Just as multiple pregnancy demands higher energy expenditure, caloric intake, and weight gain compared with singleton gestation, there is likely also a greater demand for micronutrients. Some experts have suggested that supplemental calcium, magnesium, and zinc may be important to optimal fetal growth and infant and maternal outcomes, although specific evidence for individual micronutrients is generally lacking. Table 30-8 represents a reasonable protocol regarding optimal nutritional management and micronutrient intake during twin pregnancy.

Spontaneous Preterm Birth

Patients with a multiple gestation are at significant risk for preterm labor and delivery. Although this risk is an overriding concern in the antepartum care of multiple gestations, not all multiples are delivered preterm; 40% of twins are delivered at term. **Refining the risk for preterm birth in each individual patient improves pregnancy management by selecting those patients who may benefit most from increased surveillance and interventions while simultaneously minimizing unnecessary interventions in lower-risk women.**

The use of ultrasound transvaginal cervical length measurements and fetal fibronectin (FFN) sampling can help stratify preterm birth risk in multiple gestations. The NICHD Preterm Prediction Study included 147 twin

TABLE 30-8 TWIN PREGNANCY NUTRITIONAL RECOMMENDATIONS

INTERVENTION	FIRST TRIMESTER	SECOND TRIMESTER	THIRD TRIMESTER
Maternal weight gain	Assess pre-gravid BMI, determine BMI-specific weight gain goal	Assess/counsel regarding BMI-specific weight gain goal	Assess/counsel regarding BMI-specific weight gain goal
Caloric requirements by BMI category (kcal/day)			
Underweight (<18.5)	4000	Alter as necessary for weight gain goal	Alter as necessary for weight gain goal
Normal (18.5-24.9)	3000-3500		
Overweight (25-29.9)	3250		
Obese (≥30)	2700-3000		
Protein Requirements by BMI category (g/day)			
Underweight	200	Unchanged from first trimester	Unchanged
Normal	175		
Overweight	163		
Obese	150		
Micronutrient Supplementation			
MVI with iron (tablets)	1	2	2
Calcium (mg)	1500	2500	2500
Magnesium (mg)	400	800	800
Zinc (mg)	15	30	30
Folic acid (mg)	1	1	1
Nutritional Consultation	Yes	Repeat if not at weight gain goal, anemia, GDM	Repeat if not at weight gain goal, anemia, GDM
Laboratory Nutritional Assessment	HgB, ferritin, folate, B_{12}, early GDM screening if risk factors	Follow up abnormality from first trimester	HgB, ferritin, GDM screen

Modified from Goodnight W, Newman R: Optimal nutrition for improved twin pregnancy outcome. Obstet Gynecol 114:1121, 2009.

mothers screened at 24 to 28 weeks' gestation for 50 potential risk factors for preterm delivery. They found that at 24 weeks, only a short cervix (≤25 mm) was significantly associated with an elevated risk for preterm birth in twin pregnancies. The odds ratio of preterm birth before 32 weeks was 6.9 (95% CI, 2 to 24.2) in these women, corresponding to a 27% risk for spontaneous preterm birth before 32 weeks in those women with cervical length of 25 mm or less at 24 weeks compared with a 5% risk in those women with a cervical length of more than 25 mm at 24 weeks. The risk for preterm birth before 35 weeks and before 37 weeks was also significantly elevated for those women with a 24-week cervical length of 25 mm or less.

In the same study, a positive FFN at both 28 and 30 weeks was associated with preterm birth before 32 weeks (OR, 9.4 and 46.1, respectively). Specifically, a positive FFN at 28 weeks was associated with a 29% risk for spontaneous preterm birth before 32 weeks, compared with only 3.9% for those with a negative FFN at 28 weeks.[71]

The combination of cervical length and fetal fibronectin assay has been suggested as a stronger predictor of spontaneous preterm birth than either test alone. A retrospective cohort analysis was performed on 155 asymptomatic twin pregnancies evaluated with combined fetal fibronectin and cervical length testing between 22 and 32 weeks' gestation. The authors reported that they routinely performed FFN assays and measured cervical length every 2 to 3 weeks in their twin mothers. They found that the combination of a positive FFN and a cervical length less than 20 mm (at any time between 22 weeks and the gestational age endpoint in question) had a significantly higher positive predictive value for spontaneous preterm birth than either test alone. If both tests were positive, the risk for spontaneous preterm birth before 28 weeks was 50%, compared with a 13% risk if only one test was positive and only a 1.6% risk if both tests were negative. The stepwise increase in the risk for preterm birth in women with both tests negative, only one test positive, and two tests positive remained statistically significant for spontaneous preterm birth before 30, 32, 34, 35, and 37 weeks' gestation.[72]

In addition to the absolute cervical length, the degree of change in the cervical length over time may also be an important predictor of preterm birth in twins. Fox and coworkers studied a historical cohort of 121 asymptomatic twin pregnancies who had two transvaginal cervical length measurements performed 2 to 6 weeks apart between 18 and 24 weeks' gestation. They found that cervical length shortening (defined as a decrease of ≥20%) over this interval was associated with a greater risk for preterm birth before 28, 30, 32, and 34 weeks compared with women whose cervical length remained stable (15.8% vs. 1% at <28 weeks, 15.8% vs. 2% at <30 weeks, 31.6% vs. 5% at <32 weeks, and 36.8% vs. 12.9% at <34 weeks; all P values ≤.027). Most striking was the fact that this association with preterm birth remained even when patients with cervical length less than 25 mm were excluded. Despite the overall cervical length remaining longer than 25 mm, shortening of 20% or more was still associated with a significantly higher risk for spontaneous preterm birth before 28, 30, and 32 weeks compared with women whose cervical length remained stable (18.2% vs. 1%, 18.2% vs. 2%, and 27.3% vs. 4.1%, respectively; P values = 0.026, 0.049, and 0.022, respectively).[73]

The use of these tests can help guide management decisions, such as frequency of office visits or whether work or activity restriction is prudent. Identification of a patient at particularly high risk for preterm delivery based on her cervical length, fetal fibronectin, or a combination of the two can allow for heightened surveillance and may permit timely interventions such as restricted activity, tocolysis, or steroid administration. On the other hand, documentation of an above-average and stable cervical length (>35 mm) in midgestation can allow both patient and physician to feel comfortable with a patient continuing with her normal activities, avoiding the temptation to implement unnecessary interventions.

Over the years, various interventions aimed at decreasing this high rate of preterm birth have been studied, most without clear evidence of benefit in a general multiple-gestation population. Of note, very few, if any, of these studies have been carried out in the highest-risk multiple gestations based on transvaginal cervical lengths or fetal fibronectin assays. The potential value of some of these interventions in prolonging pregnancy may be quite different in a woman with a 50% risk for delivery before 28 or 30 weeks' gestation versus a 2% risk. The following section discusses the relative merits of these proposed interventions to prevent spontaneous preterm birth in multiple gestations.

Bedrest and Hospitalization

A Cochrane review analyzed six randomized trials including 600 women and 1400 babies and concluded that routine hospitalized bedrest did not provide any benefit for multiple pregnancies. A trend toward fewer low-birthweight babies was noted, although this trend did not extend to very-low-birthweight (VLBW) infants. In fact, in uncomplicated twin pregnancies, inpatient bedrest was associated with a greater chance of delivery before 34 weeks.[74] Because there is no evidence to suggest that routine hospitalization is beneficial for patients with multiples, we believe that these women should be hospitalized only for the same obstetrical indications as singletons.

There are no prospective trials of prophylactic home bedrest in multiple gestations. Older studies that suggested a benefit of bedrest were confounded by the inclusion of undiagnosed twins among the unrestricted women. Tocodynametric studies on normal uterine activity over a 24-hour period have documented that uterine contraction frequency is greater during periods of maternal activity and ambulation. However, for asymptomatic twin pregnancies in women with reassuring cervical length and no prior history of preterm birth, we do not recommend routine rest at home or cessation of work. Nonetheless, because it is difficult to refute the possibility of benefit in higher-order multiple gestations, we generally recommend rest at home starting at about 20 weeks for women carrying triplets or more.

Cerclage

Results of studies using cervical cerclage to prolong pregnancy in multiple gestations have been disappointing. Prophylactic cerclage has been studied and found to be

ineffective in both twins and triplets. Even in the presence of cervical shortening, no clear benefit of cerclage placement in patients with twins has been demonstrated. Newman and coworkers[75] prospectively followed 147 twin pregnancies in women who underwent transvaginal ultrasonographic cervical length measurements between 18 and 26 weeks' gestation. Cerclage was offered to all 33 women with transvaginal cervical length of 25 mm or less and was placed in 21 women. There were no differences between the cerclage and no cerclage groups with regard to length of gestation, birthweight, delivery before 34 weeks, PPROM, or VLBW. A 2005 meta-analysis of ultrasound-indicated cerclage found that, in the subgroup with twins, cerclage placement was actually associated with a statistically significant increase in birth before 35 weeks (75% vs. 36%).[76] Because cerclage is a surgical procedure that may be associated with adverse sequelae for both the mother and her fetuses, it is recommended that cerclage placement in multiple gestations be restricted to women with either a strongly suggestive history or objectively documented cervical insufficiency rather than based on cervical length alone.

Tocolysis

Prophylactic tocolysis has been evaluated in multiple gestations and not found to be effective. In contrast, short-term use of these agents for acute tocolysis in preterm labor is helpful to gain time for administration of corticosteroids to enhance fetal lung maturity as well as to allow transport to a tertiary care facility. Tocolytic use in multiple gestations, however, must be accompanied by careful monitoring of the maternal condition. Because of the exaggerated maternal cardiovascular adaptations to a multiple gestation, women pregnant with multiples are predisposed to cardiopulmonary complications, most notably pulmonary edema. This risk is heightened with β-adrenergic agents and when tocolytics are used in combination with corticosteroids and intravenous fluids. At our institution, intravenous magnesium sulfate is used as a first-line acute tocolytic. When needed in patients before 32 weeks' gestation, we add oral indomethacin for 48 hours.

Progesterone

Weekly intramuscular administration of 17-hydroxyprogesterone caproate deserves special consideration as a unique approach to prophylactic therapy. After 17-hydroxyprogesterone caproate was shown to be effective in reducing recurrent preterm birth in singletons, there was interest in using it in populations with other risk factors for spontaneous preterm delivery, such as multiple gestation. Unfortunately, prospective randomized studies have not shown any effect of weekly 17-hydroxyprogesterone caproate in preventing preterm birth in women whose risk factor for preterm birth was twin or triplet gestation.[77,78] It should be mentioned, however, that those trials included very few women with a history of prior preterm birth. In the study of twins by Rouse and colleagues in which just over half of the participants were multiparous, only 6.1% of the treatment group and 9% of the placebo group had a history of previous preterm delivery.[78] In the triplet trial by Caritis and associates, none of the women in the treatment group and only 3% in the placebo group had a history of previous preterm birth.[77]

A 2007 trial by Fonseca and associates[79] examining the effect of nightly vaginal progesterone in women with short midgestation cervical length did include twin gestations, although twins made up only 10.4% ($N = 13$) of the placebo group and 8.8% ($N = 11$) of the treatment group. This study randomized women with a transvaginal cervical length of 15 mm or less at a median of 22 weeks' gestation to either 200 mg of vaginal progesterone nightly or placebo. They found that administration of nightly vaginal progesterone decreased spontaneous delivery before 34 weeks from 34.3% to 19.2%, which was statistically significant. In the subgroup of twin gestations, vaginal progesterone was associated with a similar reduction in preterm delivery, although the difference did not reach statistical significance because of sample size considerations.

The STOPPIT trial, published in 2009, randomized 500 women carrying twins to daily vaginal progesterone gel (90 mg) or placebo gel administered between 24 and 34 weeks' gestation.[80] The investigators did not find any difference in the primary outcome, which was intrauterine death or delivery before 34 weeks. Just less than 50% of the study participants were multiparous, but the incidence of prior preterm birth was not reported.

The results of these studies suggest that the mechanism for increased spontaneous preterm birth in multiples is likely different from the mechanism of spontaneous preterm birth in singletons. Whatever the mechanism, it appears to be less responsive to progesterone supplementation. However, this is a question deserving more study, especially for those multiples at particularly high risk for spontaneous preterm birth based on a short cervical length or positive fetal fibronectin assay.

Another population that has not been specifically studied includes women currently pregnant with multiples who have a history of spontaneous preterm birth with previous singleton gestations. These women are at very heightened risk for spontaneous preterm birth. Whatever factors put them at risk for spontaneous preterm delivery with a singleton are presumably still in effect and likely exacerbated by the additional demands of carrying twins. For these reasons, until better evidence is available, it is reasonable to use weekly 17-hydroxyprogesterone caproate for women pregnant with multiples who also have a history of a spontaneous preterm birth before 37 weeks with a prior singleton gestation. Additionally, based on the Fonseca trial, it is also reasonable to offer nightly vaginal progesterone to women carrying multiples who have a midgestation cervical length of 15 mm or less.

Antenatal Testing

Multiple gestations are at an increased risk for uteroplacental insufficiency, fetal growth restriction, and stillbirth, and for this reason many experts recommend antenatal surveillance in the form of nonstress tests or biophysical profiles. There are retrospective data showing that both nonstress tests and biophysical profiles are effective in detecting compromised twin gestations.[81] However, the optimal surveillance schedule is unknown because there are no prospective data on which to base a recommendation. The American College of Obstetricians and

Gynecologists 2004 Practice Bulletin on multiple gestation acknowledges these limitations and states that "further studies are needed to determine whether routine antepartum fetal surveillance provides objective benefit in the absence of other high-risk conditions." The 2009 NICHD reevaluation of antenatal testing also discusses the limits of the evidence regarding routine fetal surveillance in multiple gestations but lists weekly testing at 32 weeks as a reasonable strategy for twins with normal fetal growth.[82] Pregnancies complicated by growth restriction or other risk factors may require earlier and more frequent testing. Others have suggested an increased stillbirth risk even among apparently uncomplicated monochorionic, diamniotic twins and recommend twice weekly testing of these gestations after 34 weeks.

There are even fewer data for triplet and higher-order multiple gestations. However, because the stillbirth risk increases with increasing plurality, it is reasonable to begin antenatal testing earlier for triplets than for twins, acknowledging that these recommendations are based more on expert opinion and clinical practice than prospective evidence. Possibly the most compelling reason to perform routine monitoring in twins is the high incidence of both IUGR and discordant growth in the third trimester and the inability to reliably diagnose those conditions by ultrasound.

Fetal Growth Surveillance

Ultrasound, although imperfect, is the only method available for assessing individual fetal growth in multiple gestations. **Normal twins grow at the same rate as singletons up to 30 to 32 weeks' gestation, after which they do not gain weight as rapidly as singletons of the same gestational age.** The restriction in each twin's somatic growth is thought to be related to "crowding" in utero and competition for nutrients. The implication of this concept is that at some point in the third trimester, the placentas can no longer keep pace with the nutrient requirements of both developing fetuses. This relative uteroplacental insufficiency occurs even earlier when more than two fetuses are present. It must, however, be cautioned that most of the studies suggesting a slowing of fetal growth after 30 weeks are based on birth weight and therefore represent size rather than growth. A retrospective longitudinal study using ultrasound to follow fetal growth velocity in 131 twin gestations found that biparietal diameter growth velocities significantly slowed between 30 and 33 weeks' gestation and that growth of the abdominal circumference was significantly slowed from 30 to 37 weeks.[83] A subsequent prospective longitudinal study of fetal growth in 162 twins was performed using ultrasound every 2 weeks from 16 weeks until delivery. Similar to the retrospective analysis, this study showed that the growth velocities for biparietal diameter, femur length, and abdominal circumference were all decreased after 32 weeks.[84] Of interest, in both of these studies, chorionicity did not significantly influence fetal growth.

Discordant Growth

Significant discordance in weights between twins is typically defined as a greater than 15% to 25% difference in actual or estimated twin weights (the difference between the weights divided by the weight of the larger twin). In a series of 1370 consecutive twin pregnancies, discordances in birthweight of 15% to 20%, 21% to 25%, 26% to 30%, 31% to 40%, and more than 40% were found in 14%, 7%, 4%, 3%, and 1% of pregnancies, respectively.[85] Because DZ twins are genetically distinct individuals, it is not surprising that they might be programmed to have very different weights at birth. There are, however, several pathologic situations in which either monochorionic or dichorionic twins may develop substantial weight differences. These include TTTS, the combination of an anomalous fetus with a normal co-twin, and selective IUGR affecting only one twin because of local placental factors (Figure 30-13) or abnormalities of the umbilical cord. IUGR can also affect both twins relatively equally, in which case they would both be small, but not discordant in size. **Although it has been argued that fetal size discrepancy is not concerning if both babies' estimated weights remain appropriate for gestational age, discordance, especially when severe, suggests clinically significant growth restriction. The exact degree of growth discordance that begins to confer increased risk is debated, but an association with increased fetal and neonatal morbidity and mortality has been demonstrated when the estimated weight discrepancy exceeds 25% to 30%.**[85]

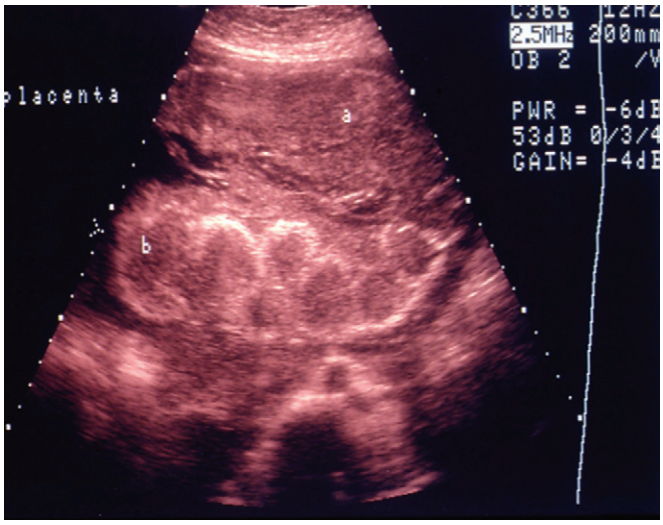

FIGURE 30-13. Normal anterior placenta of twin A and abnormal calcified grade 3 placenta of twin B in a case of selective intrauterine growth restriction of twin B. Twin B also had elevated umbilical artery S/D ratios.

Smaller degrees of discordance, not surprisingly, may be more worrisome in monochorionic compared with dichorionic gestations. In one study examining the significance of discordance, the risk for stillbirth, neonatal death, and preterm birth was not increased until discordance reached 30% or higher in different-sex twins, but these risks were increased with discordance of 15% or higher in same-sex twins.[86] A specific concern among monochorionic twins is the association between discordant growth and the occurrence of neurodevelopmental disability.

Ultrasound is the optimal method of assessing the progression of fetal growth in multiples. A survey of multiple biometric parameters on serial ultrasound examinations

provides the most accurate assessment of the size of each individual fetus in twin gestations. No single anatomic parameter evaluated at birth adequately discriminates normal twins from those with IUGR. Consequently, multiple biometric parameters should be assessed to detect growth disorders among twins in utero, especially in the third trimester. Among individual parameters, abdominal circumference is the single most sensitive measurement in predicting both IUGR and growth discordance.

Consideration of as many biometric variables as possible will maximize the likelihood of differentiating a normally grown from a growth-restricted twin fetus. A recent prospective longitudinal study from Belgium found that ultrasound estimations of fetal weight and weight discordance among monochorionic, diamniotic twins were highly correlated with actual birthweight and the degree of weight discordance at birth.[87] The same general principles can be applied to the assessment of growth in triplets and higher-order multiple gestations. Another point that should be stressed is that growth is a dynamic process and, therefore, that patients with multifetal gestations should be followed throughout pregnancy. **It is recommended that all patients with twins undergo ultrasound testing at least every 3 to 4 weeks after 20 weeks and more frequently if IUGR or growth discordance is suspected. Additionally, many experts recommend that ultrasounds be performed every 2 weeks in monochorionic twins beginning in the mid-second trimester in order to survey for the development of TTTS or selective IUGR.**

SPECIALIZED TWIN CLINICS

The value of specialized twin clinics has been described. In these clinics, where women carrying twins are seen at regular intervals by the same obstetrical team, several advantages accrue. Patients have the opportunity to develop rapport with a small group of caregivers. This results in an increased awareness of their special problems and may increase compliance with therapeutic directives. The medical personnel become adept at detecting early signs of the specific problems associated with twin pregnancies, and special emphasis is given to nutrition, weight gain, and preterm labor surveillance. Two studies have examined the effects of such clinics and found improvements in outcomes. One study demonstrated reduced rates of VLBW babies, neonatal intensive care unit (NICU) admissions, and perinatal mortality,[88] whereas the other showed improvements in gestational age and birthweight and reduced rates of PPROM, preterm labor and delivery, preeclampsia, and low-birthweight and VLBW infants, as well as reductions in NICU admissions and individual complications such as respiratory distress syndrome, necrotizing enterocolitis, and retinopathy of prematurity. Shortened length of stay was also seen for the babies, as was a reduction in cost per twin pair.[89] These studies, although lacking a prospective randomized design, suggest that intensive education, multidisciplinary care, and surveillance, combined with careful attention to maternal nutrition and weight gain, can improve outcomes in twin pregnancies. Figure 30-14 outlines a reasonable management algorithm for antepartum care unique to twin gestations.

TIMING OF DELIVERY IN MULTIPLE GESTATIONS

Concern over preterm delivery in twin pregnancies sometimes overshadows decision making regarding timing of delivery for twin mothers who remain pregnant at or near term. Numerous population-based studies suggest that the nadir of perinatal complications occurs at earlier gestational ages in multiple gestations compared with singletons.

Unfortunately, the hypothesis that elective early delivery of twins leads to better outcomes has not been subjected to rigorous prospective study. The only randomized study of elective early delivery of twins was quite underpowered, with only 17 women in the induction group and 19 in the expectant management group. Women with uncomplicated pregnancies and a cephalic first twin were randomized at 37 weeks to either labor induction or expectant management. The study found no statistically significant differences in birthweight, Apgar score, or cesarean delivery rate. There were no fetal deaths in either group.[90]

As mentioned previously, there are numerous population-based studies that suggest early delivery of twins could be advantageous. Kahn and colleagues reviewed nearly 300,000 twin pairs and found 39 weeks to be the point of intersection that minimized both the fetal and neonatal death rates.[91] They found that the prospective risk for fetal death in twins equaled that of postterm singletons by 36 to 37 weeks' gestation. Another investigation by Sairam and associates evaluated more than 4000 multiple pregnancies (of which more than 99% were twins) and found that the stillbirth risk at 39 weeks in a twin pregnancy exceeded that of a singleton postterm pregnancy. Twins at 37 to 38 weeks had stillbirth rates equivalent to postterm singletons.[92]

Given consistent evidence of increased risk in twin pregnancies extending past 38 to 39 weeks (analogous to a postdate singleton gestation), a rational delivery approach, supported by the 2011 NICHD and SMFM workshop,[34a] is to plan elective delivery at 38 weeks in well-dated, uncomplicated dichorionic twin pregnancies. Allowing a twin gestation to go past 38 weeks requires convincing evidence of normal fetal growth, amniotic fluid, and fetal testing, as well as a strong patient desire to extend the pregnancy. Prolongation of a twin pregnancy past 39 weeks is not advisable because of clear risk without any known benefit. Figure 30-15 outlines a reasonable approach to planning delivery for uncomplicated term or near-term twin pregnancies.

Twin gestations complicated by maternal or fetal abnormalities will require individualized assessment and decision making. Figure 30-16 provides general guidelines as to how twin gestations complicated by fetal growth restriction, discordant growth, or maternal complications such as mild preeclampsia or cholestasis might be managed. Of course, the timing of delivery in the face of either maternal or fetal complications is influenced by severity and clinical judgment and may require modification of the guidelines outlined in Figure 30-16. For instance, an IUGR twin in less than the third percentile or a pregnancy with more than 35% discordance in estimated fetal weights may be an indication for delivery earlier than 37 weeks even if all other testing is normal. Additionally, twin pregnancies with

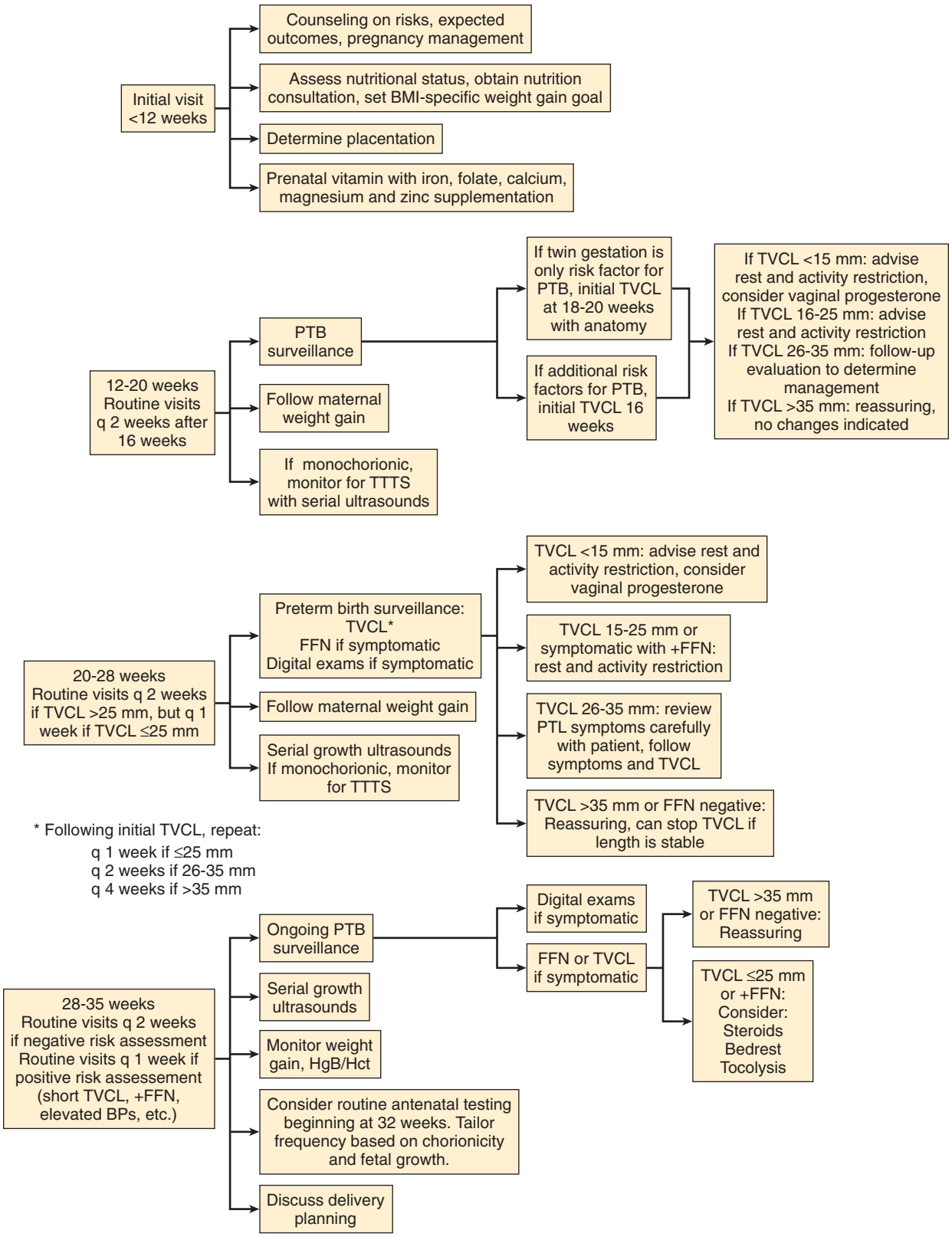

FIGURE 30-14. Suggested algorithm for antepartum management unique to twins. *BMI,* Body mass index; *BP,* Blood pressure; *FFN,* fetal fibronectin; *Hct,* hematocrit; *HgB,* hemoglobin; *PTB,* preterm birth; *TVCL,* transvaginal cervical length; *TTTS,* twin-twin transfusion syndrome.

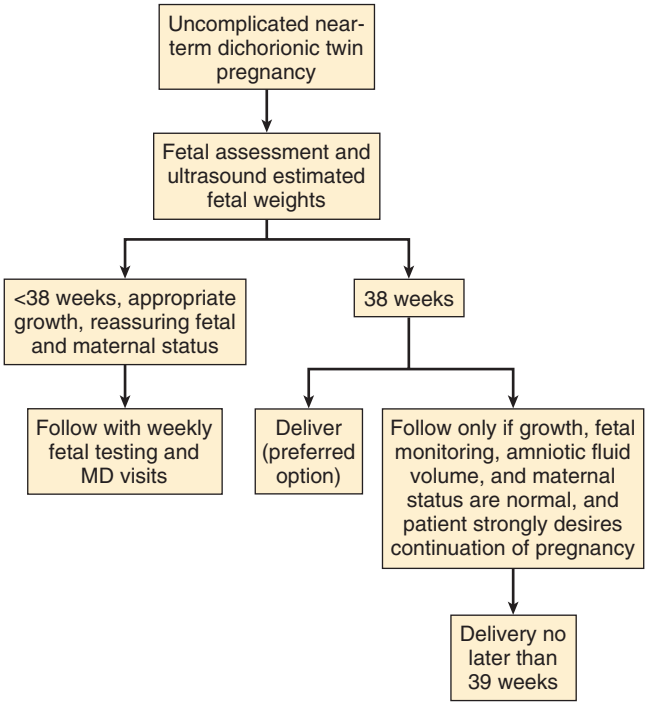

FIGURE 30-15. Timing of delivery for uncomplicated near-term twins.

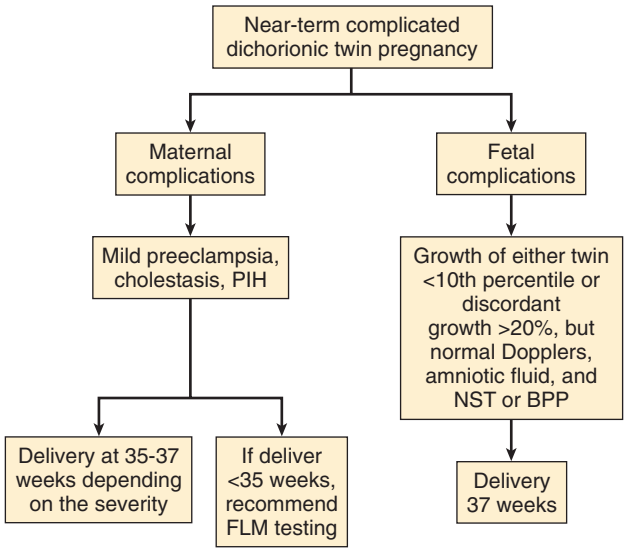

FIGURE 30-16. Timing of delivery for complicated near-term twins. *BPP,* Biophysical profile; *FLM,* fetal lung maturity; *NST,* nonstress test; *PIH,* pregnancy-induced hypertension.

more than one of the listed complications may also warrant delivery earlier than 37 weeks. Similarly, some have argued for elective early delivery of all monochorionic twins, a topic that is discussed in more detail later. Monoamniotic twins were discussed earlier in the chapter.

Monochorionic, Diamniotic Twins: Special Considerations Regarding Delivery Timing

The population-based studies outlined previously addressing the optimal timing of delivery for term and near-term twins included both dichorionic and monochorionic gestations, but they did not differentiate between the two types of placentation when evaluating outcomes. It is well established that monochorionic twins are at greater risk for a variety of pregnancy complications. **However, there is concern among some investigators that even "apparently uncomplicated" monochorionic, diamniotic twins, a term coined by D'Alton and colleagues, are at increased risk for late fetal death.** A retrospective analysis from the United Kingdom reviewed 151 uncomplicated monochorionic pregnancies in women who underwent ultrasound evaluation every 2 weeks and assessed fetal growth, amniotic fluid, and umbilical artery Doppler scans. They found that the risk for unexpected stillbirth after 32 weeks was 4.3% (1 in 23).[93] Another study of 193 monochorionic, diamniotic twin pregnancies in Portugal found that the risk for fetal death after 32 weeks in women undergoing weekly fetal testing was much lower, at 1.2%.[94] Two notable differences exist between these two studies; namely, the first study did not employ weekly fetal testing, as did the second, but rather ultrasound examination every 2 weeks. Interestingly, the authors of the second study noted that 55% of their twins were delivered preterm as a result of the surveillance program.

The latest study of "apparently uncomplicated" monochorionic, diamniotic twin pregnancies examined the records of 196 monochorionic, diamniotic and 804 dichorionic twin pregnancies. These investigators found that the monochorionic twins had higher stillbirth rates than the dichorionic twins (3.6% vs. 1.1%; $P = .004$), and this increased risk persisted in the "apparently normal" group and was seen at all gestational ages up to 37 weeks ($P = .039$).[95]

Based on these concerns, some experts recommend offering elective delivery at 34 to 35 weeks in uncomplicated monochorionic, diamniotic twins. This evidence and expert opinion were incorporated into the 2011 NICHD and SMFM workshop paper on timing of indicated late-preterm and early-term birth, which recommends delivery for monochorionic, diamniotic twins between 34 and 37 weeks. It is emphasized that this approach does not yet represent standard of care, and further data may be necessary before this more aggressive approach can be fully embraced. In the absence of early delivery for monochorionic, diamniotic twins, it would be prudent to conduct frequent antenatal testing along with periodic ultrasound assessment and fetal movement counts. Given this more intensive surveillance, it is unknown whether the stillbirth risk would be significantly different than that in uncomplicated dichorionic twins. The topic of antenatal testing for twins was discussed in more detail earlier in the chapter.

Fetal Lung Maturity in Twins

The clinical management of multiple gestations occasionally requires the assessment of fetal lung maturity. There is currently no consensus on whether pulmonary maturation differs between singletons and multiples. If elective delivery is scheduled before 37 to 38 weeks' gestation in dichorionic twins, amniocentesis for fetal lung maturity determination may be considered. Because asynchronous pulmonary maturity can occur in twins regardless of size and gender, if technically feasible, it is suggested that both gestational sacs be sampled when amniocentesis for lung maturity is required. A reasonable approach to

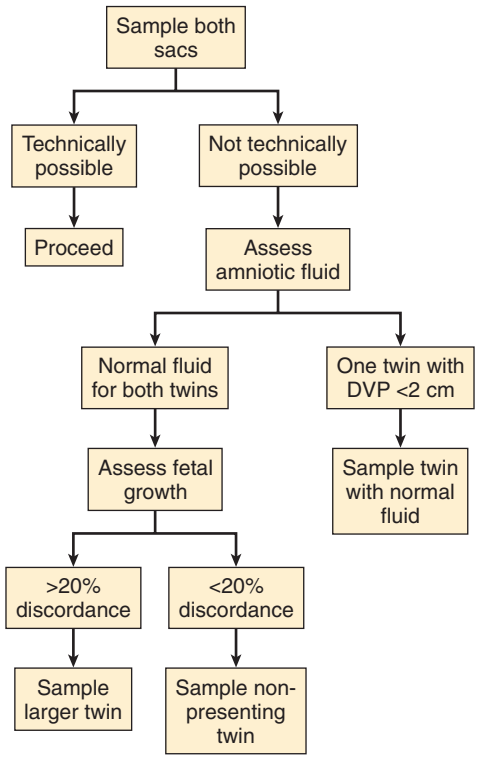

FIGURE 30-17. Assessment of fetal lung maturity in twins. *DVP,* Deepest vertical pocket.

assessing fetal lung maturity in diamniotic twins is outlined in Figure 30-17. For pregnancies with triplets and higher-order multiple gestations, there are not enough data to make recommendations regarding amniocentesis for fetal lung maturity.

Timing of Delivery in Triplets

Triplets are clearly at very high risk for significant preterm birth. However, in a review of more than 15,000 triplet pregnancies, about 15% of triplets were undelivered at 36 weeks. That same study found that the point of intersection of fetal and neonatal death for triplets occurred at 36 weeks.[91] Most experts agree that if otherwise uncomplicated, well-grown triplets remain undelivered at 36 weeks, elective delivery should be undertaken.

MODE OF DELIVERY IN MULTIPLE GESTATIONS

A number of factors must be considered when determining the mode of delivery for patients with a multifetal gestation. These variables include the gestational age, estimated weights of the fetuses, their positions relative to each other, the availability of real-time ultrasound on the labor floor and in the delivery room, and the capability of monitoring each twin independently during the entire intrapartum period. Carefully considering all these variables is essential because multiple gestations are inherently at higher risk during the intrapartum period. This risk is illustrated by a large retrospective cohort study published in 2005 that examined neonatal outcomes in all twin births of 36 weeks' gestation or more in Scotland between 1985 and 2001. They found that the odds ratio for death

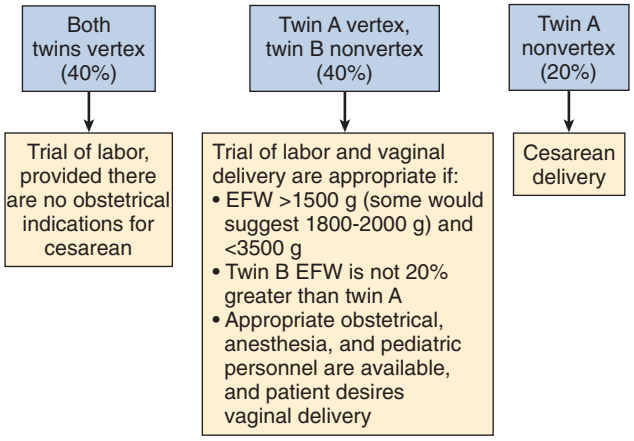

FIGURE 30-18. Algorithm for determining mode of delivery in diamniotic twins. (Monoamniotic twins should have cesarean delivery.) *EFW,* Estimated fetal weight.

of the second twin due to intrapartum anoxia was 21 (95% CI, 3.4 to 868.5) in twins delivered vaginally compared with those in which both twins underwent cesarean delivery. Death of either twin occurred in 0.14% (2 of 1472) with cesarean delivery compared with 0.52% (34 or 6601) with vaginal delivery ($P = .05$). The researchers calculated that the number of twins requiring cesarean delivery to prevent one death was 264.[96] However, it should be noted that the study had no information on fetal presentation, chorionicity, or other specific maternal or neonatal variables.

Older case series may not be applicable to current practice because our ability to monitor both twins closely during labor and delivery has improved considerably in recent years. Additionally, multiple smaller studies, including a 2003 meta-analysis, do not show a benefit of cesarean delivery for all twin deliveries.[97] At present, the evidence is inconclusive that there is a benefit to routine cesarean delivery of all twins. However, it is clear that twin gestations represent a high-risk intrapartum situation that requires expert management.

All combinations of intrapartum twin presentations can be classified into three groups: (1) twin A vertex, twin B vertex; (2) twin A vertex, twin B nonvertex; and (3) twin A nonvertex, twin B either vertex or nonvertex. In a series of 362 twin deliveries presented by Chervenak and associates,[98] these presentations were found in 42.5%, 38.4%, and 19.1% of cases, respectively. Each scenario is discussed separately next, and recommendations are summarized in Figure 30-18.

Vertex-Vertex Twins

A trial of labor and vaginal delivery is believed to be appropriate for all vertex-vertex twin gestations, regardless of gestational age or estimated fetal weight. No clear benefit to routine cesarean delivery of vertex-vertex twins has been found in the literature, including VLBW deliveries.[97] However, it is important to note that the presentation of the second twin may change in 10% to 20% of cases after delivery of the presenting twin. For this reason, the obstetrician should always discuss this possibility with the patient before delivery. Furthermore, when anticipating a vertex-vertex twin vaginal delivery, the obstetrical team

should always have a clear plan for the management of an unexpected nonvertex second twin.

Nonvertex-Presenting Twin

Twin pregnancies with a nonvertex-presenting twin are nearly always managed by cesarean delivery. Historically, this was because of a fear of interlocking fetal heads during delivery of breech-vertex twins. Interlocking fetuses, however, are exceedingly rare. Currently, in an era in which nearly all singleton breech fetuses are delivered by elective cesarean birth, cesarean delivery is also the optimal mode of delivery for twin pregnancies with a nonvertex-presenting fetus.

Vertex-Nonvertex Twins

Although the route of delivery for the previous two scenarios is noncontroversial, the management of that subset of patients whose twins are in a vertex-breech or vertex-transverse lie is subject to significant debate. When the second twin is nonvertex after delivery of the first twin, there are two options for achievement of vaginal delivery: breech extraction or external cephalic version. Although external cephalic version is an acceptable strategy, it has been shown to be associated with more fetal distress and higher rates of cesarean delivery than breech extraction.[99] Thus, provided the obstetrician is sufficiently trained in breech extraction and the fetus is of appropriate size, this is the preferable option for achievement of vaginal delivery with a nonvertex second twin.

Some obstetricians have voiced concerns regarding the safety of breech extraction and have questioned whether it is equivalent in outcome to cesarean delivery. Chervenak and colleagues[98] cite several older references in which depressed Apgar scores and increased perinatal mortality rates were associated with vaginal breech delivery of the second twin. However, in the same report, the authors analyze their own extensive experience, along with a review of the published literature, and conclude that breech extraction of a second twin is a safe and appropriate option if the estimated fetal weight is more than 2000 g. Although the data supported the safety of breech extraction for babies weighing more than 1500 g, these investigators chose 2000 g rather than 1500 g to allow for the margin of error of an ultrasound-estimated fetal weight.

The safety of breech extraction for second twins is supported by the only randomized trial of cesarean delivery versus breech extraction. Rabinovici and associates[100] randomized 66 women with vertex-nonvertex twins of more than 35 weeks' gestation to vaginal delivery with breech extraction or cesarean delivery. They found that there were no differences in neonatal outcomes and no cases of birth trauma or neonatal death. Not surprisingly, maternal febrile morbidity was greater in the cesarean delivery group.

Several other retrospective studies also support the safety of breech extraction of second twins. Gocke and colleagues[99] analyzed 136 sets of vertex-nonvertex twins with a birthweight higher than 1500 g in whom delivery of the second twin was managed by primary cesarean delivery, external version, or primary breech extraction. No differences were noted in the incidence of neonatal mortality or morbidity among the three delivery modes, although external version was associated with a higher failure rate than breech extraction, a higher rate of non-reassuring fetal heart rate patterns, cord prolapse, and compound presentation. The authors concluded that primary breech extraction of the second nonvertex twin weighing more than 1500 g is a reasonable alternative to either cesarean delivery or external version. Fishman and coworkers[101] and Greig and colleagues[102] examined the records of more than 1200 twin gestations and concluded that there was no evidence to support cesarean delivery for nonvertex second twins weighing more than 1500 g. In fact, Greig's data did not show poorer outcomes even for babies weighing less than 1500 g delivered by breech extraction. Nonetheless, most recommend avoidance of breech extractions on second twins with estimated fetal weights of less than 1500 g.

Two recent studies on mode of delivery for twins lend further support to the safety of breech extraction for second twins. Both studies were conducted in single institutions with strict protocols for active second-stage management and breech extraction. Schmitz and colleagues[103] performed a retrospective cohort study of 758 consecutive sets of twins at more than 35 weeks' gestation with a cephalic-presenting twin A. Using a strict protocol for second-stage management in which, after delivery of the vertex-presenting twin, a nonvertex second twin was immediately delivered by total breech extraction, they found that the neonatal composite morbidity for the second twin did not differ between planned cesarean delivery and planned vaginal delivery. The second, more recent study by Fox and coworkers[104] examined a retrospective cohort of 287 twin pregnancies from a single tertiary care academic medical center. The authors described a strict protocol for second-stage management of twin vaginal delivery in which all nonvertex second twins underwent immediate breech extraction and all nonengaged vertex second twins were delivered by immediate internal podalic version and subsequent breech vaginal delivery. The study found no difference in the rates of 5-minute Apgar scores lower than 7 or a cord pH lower than 7.2 between the planned vaginal delivery group ($n = 130$) and the planned cesarean delivery group ($n = 157$).

It should be kept in mind that both of these studies were conducted in a single center by experienced obstetricians using a strict protocol for second-stage management. During the past decade, concerns about outcomes associated with singleton breech deliveries have led to virtual abandonment of vaginal delivery of breech-presenting singletons. As a consequence, fewer obstetricians are acquiring or maintaining the skills needed to safely perform vaginal breech deliveries.

Triplets

Although vaginal delivery is an option for patients with triplets, there are no large prospective studies establishing its safety. Adequate monitoring of three fetuses throughout labor and delivery is challenging. As a result, elective cesarean delivery of patients with three or more live fetuses of viable gestational age is a reasonable management strategy. Vaginal delivery of triplets should only be undertaken under optimal conditions by obstetricians experienced in such deliveries.

INTRAPARTUM MANAGEMENT OF TWIN VAGINAL DELIVERY

Safe vaginal delivery of multiples requires careful preparation and multidisciplinary cooperation between obstetrics, anesthesia, nursing, and neonatology or pediatrics. On admission to labor and delivery, both fetal presentations should be confirmed by ultrasound. If a recent (within 1 to 2 weeks) ultrasound-estimated fetal weight for both babies is not available, this should be obtained and documented. As discussed earlier, knowledge of the presentation, gestational age, and estimated weight of each twin permits the establishment of a plan regarding the anticipated route of delivery.

If a trial of labor is elected, both fetuses should be continuously monitored. Although the woman may labor in a standard room, the delivery itself is best performed in an operating room, in the event that anesthesia or cesarean delivery is emergently needed. Maternal epidural anesthesia is also advisable. The pain control afforded by an epidural enhances maternal cooperation, allows a wide range of obstetrical procedures to be performed quickly, and is available for anesthesia if emergent cesarean delivery becomes necessary. Table 30-9 provides a list of personnel and equipment that should be prepared for each planned vaginal delivery of a multiple gestation.

Time Interval Between Deliveries

A variable that many investigators have historically considered to be important in the outcome of twin pregnancies is the time interval between deliveries. After delivery of the first twin, uterine inertia may develop, the umbilical cord of the second twin can prolapse, and partial separation of its placenta may render the second twin hypoxic. In addition, the cervix can constrict, making rapid delivery of the second twin extremely difficult if non-reassuring fetal status develops. Many reports have suggested that the interval between deliveries should ideally be 15 minutes or less and certainly not more than 30 minutes. Most of the data in support of this view, however, were obtained before the advent of continuous and dual intrapartum fetal monitoring capability.

TABLE 30-9 CHECKLIST FOR MANAGEMENT OF VAGINAL DELIVERY OF TWINS

Personnel and location
Availability of a fully staffed operating room for the delivery, capable of performing an emergency cesarean delivery
Skilled obstetrical attendants present
Anesthesiologist present at delivery
Sufficient neonatal personnel for resuscitation of two infants
Supplies
Capability to continuously monitor both fetuses throughout labor and delivery
Portable ultrasound for intrapartum use
Premixed oxytocin
Methergine, 15-methyl $PGF_{2\alpha}$, misoprostol for postpartum hemorrhage
Nitroglycerin and terbutaline for uterine relaxation
Obstetrical forceps and vacuum (including Piper forceps for aftercoming head)
Blood products immediately available if needed

Rayburn and associates[105] reported the outcome of 115 second twins delivered vaginally at or beyond 34 weeks' gestation after the vertex delivery of their co-twin. Continuous monitoring of the fetal heart rate was performed in all cases. Oxytocin was used if uterine contractions subsided within 10 minutes after delivery of the first twin. In this series, 70 second twins were delivered within 15 minutes of the first twin, 28 within 16 to 30 minutes, and 17 more than 30 minutes later. The longest interval between deliveries was 134 minutes. All these infants survived, and none had a traumatic delivery. All 17 of the neonates delivered beyond 30 minutes had 5-minute Apgar scores between 8 and 10. In those cases with delivery intervals in excess of 15 minutes, the birthweight differential was not in excess of ±200 g when first and second twins were compared. In another series reported by Chervenak and colleagues,[106] when the fetal heart rate of the second twin was monitored with ultrasound visualization throughout the period between twin deliveries, no difference in the occurrence of low 5-minute Apgar scores was noted in relationship to the length of the interdelivery interval.

It appears that although some second twins may require rapid delivery, others can be safely followed with fetal heart rate surveillance and remain undelivered for substantial periods of time. This less hurried approach when the second twin is not demonstrating signs of non-reassuring fetal status may reduce the incidence of both maternal and fetal trauma associated with difficult deliveries performed to meet arbitrary deadlines.

CONCLUSION

The patient carrying more than one fetus presents a formidable challenge to the obstetrician. The elevated perinatal morbidity and mortality rates seen in multiple gestations compared with singletons are due to a variety of factors, some of which cannot currently be altered. However, extraordinary technologic advances during the past 25 years have given us new insights into problems peculiar to multifetal pregnancies as well as tools with which to detect and treat those problems. Early diagnosis of multiple gestations, determination of chorionicity, and serial follow-up studies offer the potential for administering specialized regimens to selected patients, which we hope will lead to a beneficial impact on the outcome of those pregnancies.

KEY POINTS

- Twinning is one of the most common high-risk conditions in all of obstetrics. Both maternal and perinatal morbidity and mortality are significantly higher in multifetal gestations than in singleton pregnancies.
- Chorionicity is a critical determinant of pregnancy outcome and should be ascertained by ultrasound as early in gestation as possible.
- Monochorionic pregnancies are at higher risk than dichorionic, with increased rates of spontaneous abortion, congenital structural anomalies, IUGR,

and IUFD, in addition to a 10% to 15% risk for TTTS, which is a complication unique to monochorionic pregnancies.

- Multiple gestations benefit from specialized care, including attention to maternal nutrition and weight gain, serial assessment of fetal growth by ultrasound, and careful surveillance for signs of preterm labor.
- Routine bedrest, prophylactic tocolytics, prophylactic cerclage, and prophylactic progesterone supplementation have not been shown to be effective in prolonging multiple gestations. However, none of these interventions has been studied in the highest-risk women based on prior obstetrical history, current short cervical lengths, or positive fetal fibronectin assays.
- The nadir of perinatal complications and an increase in stillbirth risk occur earlier in twin gestations than in singletons. Uncomplicated dichorionic twins appear to have the best outcomes if delivered at 38 weeks. There may be a case for earlier delivery in uncomplicated monochorionic, diamniotic twins, but this issue requires further study.
- Monoamniotic twin outcomes are best when managed with a combination of prophylactic antenatal corticosteroids, hospitalization for daily fetal assessment, and elective early cesarean delivery.
- Mode of delivery should take into account gestational age, fetal presentations, estimated weights, and the experience and skill of the obstetrician. A trial of labor is appropriate when both twins are vertex. Mode of delivery should be individualized for vertex-nonvertex twins. Cesarean delivery is optimal when the presenting twin is nonvertex.

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