Sonography of multiple gestations

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Introduction

Multiple gestations account for 1-2% of all births and represent 10-14% of the overall perinatal mortality, a rate five to ten times higher than that of singletons. Because of the increase use of assisted reproductive technologies, the number of high order pregnancies has steeply increased over the past 20 years. The aim of early diagnosis of multiple gestations and their associated complications is the reduction of perinatal morbidity and mortality. Sonography allows determination of zygosity, chorionicity, amnionicity, placental location and fetal presentation, as well as the detection of complications such as growth discrepancy, abnormal vascular anastomoses, amniotic fluid volume imbalance and cord entanglement. In this chapter, we will discuss the ultrasonographic evaluation, most common complications and the role of invasive procedures in the management of multiple pregnancies.

Embryology

Two mechanisms may lead to a multiple pregnancy: fertilization of two or more oocytes or early embryonic splitting of a single ovum.

The most common mechanism is fertilization of several oocytes in a single menstrual cycle (2/3 of the cases). This type of twining results in genetically different individuals (also known as polyzygotic, non-identical or fraternal twins) and has a hereditary tendency. It is associated with a recurrence risk three times higher than that of the general population. Each zygote develops its own chorion, placenta and amniotic cavity. Every fetal-placental-amniotic compartment is individualized and there are no (or very rare) vascular communications between them. Circulatory complications are thus rare, unless the placentas become fused during pregnancy. The incidence of dizygotic twin varies in different populations while the incidence of monozygotic twins is fairly constant.

The incidence of dizygotic twin varies in different populations: from left to right: Japan, US Caucasian population, US African American population and Nigeria.
In one third of the cases, early embryonic splitting of a single ovum is the mechanism of twinning. Four situations may arise as a result of this process: dichorionic-diamniotic placentation (1/3 of the cases), monochorionic-diamniotic placentation, monochorionic-monoamniotic placentation and conjoined twins. If early embryonic splitting occurs before day three after fertilization (during the two to eight cells stage), two independent fetuses with separate placentas will result. A single placenta with two amniotic cavities occurs if splitting takes place between days four and seven (blastocyst stage). If division of the embryoblast occurs after about eight days, the twins share a single placenta and amniotic cavity (monochorionic-monoamniotic twins). Division beyond day 13 results in conjoined twins.

Fig: Schematic drawing demonstrating the outcome of twinning at different stages of early embryonic life. **Top**: Fission before the formation of the inner cell mass and any differentiation will produce two embryos with two separate chorions, amnions and placentas. **Middle**: Twinning at the early blastocyst stage, after formation of the inner cell mass, will cause the development of two embryos, with one placenta and one chorion but two separate amnions. **Bottom**: If separation occurs after the formation of the embryonic disc, the amnion has already formed, and will lead to a monoamniotic, monochorionic pregnancy. Incomplete fission at this stage or later will result in conjoined twins.
Less frequently, monozygotic and dizygotic twining may occur simultaneously in a pregnancy with 3 or more embryos.

**Dichorionic, triamniotic pregnancy in an assisted pregnancy. Note on the left image the thick septum between the 2 embryos and on the right side the barely visible septation.**

### Clinical implications of zygosity and chorionicity

Improving the outcome of multiple pregnancies is a major challenge for prenatal care. The mortality rate for twins is 4 to 11 times higher than that of singletons. Stillbirths account for approximately one third of the perinatal deaths. The remaining two thirds occur during the neonatal period, mainly as a result of prematurity.

Compared to singletons, the rate of mortality of twins is 4-11 higher, that of stillbirths, 3-13 and that of neonatal death 6-7 times.
The increased mortality of twins is already apparent in the first trimester.

Another normal dichorionic pregnancy, with appropriate early growth (in spite of vaginal bleeding). The repeat examination demonstrates demise of both twins.
The various types of twins are described in the following table (further details are in the text). The table is organized from most dissimilar on top to most similar at the bottom.

<table>
<thead>
<tr>
<th>Types of twins</th>
<th>Dizygotic twins (1/90):</th>
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<tbody>
<tr>
<td></td>
<td>Superfetation</td>
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<th>Types of twins</th>
<th>Fraternal twins</th>
<th>Monozygotic twins (1/250):</th>
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<tr>
<td></td>
<td>Same father, same cycle</td>
<td>Early separation</td>
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<tr>
<td></td>
<td>Same father, same cycle</td>
<td>Late separation</td>
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<table>
<thead>
<tr>
<th>Types of twins</th>
<th>Monozygotic twins (1/250):</th>
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</thead>
<tbody>
<tr>
<td>DiAmniotic DiChorionic</td>
<td>Same zygote, 2 separate sacs</td>
</tr>
<tr>
<td>DiAmniotic MonoChorionic</td>
<td>Same zygote, 2 separate amnions</td>
</tr>
<tr>
<td>MonoAmniotic MonoChorionic</td>
<td>Same zygote, same sac</td>
</tr>
<tr>
<td>Conjoint</td>
<td>Equally but incompletely divided</td>
</tr>
<tr>
<td>Duplicata incompleta</td>
<td>Incompletely duplicated</td>
</tr>
<tr>
<td>Ectoparasitic twin</td>
<td>Partial fetus attached to sib</td>
</tr>
<tr>
<td>Fetus-in-fetu</td>
<td>Embedded</td>
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</tbody>
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A classification of twin from most dissimilar to most identical from top to bottom.

A classification of monozygous twin according to their symmetry or lack of.
Precise determination of zygosity and chorionicity is the most important step for the proper management of multiple pregnancies. Monochorionic-monoamniotic pregnancies are associated with the highest mortality rate (50%), followed by monochorionic-diamniotic pregnancies (26%) and dichorionic-diamniotic pregnancies (9%). Mortality is even higher before 24 weeks of gestation. The elevated mortality rate seen in monochorionic placentation is caused mainly by aberrant vascular communications in the placenta leading to twin-to-twin transfusion syndrome. In monoamniotic twins, the risk is worsened by the possibility of cord accidents. Monochorionic twins are thus at a higher risk of prematurity, intrauterine death and neurological damage secondary to complications of twin-to-twin transfusion syndrome.

As illustrated below from data from the Collaborative Perinatal Project, the excess mortality in twins is predominantly due to the contribution of the monochorionic twins.
The relative risk of twins compared to singletons is not limited to mortality, but also affect morbidity.

Also important is the determination of the number of viable fetuses: higher order multiples have a greater risk of prematurity. A singleton gestation has an average length of 39 weeks versus 35 weeks for twins, 33 weeks for triplets, and 29 weeks for quadruplets. Early ultrasound evaluation at 9 to 12 weeks can precisely inform choriocity, amnionicity and the number of viable fetuses. This information is important for the development of appropriate methods of surveillance and intervention during the second trimester of pregnancy aimed at reducing the excess fetal loss in twins\(^5,7\).

Frequency and mortality according to the types of placentation\(^234\)

<table>
<thead>
<tr>
<th>Placenta Type</th>
<th>Frequency</th>
<th>Mortality</th>
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<tbody>
<tr>
<td>DiAmniotic DiChorionic Separate placentae</td>
<td>35%</td>
<td>13%</td>
</tr>
<tr>
<td>DiAmniotic DiChorionic Fused placentae</td>
<td>27%</td>
<td>11%</td>
</tr>
<tr>
<td>DiAmniotic MonoChorionic Single placenta</td>
<td>36%</td>
<td>32%</td>
</tr>
<tr>
<td>MonoAmniotic MonoChorionic Single placenta</td>
<td>2%</td>
<td>44%</td>
</tr>
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</table>
The chorionicity and zygosity of twins is expressed in the following chart compiled from the Birmingham twin survey. 65% of twins are like sex. Of these 28% are monozygotic and 37% are dizygotic. The chart also demonstrates that 80% of twins are diamniotic-dichorionic and that 90% of these diamniotic-dichorionic are also dizygotic. Further 43% of like sex twins are monozygotic. This helps answer the common question from patients: “If I have like-sex fetuses, what is the likelihood that they are identical?”

Dichorionic twins are easier to recognize from monochorionic twins in the first trimester. The criterion is simply that dichorionic twins have a thick membrane (actually some interposing tissue) while monochorionic twins have either a very thin or barely visible membrane. This is illustrated in the figure below.

The two left images are dichorionic twins, which are easily recognized from monochorionic twins on the two right images (the first trimester) by the thick intervening membrane.
Later, dizygotic twins can be suspected or identified when they have separate placenta or discordant sex.

Dizygotic twins can be suspected or identified in the second trimester when they have separate placenta or discordant sex.

The naming of twins

In the pre-ultrasound days, when the obstetrician delivered a set of twin, it was traditional to call the first one out “Twin A” and the second one “Twin B”. By some twisted extrapolation this nomenclature has been applied to ultrasound, although we have observed that the presenting twin is not always the same one from examination to examination (figure). A much better terminology, aside from the monoamniotic twins, is to describe the relative positions of the twins: Left-upper, right-lower. One of the characteristics is bound to be constant from examination to examination since the membrane prevents the twins from switching side.

The vestigial convention of naming of twins “A&B” has to be replaced by a description of the actual positions.
**Monochorionic twins**

**Definition**

Monochorionic twining is a type of gestation in which the fetuses share a single chorion (the outer membrane) and may or may not share the amnion (the inner membrane). When the amnion is shared, the twins are called monochorionic-monoamniotic (Mo-Mo) and the reader is referred to the specific topic in this chapter. When they do not share the amnion the twins are called monochorionic-diamniotic (Mo-Di). Independently from the number of amniotic sacs, all monochorionic twins are monozygotic\(^9,10\).

*The implantation of two fertilized eggs (left side of the drawing) will result in two gestational sacs that share neither the chorion nor the amnion. The drawing illustrates how the placenta can insert between the two sacs producing the “λ” sign (lambda sign). On the right side of the drawing, a single egg can either split early (before 4 days) into two embryos and the 2 embryos will then resemble the previous condition, or the fertilized egg can split between the 4\(^{th}\) and 8\(^{th}\) days at a time when the chorion is no longer divisible. Both embryos will then share the chorion, the placenta will not be able to infiltrate between the two gestational sacs and the membrane insertion will have the “T” appearance. The ultrasound images underneath the drawings illustrate the membrane insertion in both cases.*
Monochorionic placentation occurs in two-thirds of monozygous twins and represents approximately 0.3% of all spontaneous conceptions. It is highly associated with the overall adverse outcome in multiple gestations. Of all intrauterine deaths in twins, 73% are associated with monochorionic placentation, and among the live births, there is an elevated incidence of perinatal mortality, birth weight discrepancies, and intrauterine growth retardation.

Sonographic features

Determination of chorionicity and can be performed by transvaginal ultrasound as early as 5 weeks. In early pregnancy, the separate sacs are clearly visible. In monochorionic twins, there is a single placental mass, with or without a dividing membrane. When there is a dividing membrane, it is composed of two layers representing the two layers of amnion. In contrast, the inter-twin membrane of dichorionic twins is composed of a layer of chorion sandwiched between two layers of amnion. Therefore, the inter-twin membrane in dichorionic twins is thicker, especially between 6 to 9 weeks, when a septum can be observed between the chorionic sacs. After 9 weeks, the septum becomes progressively thinner; however, it remains thick and relatively easy to identify at the insertion point into the placental mass as a triangular projection called the lambda or "twin-peak" sign. Sepulveda et al. studied 368 twin pregnancies at 10 to 14 weeks gestation, classifying them as monochorionic if there was a single placental mass in the absence of the lambda sign at the inter-twin membrane-placental junction and dichorionic if there was a single placental mass but the lambda sign was present or the placentas were not adjacent to each other. In 81 (22%) cases, the pregnancies were classified as monochorionic and in 287 (78%) as dichorionic. All pregnancies classified as monochorionic resulted in the delivery of same-sex twins and all different-sex pairs were correctly classified as dichorionic.

Other authors suggest counting the number of layers of fetal membranes to determine chorionicity, however this strategy is not always possible and should be used in conjunction with other sonographic criteria. Membrane thickness is also occasionally useful to predict the type of placentation. Thick membranes suggest dichorionic placentation while thin membranes suggest monochorionic placentation.

Another important criterion of differential diagnosis is the sex of the fetuses. If they are of different sex, the odds are that the fetuses are dichorionic. There is a small risk, however, of a cytogenetic change that could result in monozygotic twins presenting as a boy and a girl. The most common cause of this rare anomaly is the early loss (during the embryo stage) of a Y chromosome in a cell line that eventually becomes a Turner syndrome.

In rare instances, not only the primordial fertilized egg divides but one of the 2 daughter cells also looses genetic material (and more commonly the Y chromosome) resulting in a heterokaryotypic monozygotic twin pregnancy consisting of a boy and a Turner girl.
Very asymmetrical growth may occur in heterokaryotypic twins

Associated syndromes

Monochorionic twins are at risk for twin-to-twin transfusion, twin embolization syndrome, higher rates of congenital malformations, growth restriction and prematurity. Death of one twin may have serious implications for the survivor because of the increased risk of preterm delivery as well as the risk neurological handicap secondary to hypotensive episodes caused by hemorrhage from the live fetus into the dead fetoplacental unit through vascular anastomoses.

Monoamniotic twins

Definition

Monoamniotic twins are those that share not only the chorion (the outer membrane) but also the amnion (the inner membrane) and thus are in the same gestational sac. They result from splitting between 7 to 13 days after fertilization and represent 1% of twin pregnancies.
Sonographic features
Monoamniotic twins can be suspected if the following features are observed:\(^{45}\):

- Single placenta and same sex twins;
- Close approximation of the cord insertions;
- Entanglement of the cords;
- Normal and identical amniotic fluid volume around both fetuses;
- Unrestricted fetal movement; and
- Absence of a dividing membrane demonstrated on two studies at least 12-15 hours apart\(^{46}\).

A single yolk sac may be a normal finding\(^{47}\).

Absence of a dividing membrane between two fetuses that are intimately in contact.

Close approximation of the cord insertions.
Counting twins with different chorionicity by counting the number of gestational sacs is easier in the first trimester when thick layers of tissue separate the sacs. However, differentiating monochorionic diamniotic from monochorionic monoamniotic twins is not easy. The amniotic membrane is very thin, and unless the ultrasound beam is perpendicular, it may be difficult to observe. A simple trick that is convincing when present is to roll the patient to the side and observe the passive motion of the embryos. If they both gravitate to the bottom of the gestational sac no matter what decubitus position, the suspicion of monoamniotic twin is high. If they do not, a dividing membrane is suspected. The findings however can be equivocal. This must be an accurate diagnosis since it identifies patients at higher risk for cord accidents.

**Differential diagnosis**

Monoamniotic twins can easily be confused with monochorionic diamniotic twins, especially when there is twin-to-twin transfusion and one of the twins is stuck (see elsewhere in this chapter). A careful search for a membrane, in particular between the limbs and the body, is the only way to ascertain the diagnosis. The absence or reduced amniotic fluid around the stuck twin should raise the suspicion of a diamniotic gestation as well.

**Associated syndromes**

Monoamniotic twins may be affected by multiple pathological conditions including twin-to-twin transfusion (although less common and less severe than in monochorionic diamniotic twins), tangled umbilical cords and increased risk of congenital anomalies (15-20%). Cord entanglement occurs in 40-70% of monoamniotic twins because of their increased mobility in the second trimester.
During the third trimester, the reduced space is usually no longer sufficient to allow the twins to move around.\textsuperscript{83,84} Cord entanglement appears to be a pathognomonic sign of monoamnionicity\textsuperscript{85} and can be seen as early as the first trimester. In cases of cord entanglement, in spite of apparent cord compression with absent end-diastolic velocities (AEDV), some fetuses may grow appropriately\textsuperscript{86}. The significance of AEDV in monoamniotic twins may thus be less predictive than in singletons. The presence of a notch in the umbilical artery velocity waveform may reflect hemodynamic alterations in the fetal-placental circulation secondary to narrowing of the umbilical vessels involved in cord entanglement. Due to these complications the overall mortality for monoamniotic twins can be as high as 50-60\%.\textsuperscript{87,88,89,90,91}

**Fetal growth**

Intrauterine growth restriction is a pathological situation, caused in the majority of the cases by placental insufficiency. Poor maternal-fetal exchange reduces the offer of nutrients to the fetus, which grows slower than normal. This condition is seen in 25\% of twin gestations, a rate ten times higher than that found in the general population. Growth rate in multiple gestations during the first and early second trimesters parallels the growth rate of singleton pregnancies, dropping off during the late second and third trimesters.

Serial growth assessment is the most accurate method to diagnose intrauterine growth retardation. Some controversy remains concerning the use of growth nomograms derived from the general population in multiple pregnancies. The expected growth of head, limbs, and abdomen for twins is discussed below.

![Graph](image)

*Twins commonly experience decreased growth after 26-28 week, and, as in this set, the effect may be more pronounced on the smaller of the twins.*

**Head**

Reece et al\textsuperscript{92} reported that the growth of the fetal head was not significantly different from that observed in singleton pregnancies. According to his findings nomograms derived from singleton pregnancies remains useful for twin gestations.
Limbs

Another study conducted by Reece et al. evaluated growth of the long bones in multiple and singleton gestations. Although a difference in fetal growth between these two groups was found, the authors concluded it was not statistically significant to justify the generation of separate nomograms for twins.

Abdomen

Neonatal differences in abdominal circumference from the normal singleton population are frequently identified. It is still unclear if these differences occur due to genetic differences in growth potential of twins or if they are secondary to decrease supplies. Our personal impression is that it is better to consider twin growth with singleton measurement. Using special twin chart increases the risk that the nomograms be established on fetuses with less than adequate growth and thus mask the presence of growth restriction in the index fetus. Despite the controversies regarding the use of nomograms in twin gestations, concordant growth should be expected between fetuses.

Appropriate growth of twins with similar sized chest and abdominal areas
Growth discrepancies

Definition
Anthony Vintzileos has pointed out that the term “growth discordance” was introduced many years ago when obstetricians had no ultrasound to estimate fetal weights or gestational ages. In these dark old days they only had a scale, so they only could measure the weights after birth. Since then, the term has been used to underline the associated increased mortality and morbidity that only affects the small (IUGR) twin. It would be inappropriate to institute fetal surveillance in the setting of discordance when one twin has an EFW at the 50% percentile and the other at the 90% percentile, because neither of these twins would have IUGR. The data has shown that there only is increased morbidity and mortality when discordance is associated with IUGR. Conversely, when both twins have IUGR, fetal surveillance is indicated because of the increased risk despite the lack of discordance. The term should thus be abandoned because it promulgates confusion, and unnecessary testing.

Fetal growth discrepancy is defined as a greater than 20% difference in the inter-twin estimated fetal weight. It is generally caused by placental insufficiency resulting in growth restriction of one twin, death of one twin after the 16th week or chromosomal abnormalities. The definition of growth discrepancy should be categorized with respect to gestational week since the level of discrepancy varies at different stages of pregnancy. Most cases of growth discrepancy are diagnosed at the second half of the pregnancy. However, pathology can be present as early as the first trimester.

Sonographic features
The standard care for twin pregnancy includes serial sonographic evaluations to assess the growth of each fetus. Findings suggestive of growth discrepancy include:

- Estimated fetal weights discordant by more than 20%. It can be classified as mild (15-25%) or severe (>25%). Cases of pre-term twin gestations with severe discrepancy are associated with a higher morbidity rate.
- Abdominal circumference diverging by 20 mm or more.
- Difference in biparietal diameter greater than 6 mm, with the smaller biparietal diameter less than 2 standard deviations below the mean.
- Head perimeter diverging by more than 5%.
- Umbilical artery S/D ratios discordant by more than 15% and elevated umbilical artery S/D ratio (≥0.4) in one or both twins.

Differential diagnosis
Twin-to-twin transfusion syndrome is the main differential diagnosis. Observation of discordant sexes or dichorionic placentation excludes this possibility. In general, twin-twin transfusion syndrome is associated with the polyhydramnios-oligohydramnios and/or anemia-polycythemia sequences. Differences in genetic growth potential between the twins are another possibility: both twins would have normal growth but significant size discrepancy. These cases have adequate growth on serial sonographic analysis plotted in a growth chart, normal amniotic fluid volume and birth weight usually above 2500g. Females of unlike-sexed pairs are more likely to present growth discrepancy.

Associated syndromes
Growth discrepancy can be associated with low amniotic fluid volume in the sac of the growth-restricted fetus. The smaller twin is at increased risk of perinatal morbidity and mortality as well as reduced physical and mental development later in life. The association with prematurity also implies a high perinatal morbidity and mortality for the affected twin. When growth discrepancy is associated with death of one of the twins, the presence of a fetus papyraceous is expected on subsequent scans. When the etiology of the condition is a chromosomal abnormality, fetal structural defects might be found at sonographic evaluation. Twin pregnancies following in vitro fertilization (IVF) or gamete intrafallopian transfer (GIFT) are more likely to result in birth weight discordance, as well as those with high serum alpha-fetoprotein levels.

Doppler evaluation
Doppler assessment of uterine and umbilical blood flows may be used to evaluate fetal well-being in multiple gestations. It has been demonstrated that fetuses with abnormal Doppler velocimetry have increased mor-
bidity and mortality rates. Some have found umbilical Doppler velocimetry useful to predict discrepancy in twins, it is certainly an important tool to diagnose congenital anomalies such as twin reversed arterial perfusion sequence, where a retrograde perfusion in the umbilical artery of the abnormal twin is found. Other important applications of Doppler velocimetry are the demonstration of superficial anastomoses in twin-twin transfusion syndrome and identification of cord entanglement, which is a pathognomonic sign of monoamnionicity.

### Chromosomal anomalies

Chromosomal abnormalities are more frequent in multiple pregnancies than in the general population. In dizygotic pregnancies two oocytes are fertilized and each oocyte has an inherent risk of a chromosomal anomaly. The result is an increased rate of chromosomal abnormalities for any given maternal age. The genetic risk is calculated as 166% the empiric maternal age risk. Rodis and co-workers constructed a nomogram for the calculation of risk of chromosomal abnormalities in twin gestations. For example, in the United States, a 33-year-old mother with a twin gestation carries the same risk of chromosomal abnormalities as a 35-year-old woman with a singleton pregnancy. This concept has clinical implications in the management of twin gestations and the maternal age at which cytogenetic studies should be offered.

When karyotyping is recommended chorionic villus sampling is an early and safe technique of prenatal diagnosis in multiple pregnancies. If the invasive procedure is performed during the second trimester, amniocentesis should be the first choice.

Fetal sex assignment can be another useful information, particularly in pregnancies at risk for severe sex-linked diseases and fetal disorders involving the genitalia. It is worth mentioning that there have been reports of discordant sex in monozygous twins (see figure above).

Monozygotic twins are highly concordant for minor anomalies, tend to be concordant for rare congenital defects and malformations, and are predominantly discordant for more common major malformations. In general, the smaller twin is the more severely affected. There are reports of discordant karyotype in identical twins, with the recommendation of sampling both sacs if one or both fetuses have ultrasound abnormalities, even if the scan is suggestive a monochorionic pregnancy. This technique must be carefully performed making sure that each sample is properly attributed to the correspondent twin.

Klinefelter syndrome with inversion of chromosome 13 in the co-twin, trisomy 13, aneuploidy and gonadal dysgenesis are some of the discordant chromosomal abnormalities reported in twins.

### Congenital anomalies

Multiple gestations have approximately twice as many congenital anomalies when compared to the expected rate for the general population. Major anomalies are seen in 2.1% of twins versus 1.2% of singletons while minor anomalies are seen in 4.1% of twins versus 2.4% of singletons.

Some of the anomalies reported in multiple gestations are: cloacal dysgenesis sequence, cyclopia, amniotic band disruption complex, cystic hygroma, cerebral and ocular abnormalities, microcephaly and Russel-Silver syndrome among others.

According to the literature, the occurrence of malformations is higher in monozygotic than in dizygotic twins. The reported incidence of anomalies in monozygotic twins is around 16.7% for minor plus an additional 16.7% for major anomalies. If a malformation is observed in one twin, the other has a high chance of being equally affected. Concordance, however, is seen in just 10 to 20% of monozygotic twins.

A careful anatomy survey is necessary to exclude a discordant anomaly, especially in monozygotic pairs. Three theories have been proposed to explain the etiology of structural anomalies in monozygotic twins.
1. The first theory postulates that the crowding of the uterine cavity may be associated with certain types of anomalies. This would explain the statistically significant concordance seen in musculoskeletal abnormalities in monozygotic twinning, predominantly clubfeet.

2. The second theory advocates the occurrence of an early defect in the process of splitting or a delay at the splitting of the embryo that should cause structural anomalies in the fetuses. The ultimate example of this theory is the conjoined twins.

3. The third theory associates fetal anomalies to a vascular compromise secondary to a shared placenta. Syndromes that relate to this etiology include twin reversed arterial perfusion, twin–twin transfusion syndrome, and twin embolization syndrome.

### Unique monozygotic monochorionic syndromes

**Twin-twin transfusion (Stuck twin)**

**Definition**

Twin-twin transfusion syndrome is a pathological condition whereby a donor fetus bleeds into the circulation of a recipient fetus through the abnormal inter-twin placental anastomoses. The donor twin becomes anemic, hypovolemic, growth restricted, and as a consequence has a reduced urinary production. Since swallowing of the fluid is not impaired, the amniotic fluid volume progressively decreases. The recipient twin becomes hypervolemic. Lacking a mechanism to remove blood, the recipient twin eliminates as much fluid as possible, thus becoming hypercytemic or even hydropic in the more severe cases. The elevated urinary production from the recipient twin leads to polyhydramnios and an overdistension of the amniotic cavity, that compresses the donor and it’s vascular supply against the uterine wall, further decreasing perfusion to the donor fetus. The reduction in amniotic fluid on the donor side results in a close apposition of the inter-twin membrane that fixes the donor fetus to the uterus, a condition nicknamed “stuck twin”\(^{181}\).

<table>
<thead>
<tr>
<th>The donor twin:</th>
<th>The recipient twin:</th>
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<tbody>
<tr>
<td>• Chronic blood loss:</td>
<td>• Chronic blood gain:</td>
</tr>
<tr>
<td>• anemic,</td>
<td>• hypervolemic</td>
</tr>
<tr>
<td>• hypovolemic,</td>
<td>• polycytemic</td>
</tr>
<tr>
<td>• hypoxia</td>
<td>• embolization</td>
</tr>
<tr>
<td>• growth restricted,</td>
<td>• hypertension</td>
</tr>
<tr>
<td>• decreased renal flow,</td>
<td>• cardiac failure</td>
</tr>
<tr>
<td>• oligohydramnios</td>
<td>• hydropic</td>
</tr>
<tr>
<td>• vascular compression</td>
<td>• polyhydramnios</td>
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</tbody>
</table>

In twin-twin transfusion syndrome (top drawing, note the artery to vein connection) the donor twin (on the left) becomes anemic, hypovolemic, growth restricted, and as a consequence has a reduced urinary production. Since swallowing of the fluid is not impaired, the amniotic fluid volume progressively decreases (yellow lines representing the interamniotic membrane. Conversely, the recipient twin (on the right) becomes hypervolemic. The elevated urinary production from the recipient twin leads to polyhydramnios and an overdistension of the amniotic cavity, that compresses the donor and it’s vascular supply against the uterine wall, further decreasing perfusion to the donor fetus. The end condition is the “stuck twin” (lower drawing)
Sonographic features
Commonly reported criteria for the diagnosis of twin-to-twin transfusion syndrome are:

- Monochorionic placentation, with visualization of a separating membrane;
- Same sex fetuses;
- Mid-trimester polyhydramnios-oligohydramnios sequence (polyhydramnios at the recipient’s sac and oligohydramnios at the donor’s sac), in the absence of other causes of abnormal amniotic fluid volume;
- Size discordance, with the larger twin in the polyhydramniotic sac and the smaller stuck against the uterine wall (abdominal circumference difference or weight discrepancy > 20%);\(^1\);\(^2\);
- Non-visualization of the donor’s bladder with enlarged recipient’s bladder;
- Abnormal Doppler S/D ratio at the umbilical cord (> 0.4). The absent end-diastolic flow in the donor’s umbilical artery accompanied by venous pulsation in the recipient’s umbilical vein are usually associated with a poor prognosis;\(^3\);\(^4\);\(^5\);\(^6\);
- Hydrops or evidence of congestive heart failure of either twin (although more common in the recipient twin);\(^7\);\(^8\);\(^9\);

As the transfusion progresses, the donor twin loses more fluid and the recipient produces more. The net effect being that the membranes become closely apposed to the donor-twin.

The difference in size of the cord is clearly visible.

The anastomosis is occasionally visible.
Before the donor twin becomes stuck, a typical intermediate stage is the “folding membrane” stage where the redundant membrane progressively folds as it wraps itself around the donor.

At some point the “folding membrane” stage could impose for an amniotic band syndrome. Awareness of the condition will prevent a misdiagnosis.

The typical appearance of the “stuck twin” immobilized in a portion of the uterus
The criteria used to select cases for the open multicentric randomized trial to evaluate serial amniodrainage versus endoscopic placental surgery in the treatment of twin-to-twin transfusion syndrome are:

- Twin pregnancy diagnosed as monochorionic during a first trimester scan and/or as having a single placental mass and concordant sex on the second trimester scan.
- Polyhydramnios in one sac with a deepest vertical pool of amniotic fluid of at least 6.0 cm at less than 20 weeks of gestation, 8.0 cm at 20 to 22 weeks, and 12.0 cm at 23 to 25 weeks. The polyhydramnios should be related to polyuria with a distended fetal bladder during most of the examination period.
- Oligohydramnios (stuck twin) in the other sac with a deepest vertical pool of amniotic fluid of at most 2.0 cm. The oligohydramnios should be likely related to fetal oliguria with a collapsed bladder during most of the examination period.

In the most severe forms, the diagnosis should not be difficult: a single placenta, massive polyhydramnios in the sac of the recipient twin, a stuck donor twin attached to the uterine wall with poor mobility and obvious growth discordance. Milder forms of the disease are more difficult to diagnose due to the lack of uniform criteria; however, one should suspect twin-to-twin transfusion in the presence of amniotic fluid discrepancy between the cavities, regardless of the percentage of weight discrepancy between the twins. An inter-twin hemoglobin difference >2.4 gm/dl in fetal blood obtained by cordocentesis has been shown to be consistent with stuck twin syndrome.

Prevalence

Twin-to-twin transfusion complicates about 15-35% of monochorial twin gestations and is responsible for 17% of the perinatal mortality in multiple pregnancies.

Pathogenesis

If embryonic splitting occurs before day three after fertilization, two independent fetuses with separate placentas will result. A single placenta with two amniotic cavities occurs if splitting takes place between days four and seven. If division of the embryoblast occurs after about eight days, the twins share a single placenta and amniotic cavity (monochorionic-monoamniotic twins). Division beyond day 12 results in conjoint twins.

When two fetuses share the same placenta, vascular anastomoses develop between their circulations. These anastomoses can be of three types: vein-to-vein, artery-to-artery, and artery-to-vein. Even when there are multiple vascular connections within a single placenta, no transfusion should occur provided the anastomoses are balanced. Placentas from pregnancies with twin-to-twin transfusion syndrome have fewer anastomoses, which are more likely to be solitary and of deep arterio-venous type than those without twin-to-twin transfusion syndrome. When the transfusion occurs, the donor or “pump” twin becomes hypovolemic due to blood loss. Hypoxia develops because of placental insufficiency, which is also responsible for intrauterine growth retardation. Poor renal perfusion leads to oligohydramnios. This latter feature, when severe, is responsible for the classical appearance of the stuck twin: the amniotic sac becomes too small, the amniotic membrane comes in close contact with the body of the “pump” twin and the fetus appears trapped to the uterine wall. Hypervolemia with increased renal perfusion leads to polyhydramnios in the sac of the recipient twin. Since there is no loss of protein or cellular components from its circulation, colloid osmotic pressure draws water from the maternal compartment across the placenta, establishing a vicious cycle of hypervolemia, polyuria and hyperosmolarity leading to high output cardiac failure, hydrops and polyhydramnios.

Prognosis

Basically, the prognosis depends on the stage of the pregnancy at which the disease manifests and the severity of the circulatory imbalance. When signs of twin-twin transfusion syndrome are seen at mid-gestation there is a higher risk of perinatal morbidity and mortality. Intrauterine hypoxia, pre-term delivery, and death of one fetus (usually the donor) with subsequent death or hypoxia-ischemia in the surviving twin are the most common complications to watch for in these pregnancies.
Management
Aggressive treatment appears to be more successful than conservative medical management\textsuperscript{213}. For many years, the most employed technique has been amnio-drainage of the recipient amniotic sac by serial amniocentesis\textsuperscript{214,215,216,217,218,219,220,221}. The aim of amniocentesis is to restore the normal amniotic fluid volume and thereby decreasing the pressure on the donor vasculature and improving its perfusion, and decreasing the risk of polyhydramnios-induced preterm labor and thus prolong the pregnancy. The number of amniocentesis and volume of fluid drained varies, depending on the severity of the polyhydramnios, degree of fetal compromise and maternal symptoms. Approximately one liter of amniotic fluid should be removed for every 10cm of amniotic fluid index elevation. Possible mechanisms of action for serial amniocentesis are:

- restoration of placental shape with realignment of maternal spiral artery entry points with placental lobules; and
- reopening of compensatory low-pressure veno-venous anastomoses.

Amniocentesis, however, only temporarily corrects the symptoms and multiple complications and does not alter or interrupt the pathological chain of event responsible for the condition. Perinatal survival with amniocentesis is quoted as 61\% ± 22\%. However, there remains a risk of serious chronic handicap in 19\% ± 5\% of the survivors\textsuperscript{222,223,224,225,226,227,228,229,230,231,232,233,234,235}. More recently, ablation of communicating vessels on the placental surface by neodymium YAG laser guided by fetoscopy has been proposed\textsuperscript{236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252}. The aim of this technique is to interrupt the abnormal placental vascular communications between the twins. Although the survival rate comparing amniocentesis with fetoscopy is similar, preliminary studies suggest a significant decrease in neurological handicap among survivors submitted to fetoscopy (Table I). A multicentric randomized trial is currently being conducted by the EUROFOETUS group in order to answer this question\textsuperscript{197}.

Although some authors advocate an intentional rupture of the intervening membrane (amniotic septostomy) to equalize the volume of fluid in both sacs\textsuperscript{253,254}, it has been argued that artificial normalization of the fluid volumes with septostomy would not change the hemodynamic status of the fetuses and disruption of the membranes could lead to death of the fetuses from cord entanglement\textsuperscript{255}. Ligation of the umbilical cord\textsuperscript{256} of the donor twin and maternal treatment with indomethacin or digoxin\textsuperscript{257,258} have also been proposed as therapeutic options in selected cases. Further information on treatment can be obtained at www.fetalmd.com.

Table I. Management of twin-twin transfusion syndrome by laser coagulation.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Study design</th>
<th>N cases</th>
<th>Technique</th>
<th>Intact survival of both twins</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Lia et al.</td>
<td>1995</td>
<td>Case series</td>
<td>26</td>
<td>Nd:YAG laser coagulation of the placental vessels crossing the interamniotic membrane</td>
<td>34.6% (9/26)*</td>
<td>34.6% (9/26)</td>
</tr>
<tr>
<td>Ville et al.</td>
<td>1998</td>
<td>Case series</td>
<td>41</td>
<td>Nd:YAG laser coagulation of the placental vessels crossing the interamniotic membrane</td>
<td>36.5% (15/41)</td>
<td>41.5% (16/41)</td>
</tr>
<tr>
<td>Hecher et al.</td>
<td>1999</td>
<td>Comparative study</td>
<td>116</td>
<td>Nd:YAG laser coagulation of the placental vessels crossing the interamniotic membrane (n=73; Hamburg)</td>
<td>42% (31/73) p=1.00</td>
<td>37% (27/73) p=0.058</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Serial amniocentesis (n=43; Bonn)</td>
<td>42% (18/43)</td>
<td>19% (8/43)</td>
</tr>
<tr>
<td>De Lia et al.</td>
<td>1999</td>
<td>Case series</td>
<td>67</td>
<td>Nd:YAG laser coagulation of the placental vessels crossing the interamniotic membrane</td>
<td>56.7% (38/67)</td>
<td>25.4% (17/67)</td>
</tr>
</tbody>
</table>

*one triplet pregnancy
**Differential diagnosis**

The differential diagnosis should mainly include twins of discordant size that do not have the transfusion syndrome as the underlying pathophysiologic mechanism for the problem. Some authors have proposed a new entity called twin oligohydramnios-polyhydramnios sequence\(^{259,260}\), of which twin-twin transfusion would be part. Histopathological studies of the placenta are required to differentiate twin-twin transfusion from the other conditions included in twin oligohydramnios-polyhydramnios sequence. Isolated intrauterine growth restriction can be considered if the growth discrepancy is less than 15% and the other features of the syndrome are not present. Dichorionic twin pregnancy with fused placetas and growth restriction of one of the fetuses is another condition that can lead to misdiagnosis. This can be excluded if the twins have different sexes or after birth, by histopathological analysis of the placenta. Other differential diagnoses to be considered are: TORCH infections restricted to one twin, asymmetrical chorionic development, feto-maternal hemorrhage, abruption, agenesis of the ductus venosus and bilateral renal agenesis\(^{261,262,263}\).

**Associated syndromes**

The over-distension of the uterus caused by the polyhydramnios can cause pre-term labor, amniorrhexis, abruptio placentae, and maternal respiratory and abdominal discomfort. Death of one twin is associated with at least a 25% risk of death or neurological handicap of the surviving twin. Although the cause of neurological handicap has been usually attributed to embolization\(^{264,265,266,267,268,269}\), currently accepted evidence points out severe hypotension with hemorrhage from the live fetus into the dead fetoplacental unit as the causative factor\(^{45,46,270}\).

**Fetus papyraceous**

Papyraceous fetus is characterized by a macerated fetus, resulting from an early loss (second trimester) of one twin, and may affect both mono and dichorionic gestations. The non-viable fetus is compressed by the expanding sac of the co-twin and partially absorbed throughout the pregnancy\(^{271,272}\). The surviving twin often has sequelae of twin embolization syndrome such as aplasia cutis, a rare disorder characterized by localized absence of skin\(^{273,274}\).

![A macerated fetus next to the live cotwin.](image)

**Twin embolization syndrome**

**Definition**

Twin embolization syndrome is a complication of monozygotic twinning following in utero demise of the cotwin\(^{275}\). It results from the embolization of placental and fetal thromboplastins or to the direct embolization of necrosed fragments of the placenta from the dead fetus, disseminated intravascular coagulation causing embolization, or even an endarteritis\(^{276,277}\). The emboli damages predominantly high vascularized organs such as the brain and kidneys, but can affect almost all organ systems. In the central nervous system these emboli can result in ventriculomegaly, porencephaly, cerebral atrophy, cystic encephalomalacia or microcephaly\(^{278}\). Extracranial abnormalities include small bowel atresia, gastroschisis, hydrothorax, aplasia cutis and renal cortical necrosis\(^{279,280}\).
Sonographic features

Dead twin associated with a surviving twin affected by:

- CNS anomalies: ventriculomegaly, porencephaly, cerebral atrophy, cystic encephalomalacia, microcephaly
- somatic anomalies
- small bowel atresia
- gastroschisis
- hydrothorax
- aplasia cutis
- renal cortical necrosis
- limb amputation

After demise of a cotwin, the survivor developed an intraparenchymal hemorrhage in the brain (echogenic area) that evolved into an area of porencephaly.

Differential diagnosis

The presence of any of the above mentioned anomalies in the surviving twin with a dead co-twin should raise the suspicion. Only fetal death occurring during the second and third terms of pregnancy is considered.

Associated syndromes

Twin-to-twin transfusion – if one of the fetuses dies due to twin-twin transfusion syndrome, a retrograde blood flow carrying thromboplastic material from the dead twin may reach the blood stream of the survivor through the placental anastomosis, causing disseminated intravascular coagulation. Another possibility is the emboli itself from the dead twin reaching the survivor’s circulation.

**Twin-reverses arterial perfusion syndrome (TRAP or Acardiac twin)**

Definition

Twin-reversed arterial perfusion (TRAP) sequence is a rare condition reported at an incidence of 1% of monochorionic twin pregnancies (0.3:10,000 births), resulting in coexistence of a normal “pump” twin and an acardiac twin.

Sonographic features

The pathognomonic feature is the presence of reversed arterial perfusion on Doppler. When imaging the umbilical cord with Doppler, arterial waveforms are observed from the placenta towards the acardiac twin. Venous blood flow takes the opposite direction. This finding results from the absence of a heart
(pump) in the acardiac twin in association with artery-to-artery communications on the placenta, allowing the acardiac twin to get its blood supply from the normal twin\textsuperscript{292}.

The abnormal fetus presents with impaired or absent development of cephalic pole, heart, upper limbs and many viscera. The lower limbs are relatively well preserved, although clubbing and abnormal toes are common. The appearance is so pathognomonic that the diagnosis has been made as early as 10 weeks\textsuperscript{293}. A 2-vessels cord is the rule (66\%)\textsuperscript{294}. The membrane development between the twins is inconsistent and varies from full sac to strips of membrane. Occasionally the umbilical artery of the acardiac twin connects to the superior mesenteric artery (instead of the iliac artery), which is the persistence of a “primitive” vitelline supply.

\textit{Reverse flow on pulsed/color Doppler: arterial flow in the vessel going in (under the base line) and venous flow in the vessel going out (above the baseline).}

\textit{This large mass is an acardiac twin (large cystic hygroma on the left) and ill-defined body parts on the right.}
Pathogenesis

The mechanism that has been proposed is the association of paired artery-to-artery and vein-to-vein anastomoses through the placenta combined with delayed cardiac function of one of the twins early in pregnancy. Some authors have also suggested that aneuploidies could lead the abnormal twin to have a slower development than the healthy twin as a possible etiological factor. Chromosomal abnormalities have been found in 33% of the acardiac twins. If one twin develops slower, the imbalance in the blood pressure of the twins will result in a retrograde transfer of blood from the healthy twin to the abnormal twin. The retrograde flow of poorly oxygenated blood through the developing heart of the abnormal twin interferes with the development of that twin’s heart that rarely goes beyond the stage of tubular heart causing the “acardia”. The upper half of the body of an acardiac twin is extremely poorly developed and, sometimes, not developed at all. Head, cervical spine and upper limbs are usually absent. Edema and sonolucent areas in the upper body, consistent with cystic hygroma, are common. In contrast, the lower half of the body, although malformed, is better developed. This pattern of development may be explained by the mechanism of perfusion of the acardiac twin. Blood that enters the abdomen of the fetus is deoxygenated blood that left the normal twin. The morphological abnormalities in the acardiac twin are consistent with perfusion of tissues supplied by the common iliac and lower branches of the aorta with deoxygenated blood. Most of the oxygen available is extracted when the blood enters the acardiac twin, allowing for some development of the lower body and extremities. Lower pressure in the retrogradely perfused upper half of the body, combined with low oxygen saturation impairs the development of this area.

The acardiac twin is thus, a parasite. It requires blood pumped from the normal twin to keep developing, putting the pump fetus at risk of high output cardiac failure. The risk is directly dependent on the size of the acardiac twin: the higher the weight of the acardiac twin, the higher the risk of cardiac failure and death for the normal twin. Overall only 50% of pump twins survive, and the mortality for acardius is 100%.
In the twin-reversed arterial perfusion syndrome the “acardiac” twin is perfused retrogradely with poorly oxygenated blood that should have gone to the placenta.

The mechanism that has been proposed is the association of paired artery-to-artery and vein-to-vein anastomoses through the placenta combined with delayed cardiac function of one of the twins early in pregnancy. If one twin develops slower, the imbalance in the blood pressure of the twins will result in a retrograde transfer of blood from the healthy twin to the abnormal twin. The retrograde flow of poorly oxygenated blood through the developing heart of the abnormal twin interferes with the development of that twin’s heart that rarely goes beyond the stage of tubular heart causing the “acardia”. The upper half of the body of an acardiac twin is poorly or not developed, while the lower half of the body, although malformed, is better developed. The acardiac twin is thus, a parasite. It requires blood pumped from the normal twin to keep developing, putting the pump fetus at risk of high output cardiac failure.

Management
The management includes conservative and invasive therapies. Conservative management includes serial cardiotocography (CTG), ultrasonography and echocardiography, and opportune delivery. Non-invasive therapies may be used supporting the cardiac function of the pump twin with digoxin and indomethacin. The more invasive management consists in termination of pregnancy or interruption of flow to the acardiac fetus, by surgical extraction (hysterotomy with selective delivery of the acardiac twin) and ligation of the acardiac twin’s umbilical cord\textsuperscript{307,308}, ultrasound-guided embolization of the cardiac twin’s umbilical artery with absolute alcohol\textsuperscript{309}, platinum coils or thrombogenic coils, laser vaporization\textsuperscript{310,311}. Large numbers are not available to compare the various techniques.

Nomenclature
Authors have had a field day at creating a nomenclature for each variant (table). This is of little significance, since the disorder is invariably fatal, and the only concern is the preservation of the pump twin.

<table>
<thead>
<tr>
<th>Name</th>
<th>Malformation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acephalus</td>
<td>No cephalic structure present\textsuperscript{312}</td>
</tr>
<tr>
<td>Anceps</td>
<td>Some cranial structure and/or neural tissue present\textsuperscript{313}</td>
</tr>
<tr>
<td>Acormus</td>
<td>Cephalic structure but no truncal structures</td>
</tr>
<tr>
<td>Amorphus</td>
<td>No distinguishable rostral or caudal structure\textsuperscript{314}</td>
</tr>
</tbody>
</table>

Differential diagnosis
Few entities can resemble an acardiac twin. Occasionally a twin-to-twin transfusion could impose for a TRAP. These can be differentiated by the recognition of a membrane (even in a stuck twin), and of course,
cardiac activity in the smaller fetus. A fetal demise in a twin pregnancy could also look like an acardiac, however, there should be no Doppler signal in the dead fetus.

Associated syndromes
None.

**Conjoined twins**

**Definition**
Conjoined twins are monochorionic-monoamniotic twins fused at any portion of their body as a result of an incomplete division of the embryonic disk, which occurs after the 13th day of conception. The term “conjoined” is actually a misnomer, since most authors consider the pathogenesis of the condition to result from failure of complete separation, instead of fusion of twin.

**Sonographic features**
The minimal sonographic criterion for the prenatal diagnosis of conjoined twins is the visualization of fused portion of the bodies of monozygotic-monoamniotic twins. Aside from this basic criterion, several sonographic signs (listed below) can be observed in this condition. Careful search for these features and serial scans for confirmation are recommended to prevent misdiagnosis. The following sonographic criteria can also be observed in conjoined twins:

- Bifid appearance of the first-trimester fetal pole ("V" or "Y" shaped twin pregnancy), continuous skin contours at the same anatomic level
- Absence of a interamniotic membrane between the twins
- Inability to separate fetal bodies
- Presence of fetal anomalies
- Abnormal number of vessels (more than three) in the umbilical cord
- The heads and bodies of both twins are seen at the same level
- Unusual extension of the spines
- Unusual proximity of the extremities
- Permanent position of the fetus relative one to another, even after external stimulation or maternal movement
- Presence of a single heart

One unusual case of conjoined twins that only shared a part of the cord has also been described.

*The presence of more than 3 vessels in a cord is a strong marker of conjoint twins.*
The heads are seen in an unnatural position at the same and constant level.

Conjoint abdomen in frontal position. Note the stomach bubbles in diagonal positions.

A shared heart is a sign of non-operability.

The presence of these signs varies according to the different types of conjoined twins. These must be considered whenever a monochorionic and monoamniotic pregnancy is suspected. Discordant presentation does not exclude conjoined twins. Although the diagnosis of conjoined twins is easier during the first trimester, the type and severity of the condition is better achieved during the second trimester, when a more precise evaluation of the shared organs can be done. The diagnosis with 3D-transvaginal sonography during the first trimester has also been described. If diagnosis is made before viability, termination of pregnancy can be offered.
Prevalence
This is a rare condition and the reported frequency varies from 0.1-0.35:10,000 births. If stillborns are excluded the estimate is 0.05:10,000. Females are more commonly affected with a male to female ratio of 1.6-3:1. No association with maternal age, race, parity or heredity has been observed. The recurrence risk is negligible.

Prognosis
Most of the conjoined twins are born prematurely, 40% are stillborn, and 35% die within 24 hours. Among the survivors, the prognosis as well as attempts of surgical separation will depend on the type of conjunction, degree of involvement of the shared organs, and the presence of associated anomalies. The most ominous prognosis is among those twins who share liver and/or heart. Attempts of separation in cases of a common liver can be done as long as two biliary tracts are seen. In the presence of a shared heart, separation is only attempted if two normal hearts coexist in a single pericardium.

Management
The method of choice for delivery is C-section to maximize survival and prevent maternal and fetal trauma.

Classifications
Conjoined twins are classified according to the area of the bodies where the fusion takes place and the involvement of internal organs. The symmetrical and equal forms, in which the twins have equal or nearly equal duplication of structures, are called duplicata completa. When there is an unequal duplication of structures they are called duplicata incompleta, and this category includes the most severe types of conjoined twins in which just few organs systems are duplicated. The most frequent varieties of conjoined twins are thoracopagus (40-74%), omphalopagus (10-33%), pygopagus (18%), ischiopagus (6%) and craniopagus (1-6%). The classification of conjoined twins is described in the table.

Classification of conjoined twins

**Duplicata incompleta**: duplication occurring in only one part or region of the body.

Examples:
- Diprosopus: one body, one head, two faces
- Dicephalus: one body, two heads
- Dipygus: one head, thorax and abdomen with two pelvis, and/or external genitalia
**Duplicata completa**: two complete conjoined twins

**Terata catadidyma**: conjunction in the lower part of the body

Examples:
Ischiopagus: joined by inferior portion of coccyx and sacrum
Pygopagus: joined by lateral and posterior portion of coccyx and sacrum

**Terata anadidyma**: conjunction in the upper part of the body

Examples:
Syncephalus: joined by the face
Craniopagus: joined at homologous portion of the cranial vault

**Terata anacatadidyma**: conjunction in the midpart of the body

Examples:
Thoracopagus: joined at the thoracic wall
Xiphopagus: joined at xiphoid process
Omphalopagus: joined in the area between the xiphoid cartilage and the umbilicus
Rachipagus: joined at the level of the spines above the sacrum


In one attempt to universalize the current nomenclature, a new classification was proposed recently based on the theoretical site of union:

**Ventral union**: twins united along the ventral aspect

**Cephalopagus**: fused from the top of the head down to the umbilicus. Two rudimentary (fused) faces, four arms and four legs. Lower abdomen and pelvis are separated. The cephalothoracopagus Janiceps type is a rare variety of conjoined twins in which the fetuses are joined face to face, the face of each fetus being split in the midline and in half turned outward, so that each observed face is made up of the right face of one fetus and the left face of the other. The name originates from Janus, in Roman mythology, the god of gates and doorways, his statue with two faces, facing east and west for the beginning and ending of the day; and caput, head.
**Thoracopagus:** united face-to-face from the upper thorax down to the umbilicus, with heart involvement always. Four arms, four legs, two pelvises.

**Omphalopagus:** joined face-to-face primarily in the area of the umbilicus, and sometimes involving the lower thorax, but always preserving two distinct hearts. There is not even a cardiac vessel in common. Two pelvis, four arms and four legs\(^{350,351}\).

**Ischiopagus:** united ventrally from the umbilicus to a large conjoined pelvis with two sacrums and two symphyses pubis. They appear more frequently joined end-to-end with the spine in a straight line, but they can also present face-to-face with a joined abdomen. Four arms, four legs, and in general, a single external genitalia and a single anus.

**Lateral union:** twins joined side-by-side with shared umbilicus, abdomen, and pelvis.

**Parapagus:** twins that share a conjoined pelvis, one symphysis pubis and one or two sacrums. When the union is limited to the abdomen and pelvis (does not involve the thorax) it is called dithoracic parapagus. If there is one trunk with two heads it is called dicephalic parapagus. If there is a single trunk and a single head with two faces they are diprosopic parapagus. Two, three or four arms, and two or three legs.

**Dorsal union:** twins joined at the dorsal aspect of the primitive embryonic disc. There is no involvement of thorax and abdomen

**Cranio-pagus:** united on any portion of the skull, except the face or foramen magnum. They share bones of the cranium, meninges, and occasionally brain surface. Two trunks, four arms and four legs\(^{352}\).

**Pygopagus:** they share dorsally the sacrococcygeal, perineal regions and occasionally the spinal cord. There is one anus, two rectums, four arms and four legs.

**Rachipagus:** twins fused dorsally above the sacrum, involving different segments of the column. This type is extremely rare.

**Differential diagnosis**
Conjoined twins have a unique presentation and the few differential diagnoses could include lymphangioma, teratoma, or cystic hygroma.

**Associated syndromes**
Congenital anomalies of organs other than the shared ones are present in 50% of the cases of conjoined twins. Cardiac defects are the most common association (20-30%) and thus echocardiography is recommended in all cases. Neural tube defects and midline fusion defects, orofacial clefts, imperforate anus and diaphragmatic hernia are also frequently seen. Polyhydramnios is observed in 50-75% of the cases.

**Fetus-in-fetu**

**Definition**
A fetus-in-fetu is an encapsulated, pedunculated vertebrate tumor. It represents a malformed monozygotic, monochorionic diamniotic parasitic twin included in a host (or autosite) twin (see Etiology below). Characteristically the fetus-in-fetu complex will be composed of a fibrous membrane (equivalent to the chorioamnionic complex) that contains some fluid (equivalent to the amniotic fluid) and a fetus suspended by a cord or pedicle. The presence of a rudimentary spinal architecture is used to differentiate a fetus-in-fetu from a teratoma, since teratomas are not supposed to develop through the primitive streak stage (12-15 days). This last criterion has been considered too stringent by many authors who regard a rudimentary body architecture (metameric segmentation, craniocaudal and lateral differentiation, body coelom, “gestational sac”), or the presence of an associated fetus-in-fetu as equivalent criteria. Although teratomas can achieve striking degrees of differentiation by the inductive effect of adjacent tissues on one another, they do not present the criteria mentioned above.
Synonyms
As for any unusual anomalies, several descriptive terms have been used. These include: cryptodidymus (κρυπτό = hidden, δίδυμος = twin), dermocyme (δέρμα = skin, κυμα = fetus), double monster, endocyme fetus (ἐνδον = inside, κυμα = fetus) [note that the word fetus is redundant], fetiform teratoma, fetal inclusion, included heteropagus twin (ἔτερος = other, πυγμα = which is fixed) and suppressed twin.

Prevalence
The prevalence is unknown. About 70 cases have been reported but this number varies according to how strictly identification criteria are used (see Definition above). Several cases have been formally recognized by some as fetus-in-fetu, while categorically rejected by others. Seven cases have been detected in utero. An estimated frequency of 0.02:10,000 is commonly reported in the literature, but this number is based on the unsubstantiated assumption that fetus-in-fetu represents 5% of conjoined twins. Further, (see Etiology) the current trend is to consider that fetus-in-fetu does not represent a form of conjoined twins. The male-to-female ratio in the 39 reports that we reviewed was M1.3:F1. This is in contrast with conjoined twin, which occurs predominantly in girls.

Historical review
Several cases of fetus-in-fetu were reported in the past, and no distinction from teratoma was done until the first quarter of this century. For this reason, those reports that did not clearly identify the presence of a spine are subject to caution. Further, because of possible confusion with abdominocyesis, cases in women of childbearing age should be interpreted cautiously. The most credible old cases are those reported by Young, Hightmore and Taylor. Only the first two reports include figures. Young reports the case of an 18-week-old boy examined for vomiting. On physical examination, a smooth, round tumor was palpated in the left upper quadrant. The patient was lost to follow-up but returned 5 months later, emaciated. The tumor had grown and extended to the scrobiculus cordis (the epigastric fossa), and the child poorly tolerated breast-feeding. Young describes episodes of enlargement and decrease of the abdominal perimeter, which he attributes to accumulation of fluid in the cyst. The child died at 9 months. On autopsy, a large mass occupying most of the abdomen was found. Opening the cyst revealed the fetus-in-fetu. Young gives a remarkably complete description of the findings.

The case reported by Highmore is even more extraordinary in that it occurred in a teenage boy. This 15-year-old boy had a 7-year history of abdominal complaints and mass. As in the previous case, the child died of malnutrition. At autopsy, a large tumor containing a fetus was discovered.

Etiology
Several etiologies have been proposed. A primordial organizer defect was once thought to explain dermoids, teratoma and embryoma. Another theory suggested that the fetus-in-fetu derived from germ cells from the host that evolved on their own. This appears to be supported by the occasional localization in an ectopic testicle. However, that localiza-
tion can also result from migration of the fetus-in-fetu along with the germ cells, when the germ cells of the host return from the yolk sac into the retroperitoneal cavity on their way to the gonads. A parthenogenetic origin has also been suspected. In this theory, germ cells from the retroperitoneal region (where they normally are located) are parthenogenetically stimulated and evolve into a rudimentary fetus. Histocompatibility studies and gene markers do not support parthenogenesis as a likely etiology.

In the continuum theory of monozygous twin, a progression from normal twin to conjoined symmetrical twins into asymmetrical twin (acardiac twins) and then into parasitic twins, included twins and then teratoma is hypothesized. As mentioned under Prevalence, the incidence is about equally divided among sexes (with a slight male predominance in this review), which is an argument against the continuum theory and the highly differentiated sacrococcygeal teratoma theory since conjoined twins and sacrococcygeal teratomas are more common in females.

Willis considered that the fetus-in-fetu did not represent a monoamniotic twin but instead an included monozygotic diamniotic parasitic twin within the host twin: “It is, I believe, a mistake to suppose that a gentle series of gradations exists between double monsters and malformed twins on one hand and teratomas on the other—a mistake widely promulgated because of the prevalent view that teratomas are included monsters or malformed twins. The sooner this misconception is abandoned, the better.” His postulate explains why in all extracranial locations the fetus-in-fetu is embedded in a gestational sac. If the fetus-in-fetu was a conjoined twin, it would have to be monoamniotic and thus would not have its own gestational sac. This theory has been widely accepted.

Pathogenesis

The currently accepted mechanism is the embedding of a twin due to vitelline circulation anastomoses. Vascular anastomoses between twins have variable repercussions, depending on the vessels anastomosed and the location of the anastomoses. The most benign anastomoses are superficial connections of similar vessels on the surface of the placenta. These connections between artery and artery or vein and vein are common and of limited significance when they occur after the first few weeks of gestation. When they occur early, and one fetus has a slight developmental delay, they result in the twin reversed arterial perfusion syndrome. Anastomoses that are between dissimilar vessels and occur in the placenta are responsible for the twin-to-twin transfusion syndrome.

Finally, anastomoses between vitelline vessels —only possible when the twins are monochorionic—are assumed to cause fetus-in-fetu by a mechanism similar to that which produces acardiac twins. The cardiac development of the affected twin is impaired by the reversal of the flow in its heart. This stunts the growth of the affected fetus, and as the host grows it progressively embeds the smaller twin around the third week.

A few intracranial cases have been described. The location in the skull results from a different embryological mechanism. To be imbedded in the ventricle, a fetus-in-fetu has to separate at a much latter date than those that are imbedded in the retroperitoneum. At 15 days, when the embryo is at the bilaminar disc level, the primitive streak develops. At the cephalic end of the streak, a depression, the primitive knot or Hensen's node, forms and extends cranially. The invagination of the cells into the depression is at the origin of the mesoderm and forms the notochordal process (or blastopore). The blastopore extends to become the notochord, which elongates towards the cranial end. If a second differentiation focus occurs in the bilaminar embryo and grows
at the same rate as the primary focus, it will form a craniopagus conjoint twin. If the second differentiation focus grows slower than the primary focus, it will be engulfed in the invagination of cells and may arrest in what will ultimately become the ventricles. A fetus-in-fetu might thus also arrest along the central canal of the spinal cord. In intracranial fetus-in-fetu, one does not expect to find a gestational sac (amnion or chorion equivalent), and indeed none of the intracranial cases have described any surrounding membranes.

The cause of intracranial and spinal fetus-in-fetu is probably due to the presence of a second differentiation focus in the bilaminar embryo.

Localization
The majority of fetus-in-fetu are retroperitoneal, but some have been found in the mesentery adrenal, cranial cavity, lateral ventricles, pelvis, coccyx, inguinal region, testicles and scrotum. Thus, most of the resting places are retroperitoneal or on the path that the germ cells follow on their way back from the yolk sac to the retroperitoneum and onto the gonads. When located on ectopic testes, they may be intraperitoneal. The affected testicle is usually ectopic or undescended, probably because the added bulk impairs the migration of the cells.

Vascularization
As expected from the etiologies, most fetus-in-fetu are connected to the host by vessels originating from or around the superior mesenteric artery, a derivative of the right vitelline artery in mammals. The artery of the fetus-in-fetu derives from the vitelline artery and thus is the equivalent of a superior mesenteric artery. In the host, if the superior mesenteric artery is not directly involved, the connection is usually with direct branches from the aorta, small retroperitoneal or diaphragmatic vessels. In a testicular location, spermatic vessels or even renal and adrenal vessels may be involved. In only a few cases, a definite vascular connection can be recognized between the fetus-in-fetu and the host. In other cases, a capillary system exists between the two circulations. Since the fetus-in-fetu does not have a cardiac system, the severe hypoxia is responsible for the lack of evolution.

Age at detection
Only a few cases have been detected prenatally. Most cases are discovered in newborns or small children.

Weight
The weight varies from a few grams up to 2000 or even 4000g. There is some inexactitude in the report of the weights since some reports mention the weight of the whole tumor, while others report the weight of the fetus-in-fetu alone.
Presenting symptoms in children
Aside from a few fortuitous discoveries, the disorder usually becomes apparent from its compression of adjacent organs, principally the gastrointestinal tract.

Number
Usually one fetus is found, but several instances of two, three, five or even more have been described. When several fetuses are present, they usually share a same sac, but some may have their own sacs.

Zygosity
Studies of gonads, blood types, chromosomes, and red cell antigens (ABO, Rh, M, N, S, P1, K, Fy and Jk) have shown the fetus-in-fetu to be monozygotic to the host. It is not surprising, however, that the fetus-in-fetu has the same blood type as the host, since it is perfused by the host. There have been no recorded cases of dizygosity. However, as in acardiac twins, the combination of a normal twin with a twin that has lost a gonosomal chromosome and thus appears as a 45,X0 could potentially be found.

Macroscopic appearance
At surgery, the fetus-in-fetu appears as a well-circumscribed mass bound by a fibrous membrane. Inside the mass the fetus-in-fetu is suspended in straw-colored fluid by a pedicle. Two vessels (an artery and a vein) travel along the pedicle. The fluid is generally not abundant and has been described as containing sebaceous material. The origin of this fluid is uncertain. Several authors have pointed out that the membranes of a normal embryo are not responsible for the production of amniotic fluid. They would more likely act as semipermeable membrane. In fetuses past 12 weeks, the urinary system produces the fluid and the gastrointestinal system reabsorbs it. Since no fetus-in-fetu has ever been described to contain a urinary system, and the segments of gastrointestinal tract that are found are too incomplete to have any reabsorptive capabilities, the fluid is probably in communication with the extra-cellular fluid of the fetus-in-fetu and maintained in the amniotic cavity solely by osmotic and oncotic pressure.
The presence of chorionic villi has only been reported in one case. Except for one quote of a 15-year-old saying “Mother, do come to me, I have something alive in my body”, and the mother being quoted as saying that she felt something resembling “the motion of a child during gestation”, no fetal movements have ever been recorded in a fetus-in-fetu. The above record of movement is somewhat doubtful since striated muscles have rarely been found around joints. Yet this host is one of the older hosts described.

What is included
Fetus-in-fetu resemble poorly formed acardiac twins. Most every organ has been recognized in various stages of development. The notable exception is the urinary tract, which does not appear to have been recognized in any of the cases that we reviewed. Some structures such as ribs, intrathoracic organs (lung, heart, thymus) and retroperitoneal organs (liver, spleen, kidneys, adrenal glands, pancreas, gonads) are rarely described. An incomplete heart has been found. In one instance, a rudimentary 2-chamber heart was found with the atrium in the caudal position and the ventricle in the cranial position. This is the stage normally reached in a 22-day embryo. Facial and cranial structures also are uncommonly seen, yet eyes, ears, mouth and poorly organized brain and cerebellum have been observed.
The cord that connects the fetus to the membrane has different characteristics than a normal cord: it contains vasa vasorum and nerve fibers.
The evolution of the fetus-in-fetu is usually arrested at the first trimester, and further evolution is by mass accretion more than by development. Overall structures derived from the ectoderm are better represented than structures derived from the other two layers. The mesoderm contributes the musculoskeletal system, which is usually well represented, but the other derivatives (the vascular and urogenital system, the spleen and adrenal glands) are uncommonly found. The most commonly represented derivative from the endodermal layer is the gastrointestinal tract, but the liver and pancreas are also often recognized.
Ultrasound appearance
The few cases detected prenatally all presented as a complex mass. The general appearance is a well-delineated capsule, with an echogenic mass suspended in fluid or partially surrounded by fluid. Occasionally, the diagnosis can be suggested by the recognition of a rudimentary spine.

A fetus in fetu, with a rudimentary spinal organization (Courtesy Caldwell K and Dix P)

Differential diagnosis
When discovered in a newborn child during physical examination, the differential diagnosis includes all the common masses such as Wilms' tumor, hydronephrosis, and neuroblastomas. Prenatally, the main differential diagnosis is with teratoma. Teratomas are disorganized congregations of pluripotential cells from all three primitive tissue layers. By differentiation and induction, they can achieve striking organization, with examples of several organs being well formed. However, teratomas do not have vertebral segmentation, craniocaudal and lateral differentiation, body coelom or systemic organogenesis. Thus the presence of a mass with a spinal organization and surrounded by fluid suggests the correct diagnosis. When spinal structures are not present, most authors have considered that the diagnosis of fetus-in-fetu can still be made when the alternate criteria described under Definition are found. These criteria are sufficiently restrictive that even well organized teratomas cannot fulfill all of them. Teratomas have a definite malignant potential, a feature that has not been reported in fetus-in-fetu. Teratomas occur predominantly in the lower abdomen, not the upper retroperitoneum. Yet, the coexistence of a fetus-in-fetu and a teratoma as well as the occurrence of a teratoma 14 years after removal of a twin fetus-in-fetu have been reported, supporting the older hypothesis of a continuum between twin and teratoma. Cases of sacrococcygeal fetus-in-fetu should probably be regarded and treated as teratoma, because of the high incidence of teratoma in this region.

Ectopic testicles have a higher incidence of germ cell tumors, and the differentiation between fetus-in-fetu and teratoma is particularly important. Although the characteristics of intracranial teratoma differ from those of intracranial fetus-in-fetu, Wakai found, in a large review of 245 intracranial teratomas, that there are some transitions between certain teratoma and fetus-in-fetu.

In the older literature, several descriptions of fetus-in-fetu were too vague to be acceptable by current criteria. For example, the case reported by Phillips does not unequivocally suggest the criteria described above and therefore should probably be considered a teratoma. Some have argued that fetus-in-fetu should be considered as teratomas since they do not evolve into lithopedion like fetuses of abdominocyesis. That argument is probably not valid since in abdominocyesis the antigen complements of the host and fetus are different, which contrasts with fetuses in fetu.

Associated anomalies
Every organ of the fetus-in-fetu has undergone hypoxic growth and is deformed. Most cases are anencephalic. Usually the body is closed, but ventral wall defects such as omphalocele are common, and a case that suggests a limb-body wall complex has also been described. The host rarely presents any anomalies, except those re-
lated to the presence of a space-occupying lesion. Those manifestations have rarely been severe, even in the case of intracranial fetus-in-fetu, although in rare cases, severe hydrocephalus was responsible for the death of the host. One case of Meckel diverticulum and another of skin hemangioma have been described. A malignant degeneration has never been reported, even in the cases that have been allowed to evolve for several years.

Evolution
If conservative management is opted for, the fetus-in-fetu do not seem harmful to the host, but in every case in which the fetal mass was not removed at the time of discovery, a slow growth has been described.

Prognosis
In the literature of the past century, fetus-in-fetu was fatal to the host because of the compression imposed to adjacent organs. In the more recent literature, the outcome for the host twin is usually favorable. Only a few cases of spontaneous or postsurgical deaths are recorded.

Recurrence risk
There is no report of recurrence.

Management
Aside from a few attempts, in the first half of this century, to marsupialize fetus-in-fetu, surgical removal is the treatment of choice. The membranous capsule can usually be enucleated from the host with minimal problems. In only a few cases, removal is difficult due to adhesions and this difficulty may precipitate the end of the operation, or even be the reason of the postoperative death of the host. Leaving the capsule, or part of it, has not led to complications, except in very rare cases in which fluid reaccumulated in it.

Heterotopic gestation

Definition
An heterotopic pregnancy is the occurrence of a multiple pregnancy in which one or more gestational sacs are implanted outside the uterine cavity (ectopic pregnancy) associated with a single or multiple intrauterine pregnancy (eutopic pregnancy). It occurs in 1-2.9% of pregnancies after in-vitro fertilization and embryo transfer. An heterotopic pregnancy is the combination of an ectopic pregnancy with an intrauterine pregnancy.
Sonographic features
Visualization of one or more intra-uterine gestational sacs associated with one or more ectopic pregnancies, which are classified depending on the site of implantation in:
- Tubal\textsuperscript{434,435}
- Cervical\textsuperscript{436}
- Cornual\textsuperscript{437,438,439,440}
- Abdominal\textsuperscript{441,442}
- Ovarian\textsuperscript{443,444,445}

The diagnosis can be made by transvaginal ultrasound during the first trimester. This diagnosis should particularly be considered in cases with abdominal pain, (vaginal bleeding may be absent\textsuperscript{446}) and those a failed pregnancy with rising $\beta$-hCG.

Differential diagnosis
The presence of a small pelvic mass associated with an early intrauterine pregnancy is also suggestive of heterotopic pregnancy. The differential diagnosis can be made by the identification of the heartbeat. Patients with diagnosis of ectopic pregnancy, in particular the ones who have undergone infertility treatment, must have the uterine cavity investigated to exclude heterotopic pregnancy. The presence of an intrauterine gestation sac in a patient without symptoms should not exclude the diagnosis of a concomitant extrauterine pregnancy until the pelvis is carefully visualized\textsuperscript{447,448}. Heterotopic pregnancies can occur even in patients without risk factors.

Associated syndromes
This condition is particularly associated with infertility cases that have undergone assisted reproductive techniques\textsuperscript{449,450,451,452,453,454,455,456}.

**Molar gestation with a concurrent pregnancy**

The recognition of twin pregnancies that include a complete hydatidiform mole and coexisting fetus have a greater malignant potential and thus should be differentiated from simple partial hydatidiform moles\textsuperscript{457,458,459,460}.

**Vanishing twin**

The three common forms of spontaneous fetal loss in multiple gestation are
1. “the vanishing twin syndrome” which occurs in the first trimester
2. “the fetus papyraceous” in the second trimester, and
3. “stillbirth” in the third trimester.

Definition
First trimester loss of a member of a twin gestation\textsuperscript{461,462}. The incidence of twinning has been reported to be 3.29\% and of these, 21.2\% demonstrated the “vanishing twin” phenomenon\textsuperscript{463}. The vanishing twin is simply reabsorbed.

Sonographic features
Small gestational sac with a fetus whose development lags compared to the other fetus, with any detectable fetal heart activity. The spectrum varies from a crescent-shaped sac adjacent to a normal early gestation (up to 10-14 weeks) to a well-formed but dead fetus (fetus papyraceous / second trimester). Early vanishing twins should be distinguished from implantation bleeds that are not surrounded by a trophoblastic ring\textsuperscript{464}. Sonographic evaluation of early gestational bleeds frequently leads to the diagnosis of a vanishing twin, and this is apparently the single complication associated to the disappearance of a twin at this stage\textsuperscript{465,466}. A vanishing
twin does not adversely affect the development of a coexisting singleton pregnancy, and therefore the exact
distinction from implantation bleed versus vanishing twin may be academic.

At 5-6 weeks 2 gestational sacs are seen. Two weeks later a single fetus is visible and the sac of the other is
already partially resorbed at the lower aspect of the image.

In this sequence of images, the first image demonstrates the 2 main gestational sacs. The upper fetus is visible but with a
questionable/slow heart beat. The lower fetus appears normal. A repeat scan 10
days later (second image) demonstrates
some growth of the first fetus but cessation of cardiac activity. The other fetus
(third image) has grown appropriately.
In those 4 images, a vanishing twin was suspected in the early examination (image 1). Both embryos had heartbeats but of different rhythms (99 and 141 bpm). A repeat examination 10 days later demonstrates resorption of the vanishing twin with normal growth of the co-twin.

**Differential diagnosis**

The differential diagnosis includes implantation bleeds in the early pregnancy, artifactual error (rectus muscle artifact), incomplete scanning technique, and poor quality ultrasound equipment as well as placental cysts after the second trimester. Tomko and Baltarowich have shown that a synechia could also impose for a vanishing twin.\(^\text{[46]}\)
Although a implantation bleed can occasionally impose for a vanishing twin, the lack of trophoblastic ring allows the distinction.

Associated syndromes

Fetus papyraceus (see above). This is a macerated fetus delivered with a normal co-twin, and usually embedded in the placental membranes.

Multifetal pregnancy reduction

Multifetal pregnancy reduction is the elective termination of a variable number of fetuses, preferably done between the 10th and the 13th week of gestation, attempting to improve the perinatal outcome of the remaining fetuses. It is well known that high order multiple gestations have increased risks for both maternal and fetal complications, and the most common are the entire pregnancy loss, maternal high blood pressure, intrauterine growth retardation, premature rupture of membranes, and pre-term delivery. The occurrence of any of these events increase the risk of perinatal death and that of sequelae, such as intraventricular hemorrhage, cerebral palsy, retinopathy, respiratory diseases, and more. The procedure may improve maternal and fetal conditions, thus reducing the risk of prematurity and its associated complications. Although it confers unequivocal benefits to the pregnancy when successful, fetal reduction itself carries risks. The risk of loss of the entire pregnancy is the major concern and occurs in approximately 12% of the cases.

Basically the procedure consists of a transabdominal needle injection of potassium chloride into the fetal thorax. If reduction of both fetuses of a monochorionic pair is desired, the procedure may be successfully accomplished with a single injection in one of the pair. A special attention should be given to the appropriate use of the terminology selective termination and elective fetal reduction. Although both are procedures applied only in multiple gestations, there are some differences between them.

Selective termination is a procedure in which an anomalous fetus in a multifetal pregnancy is terminated to improve the prognosis of the normal co-twin. It is usually a second trimester procedure that follows the same routine of a first trimester reduction.

The term elective fetal reduction is employed to describe reduction of triplets or higher order fetuses to a smaller set (in general, to twins) for medical, psychological, and socio-economic reasons, improving the outcome of the remaining fetuses and reducing the maternal risks as well. Some controversy still persists regarding the impact of fetal reduction from triplets to twins. Some authors state that triplet to twin fetal reduction significantly reduces the risk for prematurity and low birth weight, and may be even associated with a reduction at the overall pregnancy loss rate, suggesting thus that it is a medically justifiable procedure, and should
be offered in these cases. Others who recommend the maintenance of the entire pregnancy, state that bed rest starting at the 20th week of gestation, associated with special diet and close prenatal care reduces the prematurity rate and optimize fetal growth, improving the outcome to the levels of a twin pregnancy.

Selective termination can be performed any time in pregnancy with good outcome in around 90% of cases, and a total pregnancy loss rate of 11.7%.

**Amniocenteses in twins**

**Diagnostic amniocentesis**

Although amniocentesis is a well-known safe technique employed in prenatal diagnosis for many years, the risks and benefits should be considered when a multiple gestation is involved. The risk of pregnancy loss when amniocentesis is performed in twins is higher than in singletons. Some authors attribute this increased loss rate to the natural tendency of miscarriage observed in multiple gestations.

In the past, the most common technique employed the injection of dye in one of the amniotic cavities to differentiate one sac from the other. Since 1990, the avoidance of methylene dye in prenatal diagnosis has been recommended because of its fetotoxicity and a small association with intestinal atresia.

More recently Jeanty et al. have successfully used a single needle puncture with no need of dye injection and the advantages of being less invasive and less painful. Their results were reproduced by others.

*In the double stick technique, a needle is inserted in one sac, the fluid sampled (1) and blue dye injected (2). The fluid equilibrates for a few minutes (3). The second sample is then obtained (4) hopefully clear of the dye.*
In the single insertion technique, the needle is inserted near the membrane attachment at a location where both sacs are visible (1). The fluid is then obtained and transferred to the appropriate containers (2). The plastic tubing disconnected and the stylet of the needle reinserted. The needle is then advanced through the membrane (3) under ultrasound guidance. A few cc of fluid from the second sac are aspirated (4) and then the whole assembly (Syringe, and tubing discarded (5) to prevent contamination of the second sample by cells from the first sample. The proper sample is then obtained (6) and transferred to the containers.

Therapeutic amniocentesis

Amniocentesis may also have therapeutic applications particularly in acute polyhydramnios, a common complication in twin pregnancies, with elevated perinatal mortality if not treated. The overdistension of the uterus provokes maternal discomfort, premature labor, and premature rupture of membranes. The treatment consists of serial amniocenteses to normalize the intrauterine pressure, prevent premature labor, and relieve maternal symptoms. (See twin-to-twin transfusion syndrome, above).

Cervical cerclage

Cervical cerclage in multiple gestations remains a controversial matter in prenatal care. Some authors demonstrate a satisfactory fetal survival rate with minimal incidence of maternal complications post cerclage and thus recommend the routine use of the procedure in multiple pregnancies\textsuperscript{516}. Other groups show a higher risk for premature rupture of membranes with no evident benefit for the pregnancy outcome\textsuperscript{517,518,519,520,521}. We believe the twin pregnancy by itself does not justify the procedure. In multiple pregnancies with sets of triplets or more, the cerclage should be discussed with the patient, considering risks, and benefits on each case. If there is a history of cervical incompetence, the procedure must be offered independently of the number of fetus.
Membranous insertion of placenta

Membranous insertion of placenta is a complication that mainly affects higher order gestations (triplets or higher). In such pregnancies a centrally located fetus may have a trophoblast developing predominantly on the uterine tissue between the gestational sacs of the other embryos. As the sac grows that trophoblast will transform into a placenta that is predominantly over the membranes of the other embryos. Even with trophotropism (the tendency of the placenta to preferentially develop where maternal exchanges are best) this embryo is at great risk of growth restriction. Should a fetal reduction be considered, this embryo would be a prime candidate.

This triplet’s placenta is inserted on the membrane with the left-sided twin. Although part of this placenta is in contact with the myometrium (bottom right) this was insufficient for adequate growth of this fetus that was several weeks smaller than the other 2.

References

1 Originally published on www.TheFetus.net ©2000 Philippe Jeanty, MD, PhD, Jacqueline Reyes, MD, Luís Flávio de Andrade Gonçalves, MD, Sandra Rejane Silva, MD. Some images courtesy Gianluigi Pili, MD. A few drawings adapted from Lifeart from Techpool studio.


163 Reindollar RH, Byrd JR, Hahn DH, Haseltine FP, McDonough PG. A cytogenetic and endocrinologic study of a set of monozygotic isokaryotic 45,X/46,XY twins discordant for phenotypic sex: mosaicism versus chimerism.


p.183-7.
364. Phillips E: Account of a case in which parts of a foetus were found in a tumour situated in the abdomen of a girl two and a half year old. Medico-chirurgical Transactions. 6:124-7, 1815.
in vitro fertilization (IVF) gestation: twin tubal and surviving intrauterine pregnancy.

gamete intra-fallopian transfer.

treated ovarian hyperstimulation and assisted reproductive techniques

Heterotopic pregnancies after in vitro fertilization and embryo transfer - a Danish survey.

Chih

Reprod

Obstet Gynecol Reprod Biol


467 Janet Tomko, RDMS, Oksana Baltarovitch, MD Synechial band (or amniotic fold) as a differential diagnosis for vanishing twin. www.TheFetus.net


