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# Other Anomalies

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## Twin Pregnancies

### Definition

Monozygotic (MZ) or "identical" twins derive from a single fertilized ovum. They are of the same sex and have identical genotypes. Dizygotic (DZ) or "fraternal" twins arise from two different ova fertilized by two different sperms. Their genetic similarity is the same as with siblings.

### Incidence

There is considerable geographic variation in the incidence of twin births ranging from 1:25 in the Yoruba tribe in Nigeria to 1:150 in Japan. The incidence in the United States is 1:88.<sup>2</sup> This difference is attributable to changes in the rate of DZ twinning, as the MZ twinning rate remains stable (0.35 to 0.45 per 100 births) throughout different populations. Factors that alter the rate of DZ twinning include race, maternal age, use of ovulation-inducing agents, and a positive family history. Twins are more common in blacks than in whites. The incidence of twinning increases with maternal age up to the age of 35, and then decreases.<sup>1</sup> The use of clomiphene citrate is associated with a multiple pregnancy rate of 5 percent, almost all of which are twins.<sup>9</sup> Pergonal therapy is associated with a twinning rate of 30 percent, of which triplets or higher conceptional rates account for 5 percent.<sup>9</sup> The tendency for multiple ovulation seems to be an inherited trait expressed only in females. Therefore, the recurrence risk for twinning in a sibship is constant for MZ twins (0.35 to 0.4 per 1000 births), while it rises to three times that of the normal population for DZ twins.<sup>10</sup> Among white North Americans, 35 percent of all twins are unsexed DZ, 35 percent are like-sexed DZ, and 30 percent are MZ.

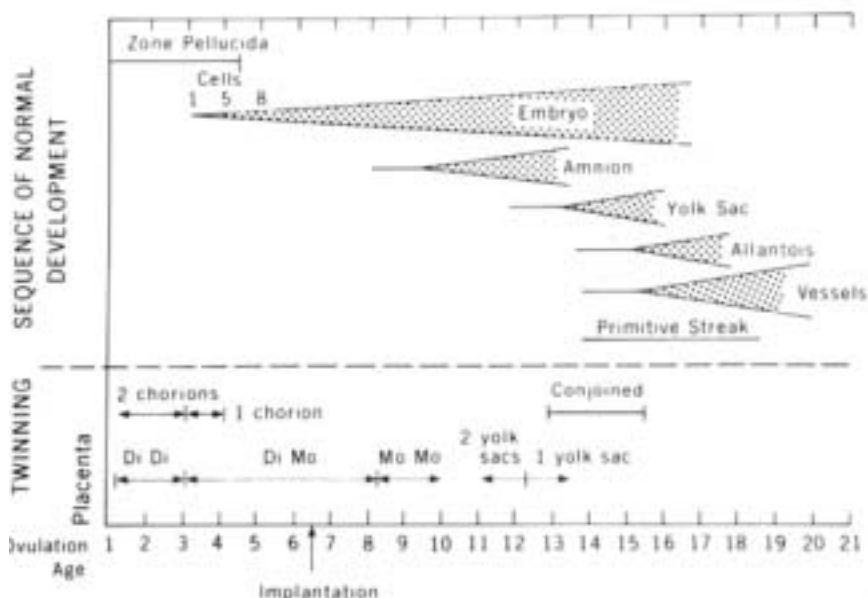
### Embryology-Pathology

DZ twinning is determined at ovulation, as it requires the availability of two ova. MZ twinning occurs after fertilization and is confined to the earliest stages of embryogenesis, because the embryo is incapable of fission once it is formed. Figure 12-1 illustrates the timing of monozygotic twinning events. If the separation occurs at the two-cell stage (approximately 60 hours after fertilization), the twins will be dichorionic diamniotic. If it occurs between the 3d and 8th days after fertilization, the twins will be monochorionic diamniotic. Separation between the 8th and 10th days results in monochorionic monoamniotic twins. Conjoined twins constitute the last type of event in the spectrum of monozygotic twinning.<sup>2</sup>

### Determination of Twin Zygosity

Determination of zygosity is important. Zygosity information will be helpful later in life if one twin develops a disease such as diabetes or requires a transplant. Zygosity assessment, therefore, should be attempted at birth. A simple approach consists of first looking at the sex of the twins, because discordant sex (35 percent of twins) indicates dizygosity. If the sex is the same, information should be obtained from microscopic placental examination. The critical area for study is a section of the dividing membranes at the placental insertion, also known as the T-zone. Twenty percent of all twins will have a monochorionic placenta, which is always a sign of monozygosity. (Sixty-five percent of MZ twins have monochorionic placentation.) For the remaining 45 percent, i.e., those of the same sex and without a monochorionic placenta, genetic studies including

**Figure 12-1.** The timing of the monozygotic twinning process. On the horizontal axis are days after fertilization. The types of placenta expected from embryonic events are: Di Di, diamniotic dichorionic; Di Mo, diamniotic monochorionic; MO MO, monoamniotic monochorionic. (Re-produced with permission from Benirschke, Kim: *N Engl J Med* 288:1276, 1973.)



blood typing and chromosomal marking will be required to determine zygosity. Molecular biology studies may help in this assessment.

### Associated Anomalies

The prevalence of congenital anomalies in twin pregnancies is higher than in singleton pregnancies. All twins are at risk for constraint deformities as a consequence of intrauterine crowding. The excess in structural congenital anomalies observed in multiple pregnancies is attributable to MZ twins.<sup>3,6,8</sup> Congenital defects in multiple pregnancies can be classified into three groups: (1) anomalies unique to multiple conception, such as conjoined twins and twin reversed arterial perfusion (TRAP) sequence; (2) anomalies not unique to multiple conception, but that occur more often in twins, such as hydrocephalus, congenital heart disease, single umbilical artery, and neural tube defects; and (3) anomalies not unique to twins, but observed with increased frequency because of mechanical or vascular factors associated with twinning, such as talipes, skull asymmetry, and congenital dislocation of the hip. The rate of concordance for congenital anomalies in twins varies from 3.6 percent to 18.8 percent.<sup>5</sup> These figures are influenced by zygosity and the specific anomaly. For example, the incidence of concordance for facial clefting is 40 percent in MZ twins and 8 percent in DZ twins.

Discrepancy for chromosomal anomalies is the rule for DZ twins and surprisingly, also occasionally for MZ twins.<sup>5</sup> Heterokaryotypes refer to the discrepant chromosomal constitution observed in some MZ

twins. Some genotypes may also be expressed differently in MZ twins. While phenotypic concordance is the rule for MZ twins with trisomy 21 or Klinefelter's syndrome, MZ twins with gonadal dysgenesis are often discordant.<sup>4,7</sup>

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# Conjoined Twins

## Incidence

The incidence is from 1 in 30,000 to 1 in 100,000 live births.<sup>3,4,8</sup> Seventy-five percent of conjoined twins are females.

## Etiology

Unknown. Monozygotic twins arise from a single blastocyst that undergoes duplication between the 1st and 10th day after ovulation. Conjoined twins are commonly regarded as an abnormality of the process of monozygotic twinning, because of an incomplete division of the embryonic cell mass at one pole or at a point between the poles. Conjoined twins are a sporadic event that tends not to recur.

## Pathology

A classification of conjoined twins is provided in Table 12-1. The most frequent types of conjoined twins are thoracoomphalopagus (28 percent), thoracopagus (18 percent), omphalopagus (10 percent), incomplete duplication (10 percent), and craniopagus (6 percent).<sup>3</sup>

Anatomic abnormalities are the rule in conjoined twins. In most cases, it is possible to assume that they derive directly as a consequence of the presumed abnormal division of the embryonic mass. In other cases, the origin of the malformation cannot be explained on a purely mechanical basis (e.g., facial clefting), and it suggests a more diffuse disturbance of morphogenesis. Figure 12-2 illustrates the different varieties of conjoined twins.

**Craniopagus.** Craniopagus may be classified, according to the area of junction, into frontal, parietal, temporal, or occipital varieties. Parietal craniopagus is twice as common as all other types combined. For surgical and prognostical purposes, craniopagus may also be subdivided into partial and complete types. In the former, brains are separated by bone or dura, and each brain has separate leptomeninges. In total craniopagus, brains are connected. Cerebral connection is most frequent in temporoparietal varieties. Successful separation depends upon the degree of connection between the brains and the presence of a superior sagittal sinus for each brain, as this is critical for adequate venous drainage.

**Thoracopagus.** Congenital heart disease is found in about 75 percent of patients. In 90 percent of cases, there is some degree of fusion of the pericardial sac.

The most frequent abnormality is a conjoined heart, with two ventricles and a varying number of atria (1 to 4), although a number of permutations have been reported. Ventricular septal defects are found in virtually all patients in addition to other deformities.<sup>13,14</sup>

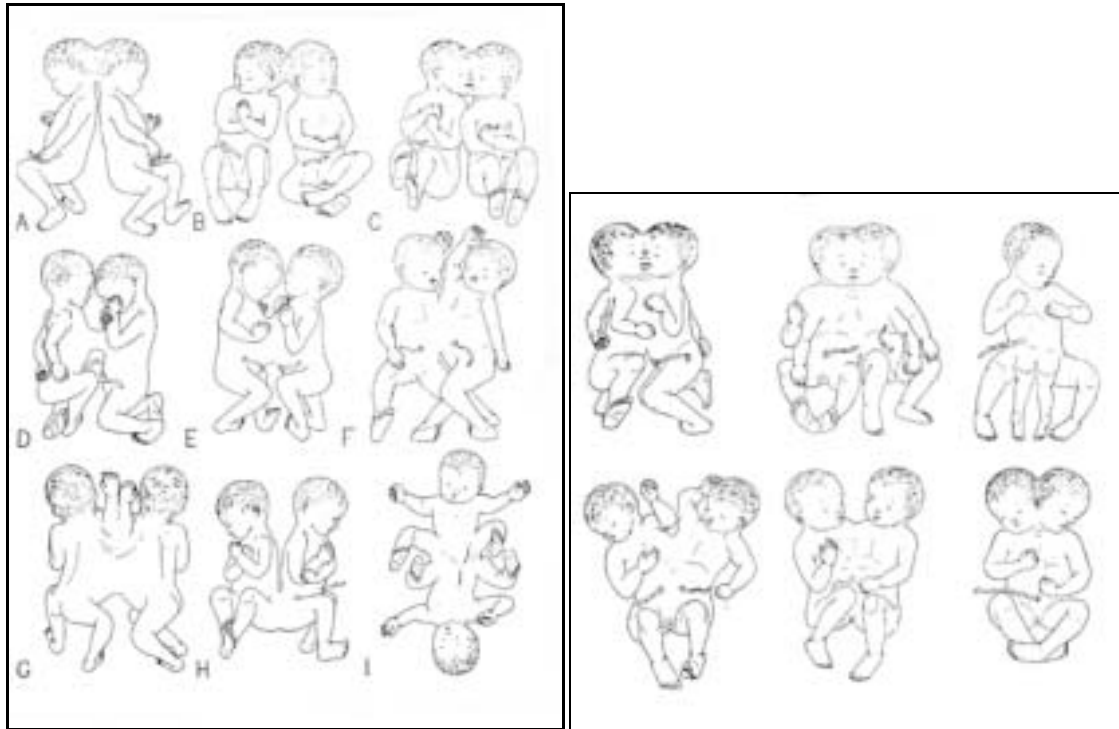
**Omphalopagus-Xiphopagus.** A review of the literature indicates that the liver is conjoined in 81 percent of patients, the sternal cartilage in 26 percent, the diaphragm in 17 percent, and the genitourinary tract in 3 percent.<sup>6</sup> The anomalies not obviously linked to the abnormal division process of the embryonic mass include malformations of the abdominal wall (usually omphalocele) in at least one of the twins in 33 percent of cases, and congenital heart disease (most frequently ventricular septal defects and tetralogy of Fallot) in at least one of the twins in 25 percent of cases. Only one of nine sets of twins had concordance of the cardiac defect in both twins.<sup>6</sup>

**Pygopagus.** Pygopagus accounts for 20 percent of all onjoined twins. They are joined at the buttocks and lower spine, and face away from each other. They may share part of the sacral spinal canal, may have a common rectum and anus, and the external genitalia are often fused.

TABLE 12-1. 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 pelves, and/or external genitalia, and/or four legs
Duplicata completa:	Two complete conjoined twins
Terata catadidyma:	Conjunction in the lower part of the body
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
Syncephalus:	Joined by the face
Craniopagus:	Joined at homologous portion of the cranial vault
Terata anacatadidyma:	Conjunction in the midpart of the body
Thoracopagus:	Joined at thoracic wall
Xiphopagus:	Joined at xyphoid process
Omphalopagus:	Joined in the area between the umbilicus and the xiphoid cartilage
Rachipagus:	Joined at any level of the spines above the sacrum

Adapted with permission from Guttmacher, Nichols: Birth Defects 3(1):3, 1967.



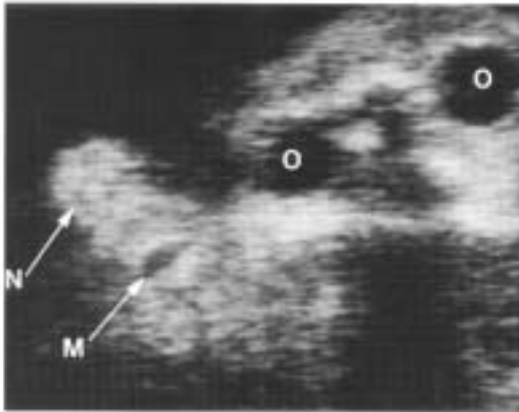
**Figure 12-2.** Drawing of the different types of conjoined twins. **Left.** This diagram illustrates cases of duplicate completa (conjoined twins where heads and limbs maintain their identity). **A-C.** Craniopagus. **D-G.** Thoracopagus. **H,I.** Pygopagus. **Right.** This diagram shows cases of duplicate incomplete (conjoined twins in which more extensive fusion takes place). (Reproduced with permission from Patten: *Human Embryology*, 3d ed. New York, McGraw-Hill, 1968.)

**Ischiopagus.** Ischiopagus represents 5 percent of all conjoined twins. They are joined at the inferior part of the sacrum and coccyx, and often have a common large pelvic ring formed by the union of the two pelvic girdles. Ischiopagus may have four legs (ischiopagus tetrapus) or three legs (ischiopagus tripus). These twins frequently share the lower gastrointestinal tract, so that the intestines join at the terminal ileum and empty into a single colon. They may have a single bladder, and urethra, and the anus can be displaced. Vaginal anomalies and rectovaginal communications are quite common.<sup>19</sup>

### Diagnosis

A detailed ultrasound examination to exclude the possibility of conjoined twins is mandatory in all multiple pregnancies. The index of suspicion should be raised when an interamniotic membrane cannot be identified, because all conjoined twins are monoamniotic. Other signs include difficulties in completely separating the twins (Figs. 12-3, 12-4), fetal spines in unusual extension or proximity, more

than three vessels in the umbilical cord, and single cardiac motion. Discordant presentation does not exclude conjoined twins. The prenatal diagnosis has been reported several times<sup>1,4,6,10,11,16,17</sup> and can be made as early as the first trimester of pregnancy.<sup>11</sup> Polyhydramnios is present in 75 percent of thoracopagus twins.<sup>8</sup> A complete examination of the twins is indicated because of the high frequency of associated anomalies. Neural tube defects, orofacial clefts, imperforate anus, and diaphragmatic hernia are the most common defects not associated with fusion. Echocardiography is indicated in all cases as congenital heart disease is a major prognostic factor for survival. Evaluation of the visceral situs is important, because abnormalities of the disposition of the abdominal organs are highly suggestive of cardiac defects.<sup>13</sup> If the diagnosis is not certain, other imaging techniques can be considered including plain radiography or amniography. Radiography may show a bony connection, but is otherwise less detailed than sonography. Amniography, especially when performed with oil soluble dyes, may allow a



**Figure 12-3.** Conjoined twins were suspected in view of the proximity between the two faces. Note the ocular fossae of one twin (O) and the mouth (M) and nose (N) of the other. The twins were thoracopagus.

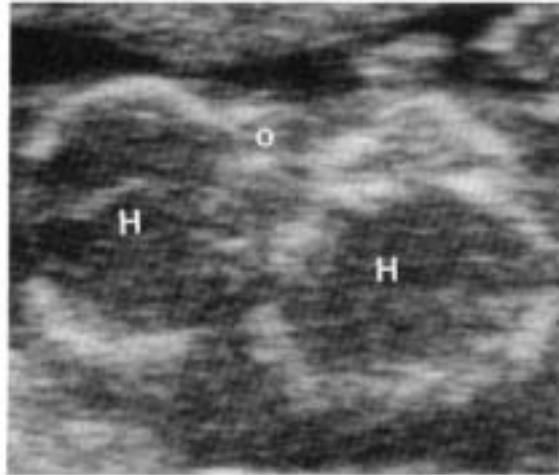
better delineation of the bridge between the twins, because these dyes adhere to the fetal skin surface.

**Prognosis**

Thirty-nine percent of conjoined twins are stillborn, and 34 percent die within the first day of life. Survival depends upon the type of conjunction and the presence of associated anomalies.

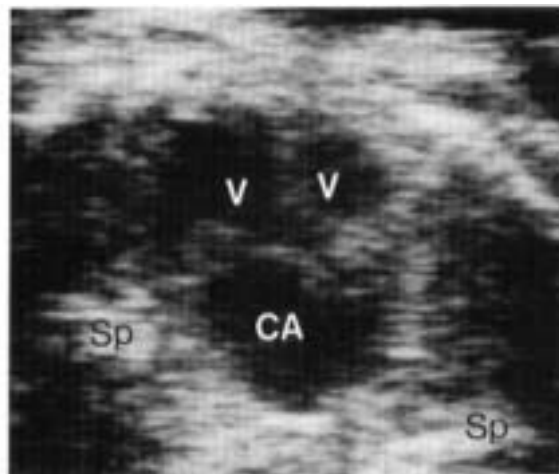
Omphalopagus twins have a reasonable chance for survival and surgical separation, unless severe associated anomalies are found. Data published in 1967 document survival of 19 of 22 twins (11 pairs). The prognosis is worse if an omphalocele is present.<sup>20</sup> In thoracopagus (Fig. 12-5), the degree of fusion of the heart determines the prognosis. When a common heart is present, the chances for a successful surgical separation are negligible. Xiphopagus twins have a better prognosis than thoracopagus, because the former has a lower incidence of cardiac lesions.

Outcome for craniopagus is unpredictable and depends mainly on the degree of fusion of intracranial structures and on the extent of venous connections at the junction site.<sup>2,18</sup> A cerebral connection is present in 43 percent of cases, but cannot be reliably diagnosed preoperatively even with modern imaging techniques, such as CT scan and MNR. In a recent review of 21 cases of craniopagus, the site of junction was an important prognostic factor for mortality and morbidity; temporoparietal and occipital junctions had a worse outcome than frontal and parietal junctions.<sup>2</sup> The perioperative mortality rate in craniopagus operated on in the past decade is 36 percent. Quality of life for the same group was good



**Figure 12-4.** Craniopagus diagnosed in the midtrimester. The two heads are joined at the level of the face. H, head; O, orbit.

(only 1 out of 9 had a severe neurological deficit), suggesting that separation of craniopagus should always be considered.<sup>2</sup> The prognosis improves when surgery is performed in the neonatal period and when craniopagus twins are separated in stages rather than in one procedure.<sup>2</sup> Improved results have been reported with the use of a shunt to prevent postoperative increase in intracranial pressure and cerebrospinal fluid leakage. Tissue expanders may help to achieve primary closure.<sup>2,18</sup>



**Figure 12-5.** Transverse section at 23 weeks of gestation at the level of the chest in a set of thoracopagus twins. Sp represents two spines. Note the single heart. V, ventricles; CA, common atrium.

Among twins conjoined in the lower part of the body, pygopagus have a fairly good outcome, because sharing of organs critical for life (e.g., heart, brain) does not occur. Although data for ischiopagus are scanty, separation is frequently difficult, because these twins often share abdominal viscera. Rehabilitation is required in most cases because of residual orthopedic, gynecologic, and intestinal disabilities. Tripus ischiopagus will need orthopedic prostheses. If male genitalia are shared, one infant will need to be raised as a female. Colostomies and suprapubic drainage may also be required to deal with the problems of a shared genitourinary and intestinal tract.<sup>5</sup>

### Obstetrical Management

When the diagnosis of conjoined twins is made before viability, the option of pregnancy termination should be offered to the parents.

After viability, serial examinations are indicated to monitor fetal growth and the development of hydrops, and to detect fetal demise. Scheduled delivery in a tertiary care center is ideal so that procedures required to evaluate the twins can be carried out shortly after birth. There is a paucity of data to assess the reliability of lung maturity studies in monoamniotic twins. The method of delivery depends upon the prenatal assessment of the likelihood of survival. Although vaginal delivery is possible,<sup>15</sup> dystocia occurs frequently<sup>12</sup>; in omphalopagus twins, it has been reported in 36 percent of cases.<sup>8</sup> Vaginal delivery should be reserved for stillbirths and for varieties that are incompatible with life. A destructive procedure (embryotomy) can be considered for stillbirths. Cesarean section is the method of choice to maximize survival of the twins, because it decreases the risk of birth trauma and hypoxia. A vertical uterine incision is recommended. In cephalic/cephalic presentation, the heads should be delivered before the rest of the bodies. The same principle is applicable to breech/breech and cephalic/breech conjoined twins.

After birth, evaluation of both twins should be conducted to assess the extent of organ system sharing. The following studies have been employed: plain and contrasted radiography, echocardiography, angiography, sonography, and CT scans.<sup>9</sup> Twins born alive fall into two categories: infants who thrive despite being conjoined, and infants whose lives are jeopardized because of the union or coexisting congenital anomalies. The former group includes twins like xiphopagus, pygopagus, and ischiopagus, whose union does not result in physiologic compromise, because they do not share critical organs. The impulsive desire to achieve separation as soon as possible

in these cases should be resisted. Over time the infants will be larger, other congenital anomalies may be identified, the risks of anesthesia should decrease, and the procedure can be carefully planned. The surgical challenges include the separation of important shared organs (e.g., liver) and the closure of the soft tissue and bony defect. The second group is constituted by those conjoined twins requiring emergency separation. Indications for this include: (1) one twin is stillborn or its critical condition threatens the other, (2) a congenital anomaly incompatible with life is present and can be corrected, and (3) there is significant damage to the connecting bridge.

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## Twin Reversed Arterial Perfusion Sequence

### Synonyms

Acardius, acardiac monster, acephalus, pseudocardiac anomaly, acephalus acardia, and holoacardius.

### Definition

Twin reversed arterial perfusion (TRAP) sequence is a specific anomaly of multiple gestations characterized by vascular communications between fetuses, a total or partial absence of the heart, and a spectrum of malformations and reduction anomalies that may affect all tissues.<sup>10</sup>

### Incidence

The incidence is 1 in 35,000 births.-, This figure may represent an underestimate of the real frequency of the problem, since TRAP sequence can be lethal for both twins in early pregnancy.<sup>10</sup> TRAP sequence is found only in twin pregnancies with fused placentas. Seventy-five percent of cases occur in monozygotic triplets and the rest in monozygotic twins.<sup>6</sup> Since fusion of the placenta may be found in dizygotic twins, there is a theoretical possibility that TRAP sequence occurs in these twins, and a few cases have been reported.<sup>2,10</sup> This condition is sporadic and family recurrences have not been reported.<sup>11</sup>

### Etiopathogenesis

The pathogenesis of TRAP sequence is controversial. Umbilical anastomoses have been found in all cases where placentas were available for examination.<sup>10</sup> This finding suggests two main etiopathogenetic hypotheses: (1) anastomosis of the umbilical arteries of the two twins in early embryogenesis would lead to reversed circulation in the perfused twin, with secondary disruption of organ morphogenesis caused by deficient oxygen and nutrient contents in the perfused blood, and (2) a primary disorder in the development of one twin early in embryogenesis, because of chromosomal abnormality, polar body twinning,

or other reasons, usually leads to reabsorption of the embryo or, if demise occurs later, to a fetus papyraceous. However, if a vascular anastomosis is present between the two circulations, the failing twin would be saved and become the malformed perfused fetus.

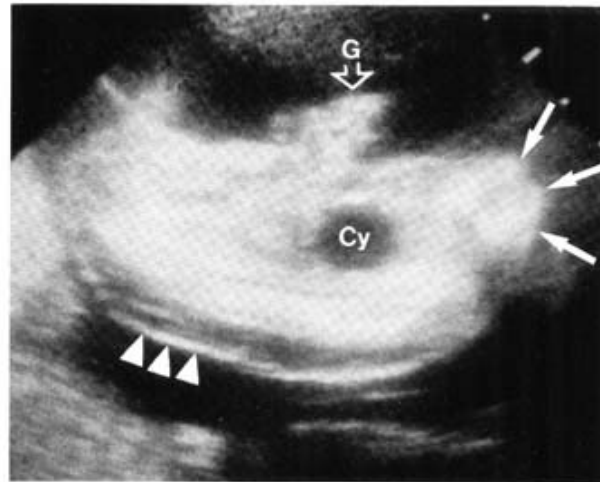
### Pathology

The members of a TRAP sequence are known as the perfused twin and the pump twin. The perfused twin exhibits a wide range of abnormalities, while the pump fetus is morphologically normal. Figure 12-6A illustrates representative examples of perfused twins. A wide range of anomalies involving virtually all organ systems has been reported in the perfused twin. They include total or partial absence of the cranial vault, holoprosencephaly, anencephaly, absent facial features, anophthalmia, microphthalmia, cleft lip/cleft palate, absent or rudimentary limbs, absent thorax, diaphragmatic defects, absent lungs and heart, esophageal atresia, short intestine, omphalocele, gastroschisis, ascites, absent liver, gallbladder, and pancreas, exstrophy of the cloaca, edema of the skin, and single umbilical artery.<sup>10</sup> Typically the most severe abnormalities are found in the upper part of the body. This has been attributed to the retrograde pattern of fetal perfusion through the umbilical and iliac arteries, which would relatively spare the lower part of the body. An absent or rudimentary heart is frequently found in these fetuses, explaining the term "acardius," which is classically used in referring to such fetuses. In a series of 14 cases, no heart tissue could be found in 5, an unfolded heart tube was seen in 7, and a folded heart with a common chamber was seen in <sup>2,10</sup>

Chromosomal abnormalities have been found in 50 percent of cases.<sup>1,2,3,10</sup> However, the pattern of abnormalities did not conform to the expected phenotype of the chromosomal aberrations. It has been suggested that the abnormal karyotype per se is not responsible for the malformation complex but rather that it increases the likelihood of a discordant development between the twins, thus creating a favorable



**Figure 12-6.** **A.** Drawings showing various examples of acardiac monster. Note the presence of limbs and absence of the upper trunk and head. **B.** Longitudinal scan of an acardiac fetus in the midtrimester. The cephalic pole is almost entirely absent. Only a few remnants of the splanchnocranium can be seen (*arrows*). A large cyst (*Cy*) occupies most of the chest, and gastroschisis (*G*) is present. Note diffuse soft tissue edema (*arrowheads*). The upper extremities could not be demonstrated. (Fig. A reproduced with permission from Van Allen, Smith, Shepard: *Semin Perinatol* 7:285, 1983.)



**B**

ground for the TRAP sequence to occur.<sup>10</sup> In a pregnancy complicated by TRAP sequence, analysis of the histocompatibility antigen haplotypes indicated that the perfused acardiac twin was probably derived from the fertilization of a polar body.<sup>2</sup>

The pump twin was morphologically and chromosomically normal in all the reported cases. However, signs of intrauterine cardiac overload, including overt hydrops, intrauterine growth retardation, hypertrophy of the right ventricle, and hepatosplenomegaly, were always present. Ascites may result in

overdistention of the abdominal wall and prune-belly phenotype.

### Diagnosis

The prenatal diagnosis of TRAP sequence has been made in a handful of cases,<sup>4,8,9</sup> but it is not always an easy task. The condition should be suspected when one of the members of a multiple gestation has a grotesque malformation (unidentifiable head, trunk, or extremities) (Fig. 12-6B). TRAP sequence should also be considered in singleton gestations associated



with an intraamniotic tumor. The identification of a pulsating heart in the malformed twin does not exclude the diagnosis. We have seen one case in which the perfused twin presented with a sonographic image similar to cystic hygromas and oligohydramnios. Death occurs in utero and progressive skin edema develops. Polyhydramnios is a frequent finding. Signs of congestive heart failure may be present in the pump twin.<sup>4,9</sup>

### Prognosis

The mortality rate of the perfused twin is 100 percent. The mortality rate of the pump twin is 50 percent.<sup>10</sup> Causes of death include intrauterine heart failure and prematurity. Parents may be reassured that embolic phenomena from the perfused twin do not occur in the pump twin.

### Obstetrical Management

Serial ultrasound scans are mandatory to assess the growth rate and the cardiovascular status of the pump twin. A detailed investigation for signs of heart failure (polyhydramnios, enlargement of the cardiac chambers, hepatosplenomegaly, ascites, hydrothorax, pericardial effusion) and IUGR should be performed at each examination. Tocolytic agents to treat preterm labor are indicated, preferably magnesium sulfate, since beta-adrenergic agents could exert adverse effects on the cardiovascular system of the pump fetus. Therapeutic amniocentesis may be considered in cases of preterm labor associated with hydramnios. The development of signs of congestive heart failure in the pump twin is serious. Maternal digoxin administration has been effective in controlling the heart failure of the pump twin in a case diagnosed at 28 weeks of gestation. Pregnancy was continued for 6 weeks, allowing the survival of the pump infant.<sup>9</sup> A surgical approach could be considered for those cases in which medical therapy has failed. Ligation of the umbilical circulation could be

undertaken by hysterotomy or under endoscopic control. Some experimental evidence in animal models suggests that laser electrocoagulation may be of use for intrauterine surgery. The delivery of a perfused twin may be associated with significant soft tissue dystocia. In one case, delivery occurred 8 hours after the birth of the pump twin and required oxytocin administration, drainage of multiple cystic structures under ultrasonic guidance, and intrauterine manipulation.<sup>10</sup> Delivery of a perfused twin is one of the few indications in obstetrics for a destructive procedure (embryotomy) to avoid a cesarean section.

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## Amniotic Band Syndrome

### Synonyms

Aberrant tissue bands, Adam complex, amniochorionic mesoblastic fibrous strings, amniogenic bands, amniotic band disruption complex, congenital annular bands, congenital annular constrictions, congeni-

tal constriction band syndrome, congenital ring constrictions, and congenital transverse defects.

### Incidence

The incidence is 1 in 1,200 to 1 in 15,000 live births.<sup>9</sup>

**TABLE 12-2. ABNORMALITIES ASSOCIATED WITH AMNIOTIC BAND SYNDROME**

Limb defects, multiple, asymmetrical
Constriction rings of limbs or digits
Amputation of limbs or digits
Pseudosyndactyly
Abnormal dermal ridge patterns
Simian creases
Clubfoot
Craniofacial defects
Encephalocele, multiple, asymmetrical
Anencephaly
Facial clefting—lip, palate
Embryologically appropriate
Embryologically inappropriate
Severe nasal deformity
Asymmetrical microphthalmia
Incomplete or absent cranial calcification
Visceral defects
Gastroschisis
Omphalocele



**Figure 12-8.** Amputation of fingers in a fetus with amniotic band syndrome.

### **Etiology**

Amniotic band syndrome is a sporadic condition.

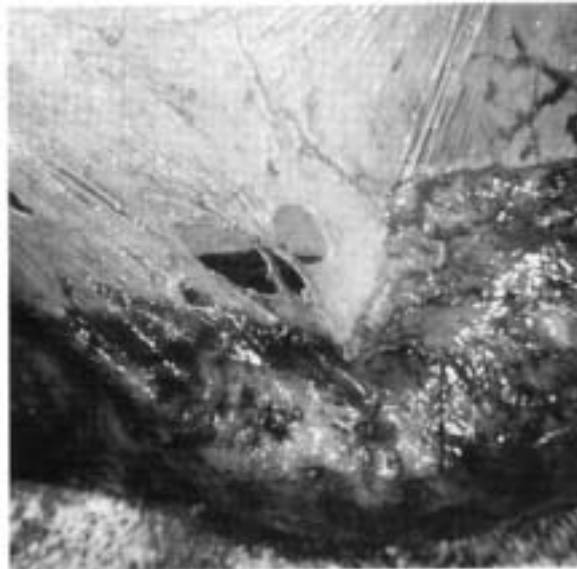
### **Etiopathogenesis**

Although several theories have been proposed to explain the genesis of amniotic band syndrome, the

most widely accepted view is that early rupture of the amnion results in mesodermic bands that emanate from the chorionic side of the amnion and insert on the fetal body, leading to amputations, constrictions, and postural deformities secondary to immobilization.<sup>10</sup> It has been suggested that the earlier the insult occurs, the more severe the lesion. Amniotic rupture in the first weeks of pregnancy results in craniofacial and visceral defects, whereas during the second trimester, it may lead to limb and digital constriction



**Figure 12-7.** Amniotic band syndrome. An amniotic band is seen inserting on the fetal head. There is great distortion of the fetal face. The hand is forced against the fetal face and deformed. AB, amniotic band.



**Figure 12-9.** Fibrous strings originating from the surface of the placenta.



**Figure 12-10.** Fibrous string inserting into the fetal body.

and amputations.<sup>4</sup> An alternative view is that amniotic band syndrome is the consequence of an insult that results in typical malformations as well as ectodermal and mesenchymal disruption. Vascular compromise may have a pathogenetic role in the genesis of external deficits. Amniotic band syndrome has been reported after amniocentesis.<sup>1,7,8</sup>

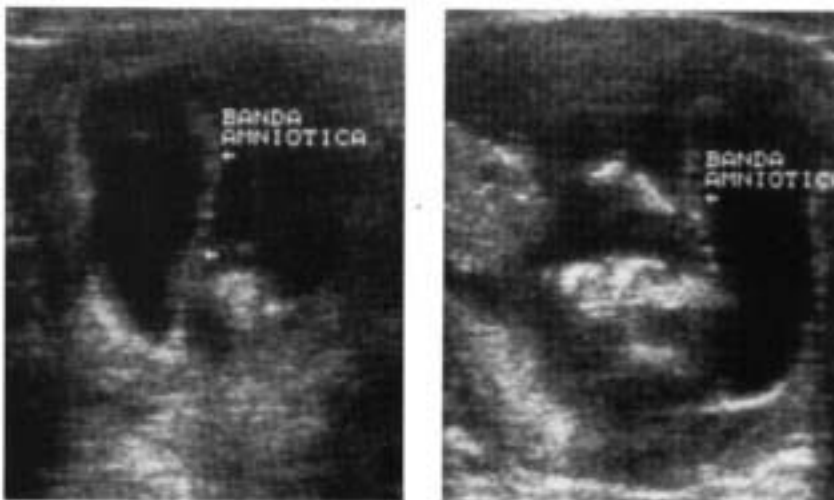
### Pathology

The pathologic findings of amniotic band syndrome have been extensively described.<sup>4,9</sup> Table 12-2 illustrates the abnormalities most commonly associated with this condition. Multiple anomalies are present in

77 percent of cases.<sup>2</sup> When encephaloceles are present, they are often asymmetrical and may be multiple (Fig. 12-7). Such a configuration is almost pathognomonic of amniotic band syndrome, since these lesions are usually single and located in the midline (see section on cephaloceles). Grotesque facial anomalies, including anophthalmia, microphthalmia, and irregular and multiple clefts, may be found (Fig. 12-7). Ring deformities encompass two groups of lesions: those that can be related to the disruptive effect of the amniotic bands, such as amputations and ring constrictions (Fig. 12-8) and those related to immobilization of the fetus, such as clubfoot, which is seen in two-thirds of the cases.<sup>9</sup> Internal organs are generally normal. However, if amniotic disruption occurs around the time of physiologic evisceration of abdominal contents, entanglement with mesodermic bands can result in ventral wall defects, such as gastroschisis and, less frequently, omphaloceles. Kyphoscoliosis can be seen.<sup>9</sup> Fibrous strings originating from the surface of the placenta (Fig. 12-9) are frequently seen inserting into the fetal body at the level of the defects (Fig. 12-10). In some fetuses, amniotic rupture allows communication between the amniotic cavity and the extraembryonic coelom. The fetus may escape from the amniotic cavity (extraamniotic pregnancy), and the amnion does not grow and can be found after delivery as a small sac connected to the umbilical cord.<sup>10</sup>

### Diagnosis

Prenatal diagnosis of this condition has been made.<sup>3,6</sup> Amniotic band syndrome encompasses a broad constellation of anomalies that are different in each case. Suspicion should arise when two or more of the anomalies indicated in Table 12-2 are encountered.



**Figure 12-11.** Sonogram of a fetus with amniotic band syndrome. Note a thick band inserting into the uterine wall (left) and fetal body (right). The fetus was born with multiple congenital amputations. (Courtesy of Dr. Heriberto Alarcon and Dr. Carlos Alarcon, Puebla, Mexico.)

Asymmetrical or multiple encephaloceles in combination with amputations, ventral wall defects, and postural deformities should strongly raise the index of suspicion.

At times, amniotic bands can be seen as linear echoes floating in the amniotic fluid and connected to the fetal body (Fig. 12-11).<sup>6</sup> However, oligohydramnios may interfere with visualization of the bands. Confusion may arise with two conditions that may cause linear echoes crossing the amniotic cavity: chorioamniotic separation and intrauterine synechia. In these cases, meticulous scanning will demonstrate that these structures do not insert into the fetal body and that there are no structural anomalies.

### Prognosis

The prognosis depends on the severity of the anomalies. The spectrum varies from individuals with normal intelligence whose only defect is a minor digital constriction to multiple severe anomalies incompatible with life.

### Obstetrical Management

Fetal karyotype is indicated because the multiple congenital anomalies may be due to a chromosomal abnormality. The option of pregnancy termination should be offered before viability. In those cases diagnosed after viability, obstetrical management is not altered unless associated anomalies incompatible with life are visualized (e.g., anencephaly). In such instances the option of pregnancy termination can be offered to the parents any time in gestation.

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## Nonimmune Hydrops Fetalis

### Incidence

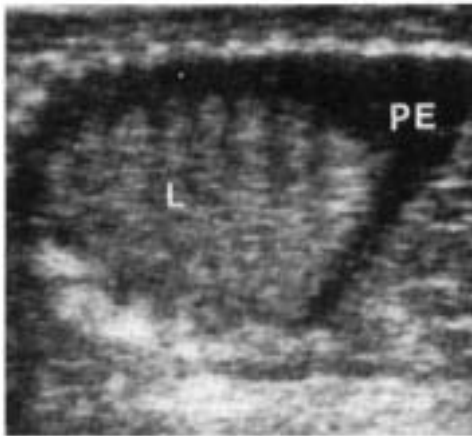
Nonimmune hydrops (NIH) fetalis has been reported with an incidence of 1 in 1500 to 1 in 4000 deliveries<sup>59,60,70,74,80,109</sup>

### Definition

NIH implies an excess of total body water, which is usually evident as extracellular accumulation of fluid in tissues and serous cavities, without any identifiable circulating antibody against red blood cell (RBC) antigen. With the decreasing frequency of Rh isoimmunization, NIH has become a relatively more frequent cause of hydrops.<sup>90</sup>

### Diagnosis

The sonographic diagnosis of hydrops is easy. The excessive body fluid accumulation can be seen as subcutaneous edema (skin thickness 5 mm), pleural and pericardial effusions, ascites, polyhydramnios, or placental thickening (>6 cm). Fluid accumulation must involve more than one site for the term "hydrops" to be used (Figs. 12-12 through 12-17). When the fluid accumulation is limited to only one cavity, the situation should be described in terms of the involved site (e.g., ascites), since this may be helpful in narrowing the differential diagnosis. The first site to show excessive fluid accumulation may

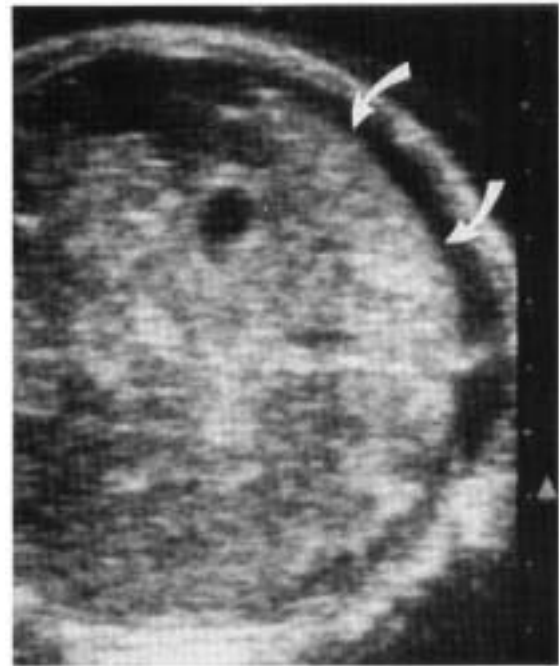


**Figure 12-12.** Longitudinal scan of a fetus with nonimmune hydrops showing pleural effusion (PE) surrounding lung tissue (L).

vary with the cause of the hydrops. For example, cystic adenomatoid tumor of the lung will first cause a pleural effusion. When the intrathoracic pressure is sufficiently elevated to impair venous return, generalized hydrops will develop. Therefore, depending on when the fetus is examined, it may be possible to detect excessive fluid accumulation in a single site before it becomes generalized. In systemic conditions (anemia, congestive heart failure), fluid accumulation tends to be more evenly distributed and can be detected simultaneously in multiple sites. Many factors, such as lymphatic drainage, venous return, surface area and potential volume of serosal cavities, tissue pressure in the skin, and, finally, accessibility to ultrasound evaluation, affect the detection of fluid accumulation with ultrasound. A pericardial effusion may be the first sign of fluid overload. This is probably due to the volume limitations of the pericardial



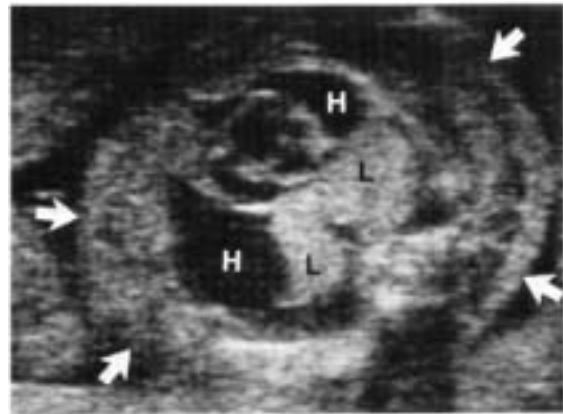
**Figure 12-13.** Skull of fetus with NIH. Edema is indicated by arrows.



**Figure 12-14.** Ascites (arrows) in abdomen of fetus with NIH.

cavity as opposed to the ease of fluid distribution within the pleural and abdominal cavities.<sup>90</sup>

Fetal ascites may be so large as to cause prune belly.<sup>69,94</sup> Several cases of isolated ascites have been reported. Meconium peritonitis and viral infections (CMV) can present in this form. Isolated ascites can also be the first stage of NIH in progress. The workup for isolated ascites is similar to that of NIH (see Table



**Figure 12 --15.** Cross section of a fetal thorax with hydrothorax (H) and subcutaneous edema (arrows). L, lungs.



**Figure 12-16.** Transverse section across the chest of a fetus with NIH. Note the pericardial effusion (*arrowheads*) surrounding the fetal heart.

12-5). In some instances this condition has resolved spontaneously.

Polyhydramnios is associated with hydrops fetalis in about 75 percent of cases studied.<sup>70</sup> When polyhydramnios is detected, incipient hydrops fetalis should be excluded by careful examination of the fetal serosal cavities. In some cases, the amount of fluid may be so massive as to preclude appropriate visualization of the fetus with real-time ultrasound because the infant is beyond the depth field of the transducer. This problem can be solved either by using a static scanner or by examining the patient in the knee-chest position with real-time ultrasound.

### **Etiology**

In about 44 percent of fetuses, NIH is an idiopathic condition, and no cause can be elicited.<sup>59</sup> Table 12-3 is an outline of conditions associated with the presence of NIH. For some of these, a direct pathophysiologic mechanism has been postulated, whereas in others, a mere association has been reported without implying a causal relationship.

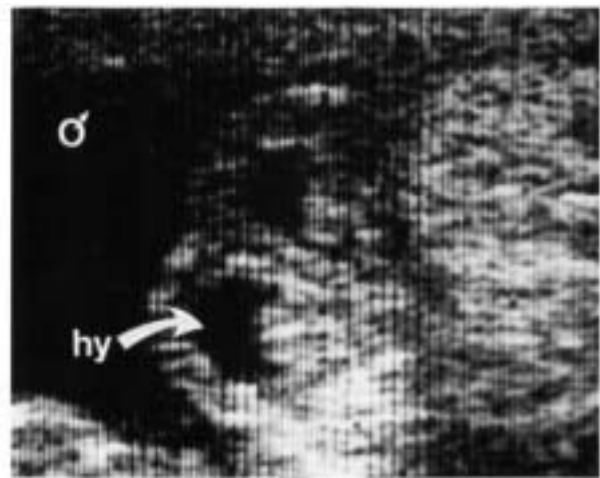
**Hematologic Causes.** The common pathway of NIH of hematologic origin is fetal anemia. This can be the

result of hemoglobinopathies, hemolysis, fetal blood loss, or in one report, red blood cell (RBC) aplasia.<sup>85</sup>

Among hemoglobinopathies, alpha-thalassemia is the leading cause of NIH fetalis. The globin portion of hemoglobin is normally built from two pairs of polypeptide chains. In the adult, the predominant form is hemoglobin A, consisting of two alpha-chains and two beta-chains, whereas the predominant form in the fetus is hemoglobin F, formed from two alpha-chains and two gamma-chains. If the synthesis of one of the chains is decreased or completely absent, abnormal hemoglobins are produced, giving rise to the clinical syndromes called "thalassemias." The two major groups of thalassemias are called "alpha" and "beta," corresponding to the involved chain. Thalassemias have a wide clinical spectrum ranging from the asymptomatic carrier (e.g., beta-thalassemia minor) to the invariably fatal disease.

Alpha-thalassemia is due to the absence of one or more of the genes controlling the synthesis of alpha-chains. In the homozygotic condition, all four genes are deleted, and, therefore, no alpha-chains are produced. Consequently, no hemoglobin F or A can be produced, and the result is that tetramers of gamma-chains are formed (beta-chains are not produced in significant quantities during fetal life). These tetramers are called "hemoglobin Bart," which has a higher affinity for oxygen than hemoglobin F—so high that it does not release its oxygen to fetal tissues sufficiently. Fetal tissue hypoxia leads to a high output cardiac failure state and hydrops fetalis.<sup>17,24,53,59,71,73,81</sup>

Beta-thalassemias do not become clinically evident until approximately the third month after birth. This is because the switch from hemoglobin F to reliance on hemoglobin A (requiring beta-chains) does not occur until the postnatal period.



**Figure 12-17.** Hydrocele (hy), fluid accumulation in the scrotum.

**TABLE 12-3. CONDITIONS ASSOCIATED WITH NONIMMUNE HYDROPS FETALIS**

<b>Hematologic</b>	<b>Cardiovascular</b>
Anemia due to maternal acquired pure red cell aplasia <sup>65</sup>	<b>Cardiac structure</b>
Anemia due to blood loss	<b>Atrioventricular canal defect</b>
Fetomaternal bleeding <sup>33,73,80,85,117</sup>	With abdominal situs inversus and complete heart block <sup>67</sup>
Twin-to-twin transfusion <sup>37,56,59,60,69-71,80,120,122</sup>	With transposition of great arteries <sup>60</sup>
Hemolysis: Glucose-6-phosphate dehydrogenase deficiency <sup>70,87</sup>	With transposition of the great vessels and asplenia <sup>67</sup>
Hemoglobinopathy: Homozygous alpha-thalassemia <sup>24,53,59,71,73,81</sup>	With transposition of the great vessels and polysplenia <sup>74</sup>
<b>Pulmonary</b>	With double outlet right ventricle and pulmonic stenosis <sup>108</sup>
Congenital cystic adenomatoid malformation (CCAM) <sup>12,32,37,46,51,59,67,77</sup>	With overriding aorta, tracheoesophageal fistula <sup>12</sup>
Pulmonary lymphangiectasia <sup>59,73</sup>	With complex bradyarrhythmia, AV valve insufficiency, interrupted IVC <sup>108</sup>
Pulmonary leiomyosarcoma <sup>48</sup>	Complete communication with common AV valve <sup>90</sup>
Alveolar cell adenoma of the lung <sup>28</sup>	<b>Tetralogy of Fallot<sup>67,73</sup></b>
Diaphragmatic hernia <sup>50,59,70,88</sup>	Absent pulmonary valve or pulmonary atresia <sup>67,158</sup>
Extralobar pulmonary sequestration <sup>67</sup>	Aortic atresia, diminutive left ventricle and mitral valve <sup>73,108</sup>
Enlargement of one lung <sup>69</sup>	Aortic valve stenosis with mitral insufficiency <sup>110</sup>
Chylothorax <sup>4,34,62,114</sup>	Aortic arch interruption <sup>75</sup>
<b>Neurologic</b>	Tricuspid dysplasia <sup>90</sup> and Ebstein's anomaly <sup>108</sup>
Fetal intracranial hemorrhage <sup>18</sup>	Tricuspid and pulmonary atresia <sup>60</sup>
Encephalocele <sup>69</sup>	Myocardial infarction with coronary artery embolus <sup>8</sup>
Porencephaly with absent corpus callosum <sup>59</sup>	Intrapericardial teratoma <sup>8,73,80</sup>
<b>Gastrointestinal</b>	Cardiac rhabdomyoma <sup>50,67</sup>
Midgut volvulus <sup>103</sup>	Myocardial tumors involving ventricular septum, aortic outflow and left atrium, not requiring surgery <sup>118</sup>
Diaphragmatic hernia <sup>12,40,45,59,70,88</sup>	Intrauterine closure of foramen ovale <sup>14</sup>
<b>Atresia</b>	Intrauterine closure of ductus arteriosus <sup>5</sup>
Esophageal with imperforate anus <sup>57</sup>	Endocardial fibroelastosis <sup>12,38,90</sup>
Duodenal <sup>28,38</sup>	With mitral valve insufficiency <sup>78</sup>
Bowel <sup>73</sup>	With subaortic stenosis <sup>79</sup>
Ileal with meconium peritonitis <sup>12,37</sup>	Ventricular septal defect (VSD) <sup>12,73</sup>
Meconium peritonitis with gut herniated into peritoneal sac <sup>12</sup>	With atrial septal defect (ASD) <sup>79</sup>
Meconium peritonitis of unknown etiology <sup>28,68</sup>	With ASD and right atrial conduction system hamartoma <sup>118</sup>
Duodenal diverticulum <sup>59</sup>	With patent ductus arteriosus <sup>37</sup>
Imperforate anus <sup>50</sup>	With absent right hemidiaphragm <sup>12</sup>
<b>Hepatic</b>	<b>Cardiac Rhythm</b>
Cirrhosis with portal hypertension <sup>59</sup>	<b>Atrial</b>
Giant cell hepatitis <sup>12</sup>	Bradycardia and bradyarrhythmia <sup>60,107</sup>
Hepatic necrosis <sup>59</sup>	Tachycardia <sup>10,23,52,73,82,105,116</sup>
Hemangioendothelioma of the liver <sup>23,80</sup>	Paroxysmal (PAT) <sup>28,42,59,60,67,92,107,118</sup>
<b>Genitourinary</b>	Wolff-Parkinson-White (WPW) <sup>81</sup>
Congenital nephrotic syndrome (Finnish type) <sup>54,80</sup>	Flutter with block <sup>58,67,107</sup>
Pelvic kidney <sup>79</sup>	Complete heart block <sup>2,28,55,73</sup>
Hypoplastic kidney (with microcephaly) <sup>70</sup>	<b>Vascular</b>
Urethral obstruction with renal dysplasia <sup>30</sup>	Vena cava thrombosis <sup>99</sup>
Hypoplastic uterus, imperforate hymen, bilateral accessory renal arteries <sup>70</sup>	Hemangioendothelioma <sup>99</sup>
Polycystic kidneys, vaginal atresia, and hydrocolpos <sup>12,59</sup>	Arterial calcification <sup>12,21,50,59</sup>
Urogenital sinus, hydronephrosis, bifid uterus, hydrocolpos <sup>59</sup>	Arteriovenous malformation <sup>49,113</sup>
Adult polycystic kidney disease <sup>124</sup>	Cerebral angioma <sup>90</sup>
<b>Infectious</b>	<b>Metabolic</b>
Coxsackievirus pancarditis <sup>9</sup>	Gaucher's disease <sup>60,60,80</sup>
Secondary syphilis <sup>22,70</sup>	Sialidosis <sup>11,113</sup>
Toxoplasmosis <sup>7</sup>	Gangliosidosis GM1 <sup>57</sup>
Cytomegalovirus hepatitis, myocarditis, encephalitis <sup>37,40,59,60,91</sup>	Mucopolysaccharidosis <sup>73</sup>
Parvovirus <sup>21</sup>	<b>Skeletal dysplasias</b>
Herpes simplex type (H) <sup>60</sup>	Achondroplasia <sup>113</sup>
Respiratory syncytial virus <sup>50</sup>	<b>Achondrogenesis</b>
<b>Neoplastic</b>	Parenti-Fraccaro (or type I) <sup>13,15,47,80</sup>
Neuroblastoma <sup>3,64,79,83,88,111,115</sup>	Langer-Saldino (or type II) <sup>15</sup>
<b>Teratoma</b>	Osteogenesis imperfecta <sup>59,80</sup>
Sacral <sup>59,80,88</sup>	Thanatophoric dwarfism <sup>113</sup>
Mediastinal <sup>12,42,48</sup>	Short rib-polydactyly syndrome
Malignant <sup>59</sup>	Saldino-Noonan type <sup>74</sup>
Congenital leukemia with Down syndrome <sup>32</sup>	Majewski type <sup>15</sup>
Hemangioendothelioma of the liver <sup>23</sup>	Asphyxiating thoracic dysplasia <sup>59</sup>
Pulmonary leiomyosarcoma <sup>48</sup>	<b>Chromosomal</b>
Tuberosclerosis <sup>59,88,116,121</sup>	Triploidy <sup>59</sup>

(Continued)

TABLE 12-3. (Continued)

Trisomies	45XO (Turner syndrome) <sup>80,80,84</sup>
13 <sup>73</sup>	dup(11p) <sup>84</sup>
21 (Down syndrome) <sup>22,28,30,73,80,84,88,108</sup>	Hereditary
E <sup>12</sup>	Pena-Shoker type I <sup>25,79</sup>
18 (Edward's syndrome) <sup>17</sup>	Lethal multiple pterygium syndrome <sup>81,81,73</sup>
Translocation E <sup>12,70</sup>	Idiopathic <sup>101</sup>
47XY+der, <sup>22</sup> t(11;21)(q23;q11)mat <sup>84</sup>	Noonan syndrome with congenital heart defect <sup>123</sup>
Abnormal chromosome 11 <sup>87</sup>	Placental
Mosaic 45X/XY <sup>72</sup>	Chorioangioma <sup>70,72,80,80,80,70,74,112</sup>
Mosaic 46XY/92XXYY <sup>84</sup>	

Thalassemia syndromes are transmitted as autosomal recessive traits. For a fetus to be affected with alpha-thalassemia, both the parents must be carriers. A simple screen for the carrier of thalassemia is to check the complete blood count with RBC indices. If the mean corpuscular volume (MCV) is above 80 femtoliters, the diagnosis is effectively excluded. If the MCV is less than 80, microcytosis is present, and the differential diagnosis includes iron deficiency anemia, anemia of chronic disease, thalassemia, and sideroblastic anemia. Performing serum iron studies (iron concentration, total iron-binding capacity and saturation) will permit differentiation of these syndromes. The most common cause of microcytic anemia is iron deficiency, but if the serum iron concentration is greater than 50 µg/dl and the saturation greater than 15 percent, this diagnosis is excluded. At this point, a hemoglobin A<sub>2</sub> level determination should be ordered. If the concentration is above 3.5 percent, the diagnosis is beta-thalassemia, which is not a cause of hydrops. If the concentration is below 3.5 percent, the diagnosis is alpha-thalassemia-1 (two of the four genes are missing). Since this mother is at risk of having an infant with homozygous alpha-thalassemia, the father must be similarly evaluated. Unless the father is also affected with alpha-thalassemia-1, the fetus cannot have alpha-thalassemia major as the cause of hydrops. Fetal diagnosis can be accomplished via percutaneous umbilical blood sampling or by amniocentesis, and culturing of amniotic fluid cells and DNA analysis for the alpha-chain gene.<sup>95</sup>

Glucose-6-phosphate dehydrogenase (G-6PD) deficiency has been reported as causing NIH in two fetuses.<sup>76,87</sup> The mechanism of hydrops appears to be intrauterine hemolysis related to the impaired production of reduced glutathione by the affected RBC. This compound is essential to protect the RBC membrane from oxidative agents. Hemolysis can occur spontaneously or in response to maternal ingestion of oxidative agents that cross the placenta. A list of

frequently encountered compounds that can trigger a hemolytic crisis is given in Table 12-4.

G-6PD is inherited as an X-linked recessive disorder. The frequency of the gene in the population is highly variable. In Southern China it is 5.5 percent, in American blacks 10 to 15 percent, in Greece 30 percent, and in some areas of Sardinia 35 percent.<sup>119</sup> The two reported cases of NIH apparently related to G-6PD, involved carrier mothers ingesting oxidative agents; one ingested fava beans,<sup>76</sup> the other sulfisoxazole.<sup>87</sup>

Diagnosis of G-6PD deficiency in the fetus would require examination of fetal blood, which is rarely justified. If the fetus is female and the father is not affected, the diagnosis is excluded. The most sensitive test for detection of the carrier state is the hemoglobin reduction test, which unfortunately is positive in only 75 percent of carriers.<sup>20</sup>

Another cause of severe anemia fetalis has been reported in a woman with acquired pure RBC aplasia.<sup>85</sup> In this disease, there are serum inhibitors of erythropoiesis, probably IgG antibodies, directed against bone marrow erythroblasts, erythroid stem cell differentiation, or erythropoietin. These antibodies may be transferred to the fetus, leading to severe anemia. The Coombs test remains negative both in the mother and in the fetus. Should the baby survive, the RBC aplasia lasts for about 3 months.

Fetal anemia due to blood loss has been described in association with hydrops fetalis in two circumstances: fetomaternal bleeding and twin-to-twin transfusion syndrome.

Fetal erythrocytes have been found in the maternal blood at least once during pregnancy in 39 percent of normal subjects.<sup>100</sup> However, the volume of such bleeding is small in virtually all cases (98 percent < 0.1 ml). Perlin et al.<sup>88</sup> reported well-documented cases of NIH associated with severe fetomaternal hemorrhage. The magnitude of the hemorrhage must not be enough to produce death due to acute hypovolemia and is generally chronic.



**TABLE 12-4. COMPOUNDS ASSOCIATED WITH HEMOLYSIS IN G-6PD**

Acetylsalicylic acid (aspirin)
Phenacetin
Sulfas
Antimalarials
Primaquine
Quinidine
Nitrofurantoin
Chloramphenicol
Paraaminosalicylic acid
Naphthalene (mothballs)
Methylene blue
Nalidixic acid
Ascorbic acid (vitamin C, massive doses required)
Quinine
Quinidine
Dapsone

Several tests are available to screen for fetal bleeding into the maternal circulation. The Kleihauer-Betke test is an acid elution test based on the relative sensitivity of adult and fetal hemoglobin to the presence of a strong acid. When maternal erythrocytes are exposed to an acid solution, adult hemoglobin is washed through the cell membrane, whereas fetal hemoglobin is not. After fixation and staining, the maternal RBCs appear as unstained ghost cells and are easily distinguished from the stained fetal cells. The volume of the transplacental hemorrhage (TPH) can be calculated using the following formula:

$$\text{TPH (ml)} = (\text{Estimated maternal blood volume}) \times (\# \text{ Stained cells}) \div (\text{Maternal cells})$$

Other available tests to quantify fetomaternal bleeding include the Fetaldex (Ortho Diagnostics) and BMC Reagent Set (Boehringer Mannheim Corporation), both of which are variations on the original Kleihauer-Betke methodology and are of sufficient accuracy for clinical use.<sup>100</sup> Measurement of the serum alpha-fetoprotein has been used to quantify transplacental hemorrhages.<sup>39</sup> If a significant fetomaternal bleed has occurred, it is important to carefully examine the placenta at the time of delivery, since such macrotransfusions have been reported in association with placental chorioangiomas and choriocarcinomas.<sup>39</sup>

Another cause of hydrops related to blood loss occurs in monozygotic twins with twin-to-twin transfusion. Although the traditional concept has been that the recipient, or plethoric, infant is the one to become hydropic, NIH has also been described in the donor twin.<sup>37,69,70,122</sup> The mechanism for the develop-

ment of hydrops has not been clearly established. Anemia has been suggested as the etiology of NIH in the donor, although the extent of the hydrops is greater than that observed in isoimmunized infants with comparable hemoglobin levels.<sup>70</sup> Volume overload may be the explanation of hydrops in the recipient.<sup>113</sup> NIH has also been described in the donor twin when the recipient is an acardius with parabiotic parasitism.<sup>56</sup> A twin-to-twin transfusion can be suspected antenatally in the presence of a weight difference greater than 20 percent of the weight of the larger twin and with a single placenta. NIH can be identified in one member of a multiple gestation, but it is important to bear in mind that this does not necessarily represent a twin-to-twin transfusion syndrome. The diagnosis can be confirmed postnatally by a blood hemoglobin difference of more than 5 g/100 ml, a higher reticulocyte count in the donor twin, and contrast studies showing anastomotic links between the two circulations in the placenta.

**Cardiac Causes.** Cardiac problems are relatively common causes of NIH,<sup>113</sup> accounting for 40 percent of cases in the series of Allan et al.<sup>1</sup> Some of them are amenable to intrauterine medical therapy.<sup>19,58,66,67,107,118</sup> They can be divided into those related to cardiac dysrhythmias and those due to structural abnormalities. The common mechanism in the development of hydrops regardless of the specific cause is intrauterine congestive heart failure. Chapter 4 provides a detailed discussion of the diagnostic approach to fetal congenital abnormalities and arrhythmias by echocardiography.

When a cardiac dysrhythmia is suspected, its nature can best be elucidated with M-mode echocardiography.<sup>36,66</sup> It should be stressed that both tachyarrhythmias and bradyarrhythmias can be the cause of NIH and can be treated with transplacental pharmacologic manipulation. These fetuses have the best prognosis. An intrauterine dysrhythmia should be suspected when postmortem examination fails to show a cause for NHI. Identification of a fetal third degree heart block is an indication for screening the mother for manifestations and laboratory evidence of connective tissue disorders, such as systemic lupus erythematosus<sup>55</sup> and Sjogren's syndrome,<sup>108</sup> since these associations have been well established. Digoxin, propranolol, and procainamide all cross the placenta and have been used to treat tachyarrhythmias.

The association of a structural cardiac abnormality and NIH usually has a poor prognosis. Of the reported cases, the only long-term survivor was an infant born with an intrapericardial teratoma that was successfully resected in the neonatal period.<sup>8</sup> Intrinsic

cardiac defects are generally associated with poor

the mother was known to have a positive toxoplasmosis

perinatal outcome. This observation may be a reflection of the severity of the defects (serious enough to cause intrauterine congestive heart failure), as well as the condition of these frequently premature babies at delivery. Neonatal congestive heart failure with pulmonary edema may aggravate the severity of respiratory distress syndrome and delay permanent surgical correction of the underlying structural defect. It should be added that intrauterine myocardial infarction has been reported in association with NIH.<sup>6</sup> This may be diagnosed postnatally by electrocardiographic changes, creatine-phosphokinase elevation in the case of a recent event, or at autopsy.

Calcifications in the pericardial sac can occur with intrauterine Coxsackie B3 viral infection.<sup>9</sup> If such calcifications are seen, a viral infection should be suspected, and acute phase viral titers drawn on the mother.

The underlying mechanism in the development of most NIH of vascular etiology is high output cardiac failure. Vascular tumors increase cardiac work, as do arteriovenous malformations, and occur in a variety of sites, including the pulmonary artery system,<sup>113</sup> the great vein of Galen,<sup>49</sup> and the celiac trunk.<sup>30</sup> The antenatal detection of a tumor mass should prompt Doppler ultrasound examination to investigate the possibility of a vascular tumor. Other causes, such as thrombosis of the inferior vena cava,<sup>99</sup> have been reported, although the mechanism for the development of NIH remains obscure.

**Infectious Causes.** NIH has been associated with a number of viral, bacterial, and spirochetal organisms without any clear pathophysiologic mechanisms. Isolated case reports of toxoplasmosis,<sup>7</sup> parvovirus,<sup>21</sup> cytomegalovirus,<sup>37,40,59,80,91</sup> Coxsackievirus,<sup>9</sup> and syphilis<sup>22,70</sup> are available with good documentation. Less certain are passing references in some reviews to associations with trypanosomiasis, herpes simplex type 1, respiratory syncytial virus, and leptospirosis.<sup>32,36,50,60</sup> Intrauterine infections with human parvovirus leading to NIH seem to be associated with aplastic crisis in the fetus and may be suspected by raised maternal serum alpha-fetoprotein.

Toxoplasmosis was reported in a series of three cases in association with NIH, each of which appeared to have excessive extramedullary hematopoiesis.<sup>7</sup> Since most cases of maternal toxoplasmosis are asymptomatic, the diagnosis rests on serologic changes or pathologic demonstration of the organisms.<sup>102</sup> A twofold increase in titer is significant and suggests acute infection. The inability to demonstrate acute seroconversion in the mother does not exclude toxoplasmosis as a cause of NIH, since the infection could have occurred some weeks earlier. If, however,

titer before conception, the diagnosis of congenital infection can be ruled out. Any patient with a positive titer should have the placenta carefully examined histologically for the presence of toxoplasma cysts. For this examination, the placenta should be immediately fixed in formalin and not refrigerated or frozen, since this may cause lysis of the organisms and lead to false negative results. A positive identification of the characteristic cysts is predictive of neonatal toxoplasmosis. Cord blood for IgM toxoplasma serology should be obtained, but 50 percent of infants with definitive congenital toxoplasmosis have negative serology by fluorescent antibody testing for IgM.<sup>102</sup>

Cytomegalovirus infections of the fetus can occur with primary infection and reinfections of the mother. Maternal serologic results are of little help unless they are negative.<sup>102</sup> Viral isolation from neonatal urine, cerebrospinal fluid, nasopharynx, or conjunctiva remains the best method of establishing the diagnosis.

Screening for syphilis can be performed with VDRL or RPR tests, with confirmation by specific treponemal antibody testing (e.g., FTA-ABS).

**Renal Disorders.** Congenital nephrotic syndrome (Finnish type) with resultant hypoproteinemia is a cause of NIH, reported primarily from the Scandinavian countries.<sup>54,80</sup> It is inherited with an autosomal recessive pattern, and over 100 kindreds have been reported. The infants have normal or slightly elevated BUN values, but massive proteinuria is uniformly present, and microscopic hematuria is often seen as well.

Although other abnormalities of the urinary tract, such as obstructive uropathy,<sup>32,43</sup> polycystic kidney disease with hydrometrocolpos,<sup>12,59</sup> hypoplastic kidney,<sup>70</sup> and pelvic kidney<sup>70</sup> have been reported in association with NIH, these are likely to reflect reporting bias because an underlying mechanism is unclear. In our experience with relatively large numbers of fetuses with obstructive uropathy and infantile polycystic kidney disease, NIH is uncommon.<sup>98</sup>

**Gastrointestinal Disorders.** A number of gastrointestinal disorders have been associated with NIH, including diaphragmatic hernia,<sup>12,42,45,59,70,88</sup> midgut volvulus,<sup>103</sup> gastrointestinal obstructions,<sup>12,37,38,57,59,73</sup> meconium peritonitis secondary to herniation of the gut into a peritoneal sac,<sup>12</sup> and meconium peritonitis of unknown etiology.<sup>59,68</sup> Whether these represent mere associations or an underlying common etiology has not been determined.

Hepatic disorders, such as cirrhosis and hepatic necrosis, were reported by Hutchinson et al.<sup>59</sup> along

with NIH. A single case of giant cell hepatitis has also

formation or an obstruction to venous return. The

appeared in the literature.<sup>12</sup> These are all pathologic diagnoses and were not made antenatally. The common mechanism in the development of hydrops may be hypoproteinemia,<sup>113</sup> although analbuminemia alone is not a sufficient cause.<sup>27</sup> Two reports of hemangioma of the liver associated with NIH may be explained by arteriovenous shunting within the hepatic mass, leading to heart failure.<sup>23,50</sup>

**Chromosomal Abnormalities.** Turner syndrome (45XO) is one of the most common causes of NIH among the chromosomal abnormalities associated with hydrops.<sup>60,80,84</sup> In this syndrome there are often multiple, septated cysts in the paracervical region ("cystic hygroma"), related to a lack of communication between the lymphatic system and venous drainage in the neck. For unclear reasons, infants with Turner syndrome may also have lymphedema of the hands and feet as well as chylothorax, giving a picture resembling NIH.

NIH has been reported in association with other genetic abnormalities, including trisomy 13,<sup>73</sup> trisomy 18,<sup>12</sup> trisomy 21,<sup>32,59,60,73,80,84,88,108</sup> dup (11p),<sup>44</sup> mosaicisms, unbalanced translocations, and triploidy.<sup>12,37,59,70,84</sup>

The diagnosis of NIH is an indication for genetic amniocentesis. The identification of trisomy 18 (Edward's syndrome) could change the management, since 50 percent of these infants die within 2 months of birth, and only 10 percent survive the first year as severely mentally handicapped infants.<sup>15</sup> Of course, early identification offers the parents the option of elective termination of pregnancy.

**Hereditary Syndromes.** Pena-Shokeir syndrome type 1 is an autosomal recessive condition characterized by neurogenic arthrogryposis, pulmonary hypoplasia, and hypertelorism, which has been described in association with hydrops fetalis.<sup>25,72</sup> Another autosomal recessive disorder associated with NIH is the lethal type of multiple pterygium syndrome.<sup>41,61,73</sup> A recurrent NIH within a sibship of idiopathic origin has been described as well.<sup>101</sup> In one case, Noonan's syndrome has been associated with NIH, but the cause of the fetal effusions was probably the associated heart anomalies.<sup>123</sup>

**Neoplasms.** Neoplastic diseases can occur in utero, and two in particular have been associated with NIH: neuroblastomas<sup>3,64,79,83,88,111,115</sup> and teratomas.<sup>12,42,48,59,80,88</sup> Single cases of NIH associated with congenital leukemia,<sup>32</sup> pulmonary leiomyosarcoma,<sup>48</sup> and hemangioendothelioma of the liver<sup>23</sup> have also been reported. This latter tumor causes a hemodynamic state similar to that of an arteriovenous mal-

reported cases of teratomas were localized in the mediastinum, in the pericardial sac, and in the sacrococcygeal area. These tumors are potentially identifiable if they are of sufficient size or if they cause a shift in the location of other organs (e.g., the heart). Hutchinson et al.<sup>59</sup> noted one case of malignant teratoma without reporting any details of the case.

Tuberous sclerosis is an autosomal dominant disease characterized by fibroangiomatous tumors in multiple organs of the body. The most frequently affected organs are the cortex of the brain, the skin, and the kidneys. Occasionally, the heart may be involved with rhabdomyomas. Fibrosis of the liver may occur as well. The mechanism for the development of hydrops is probably heart failure in those with intracardiac rhabdomyomas or hepatic failure in those with cirrhosis. Antenatal diagnosis is not possible, and although the disease is inherited as an autosomal recessive disorder, 86 percent of the cases represent new mutations. Therefore, the parents are not involved in the disease process. Several cases of NIH in association with tuberous sclerosis have been reported.<sup>59,86,116</sup> In a series of 21 cases of tuberous sclerosis diagnosed within 1 week of birth, there was only 1 with NIH.<sup>86</sup>

**Metabolic Disorders.** The metabolic derangements associated with NIH are drawn from a number of pathways that involve either synthesis or storage disorders. The mechanisms for the development of hydrops in cases of storage diseases may involve visceromegaly and obstruction of venous return.<sup>11</sup> The storage diseases that have been reported include Gaucher disease (cerebrosidosis), gangliosidosis GM1 type I, Hurler syndrome (mucopolysaccharidosis type I), and mucopolipidosis type I (sialidosis).

Gaucher disease results from an accumulation of glucocerebrosides in the histiocytes due to a tissue deficiency of beta-glucosidase. It is an autosomal recessive disease that can be diagnosed in cell culture of fibroblasts from amniotic fluid.<sup>95</sup> Heterozygote (carrier) identification can be accomplished by betaglucoisidase analysis of white blood cells or culture of skin fibroblasts. NIH is rare in infants with Gaucher disease. This diagnosis should be considered primarily in patients of Ashkenazi-Jewish ancestry, since two thirds of cases occur in this group.<sup>15</sup>

Gangliosidosis GM1 is an autosomal recessive disorder that is due to the absence of beta-galactosidase, and gangliosides collect diffusely in storage cells in many organs.<sup>15</sup>

Hurler syndrome is an autosomal recessive condition characterized by an accumulation of acid

mucopolysaccharides due to deficiency in alpha-L-iduronidase.<sup>15</sup>

Sialidosis (mucopolipidosis type I) is an autosomal recessive disease due to a deficiency in alpha-N-acetylneuraminidase, leading to accumulation of sialic acid.<sup>15</sup>

It is unclear if these metabolic disorders are associated with NIH or simply with soft tissue excess that leads to gross appearance resembling NIH.

These conditions are amenable to prenatal diagnosis and to detection of the carrier state.<sup>95</sup> In patients with NIH of unknown origin, a screening of urine by thin-layer chromatography and enzymatic assays on cultured fibroblasts is essential for accurate genetic counseling and prenatal diagnosis in subsequent pregnancies.

**Skeletal Dysplasias.** Skeletal dysplasias associated with NIH are achondroplasia,<sup>113</sup> achondrogenesis,<sup>13,47,80</sup> osteogenesis imperfecta<sup>59,80</sup> thanatophoric dwarfism,<sup>113</sup> short rib-polydactyly syndrome, and asphyxiating thoracic dysplasia.<sup>59</sup> In all of these, the mechanism for the production of NIH is unknown.

When performing real-time ultrasound evaluation of the hydropic fetus, careful attention to proximal and distal long bone lengths and mineralization will permit screening for some of these disorders.<sup>63</sup> Further discussion is available in Chapter 10.

**Neurologic Conditions.** There have been isolated reports of NIH along with an encephalocele,<sup>59</sup> and with porencephaly and absence of the corpus callosum.<sup>59</sup> All of these probably represent chance associations. An additional case documents the occurrence of NIH in an infant with intracranial hemorrhage and severe anemia.<sup>18</sup>

**Pulmonary Causes.** The most frequent cause of NIH among pulmonary lesions is congenital cystic adenomatoid malformation (CCAM).<sup>12,32,37,48,51,59,67,77</sup> Antenatal diagnosis of this condition has been reported (see Chapter 5). Other conditions that have been associated with NIH include pulmonary lymphangiectasia,<sup>59,73</sup> pulmonary leiomyosarcoma,<sup>48</sup> alveolar cell adenoma of the lung,<sup>29</sup> extralobar pulmonary sequestrations and diaphragmatic hernia.<sup>50,59,70,88</sup> An unusual cause of NIH is enlargement of one lung with shift of the mediastinal structures.<sup>89</sup> The mechanism for hydrops in all these conditions is probably obstruction of venous return. Congenital chylothorax may lead to hydrops as well.<sup>4,34,62,114</sup>

**The Placenta.** Chorioangiomas of the placenta act as high volume arteriovenous shunts to produce hydrops.<sup>10,12,50,55,60,70,74,112</sup> Small chorioangiomas may

TABLE 12-5. LABORATORY TESTS FOR HYDROPIC FETUS

Blood tests
CBC with differential and RBC indices
Kleinbauer-Betke stain
ABO type and rhesus antigen status
Indirect Coombs (antibody screen) test
Acute phase titers
Toxoplasmosis
Cytomegalovirus
Serologic test for syphilis (VDRL or RPR)
G-6PD deficiency screen
Amniotic fluid tests
Karyotype
L:S ratio after viability

not be visualized, and the true incidence of these placental tumors may be higher than has been determined in the past.<sup>106</sup> In the larger lesions, there may be vascular stasis, with resultant loss of plasma proteins into the amniotic fluid and hydrops.<sup>112</sup>

### Prognosis

Although some cases of spontaneous intrauterine remission of NIH fetalis are reported in the literature,<sup>68,93,96,104</sup> the prognosis for the majority of these infants is gloomy. The perinatal mortality rate in these infants is very high, ranging from 70 to 90 percent.<sup>37,50,59,60,73</sup>

### Obstetrical Management

Identification of the hydropic infant is not a diagnostic challenge. The real problem is to establish the underlying cause and to determine appropriate therapy and optimal timing of delivery. Once a hydropic infant is identified, the first step is to investigate the possibility of isoimmunization and whether it is due to rhesus or other irregular antibodies. This can be done easily by performing an indirect Coombs test on maternal serum. A negative Coombs test rules out isoimmunization.

A comprehensive ultrasound examination is the next step in the management of the pregnancy, along with appropriate investigative blood and amniotic fluid tests, as outlined in Table 12-5. Interpretation of these blood tests was discussed in the preceding sections. Ultrasound examination should include fetal echocardiography and a careful survey for congenital anomalies of the fetus and placenta. Most commonly, the workup (both ultrasound and laboratory) fails to reveal the etiology. Management decisions at this juncture are dependent on gestational age.

Before viability, the option of pregnancy termination should be offered to the parents. They should be counseled that the prognosis in cases of previable NIH is poor. If a decision to continue the pregnancy

is made, the clinician is faced with the dilemma of either delivering the baby to prevent intrauterine death or continuing expectant management to allow fetal maturation. Immediate delivery of an immature fetus is likely to result in a newborn with increased total lung water, thus compounding the problems in treating respiratory distress syndrome by adding pulmonary edema.

Expectant management, on the other hand, raises the questions of ensuring fetal well-being and defining the end-point for delivery. Obstetricians usually elect to defer delivery until fetal lung maturity appears as measured by the lecithin:sphingomyelin (L:S) ratio. However, the natural evolution of surfactant production in hydropic infants is unknown. In other conditions associated with pulmonary hypoplasia, such as diaphragmatic hernia, immature L: S ratios have been obtained close to term.<sup>16</sup> Furthermore, NIH is often associated with polyhydramnios, and uterine overdistention may precipitate premature labor.

A reasonable approach to management of the very premature infant is to follow the fetus with frequent ultrasound evaluations, including biophysical profiles, and to defer delivery until the clinical picture appears to deteriorate. If such a course is chosen and premature labor due to polyhydramnios occurs, the option of therapeutic amniocentesis is available. In 40 to 50 percent of the cases, preeclampsia occurs with NIH for unclear reasons.<sup>70</sup> We consider the appearance of this complication to be an indication for delivery, since the mother's health may be seriously threatened and the chance of the infant's survival is extremely small.

If the pregnancy is close to term, elective delivery would decrease the risk of intrauterine fetal demise. Because fetal ascites may cause soft tissue dystocia, cesarean section should be considered as a way of minimizing birth trauma and maximizing the likelihood of survival. On the other hand, patients should be informed that the chances of survival for these infants are minimal. Thoracentesis and abdominal paracentesis may be considered prior to delivery.

The prognosis for the hydropic fetus is improved in selected groups. Cardiac dysrhythmias amenable to transplacental medical therapy usually carry a good prognosis, provided they are not associated with a serious congenital anomaly. Another potentially treatable cause in the antepartum period is a significant fetomaternal hemorrhage, which may be treated with current techniques of in utero transfusion. This is possible when the risks of prematurity outweigh the risks of transfusion. Alternatively, elective delivery and neonatal transfusion may be chosen. In the rare case of G-6PD as a cause of hemolysis, it should be sufficient to remove the offending agent

and depending on the gestational age, either deliver or transfuse the fetus.

It is necessary to develop a systematic approach to establish the etiology. Autopsy should be performed in every case to help reach this goal.

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## Sacroccygeal Teratoma

### Definition

Sacroccygeal teratoma (SCT) is a congenital germ cell tumor arising from the presacral area.

### Incidence

SCT is the most common tumor encountered in the newborn. The estimated incidence is 1 in 40,000 births. Eighty percent of affected infants are females.<sup>5</sup>

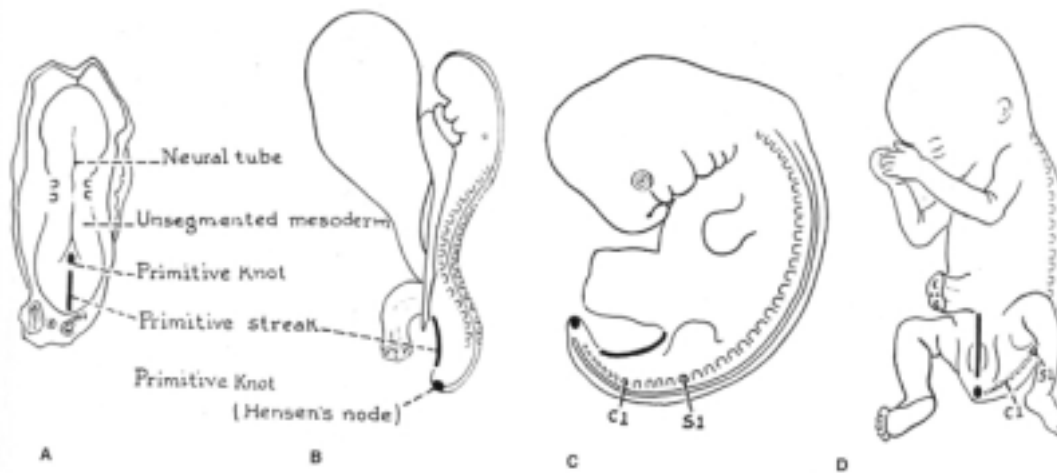
### Etiopathogenesis

SCTs arise from the primitive knot or Hensen's node. Hensen's node is an aggregation of totipotential cells that are the primary organizers of embryonic devel-

opment (Fig. 12-18). Originally located in the posterior portion of the embryo, it migrates caudally during the first weeks of life inside the tail of the embryo, finally resting anterior to the coccyx.<sup>11</sup> Segregation of totipotential cell from Hensen's node probably gives rise to SCTs. This theory provides an explanation for the more frequent occurrence of teratomas in the sacral area rather than in other parts of the body.<sup>11</sup>

Although the majority of SCTs occurs sporadically, the association of SCT, anorectal stenosis, and sacroccygeal defects has been reported and appears to be inherited in an autosomal dominant pattern.<sup>2,16</sup>





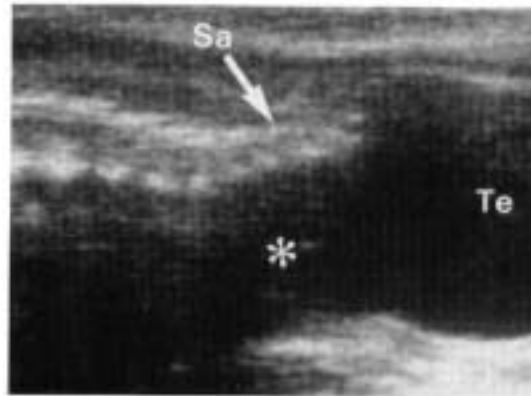
**Figure 12-18.** Sacrococcygeal teratomas presumably arise from totipotent cells that are initially derived from the primitive knot (Hensen's node). These primordial cells are most apt to be found close to the pathway traversed by the primitive node or to its final resting place in the sacrococcygeal area. **A.** The human embryo at the beginning of somite formation. The primitive node is located at the caudal end of the neural tube. **B.** A 17-somite human embryo demonstrates the apparent caudal migration of the primitive knot while somites are formed and pushed cephalad. The primitive streak is now ventral. The primitive node remains at the tip of the neural tube. **C.** Human embryo at the middle of the 6th week, at which time the tail is of maximal length. Forty-two somites are present, and the primitive node is now pushed to the tip of the tail. **D.** The fetal form reached in the 10th week after the resorption of the tail. Thirty-four somites, including the coccyx, remain. The tail does not drop off, but a retraction of it takes place as fragmentation and resorption of the ependymal canal somites and tail duct take place. The primitive knot comes to lie at the tip of the coccyx, and any teratoma arising from it would be similarly located. (Reproduced with permission from Gonzalez-Crussi et al.: *Arch Pathol Lab Med* 102:420, 1978.)

However, it is unclear if the SCT in these cases is congenital or arises in the postnatal period.

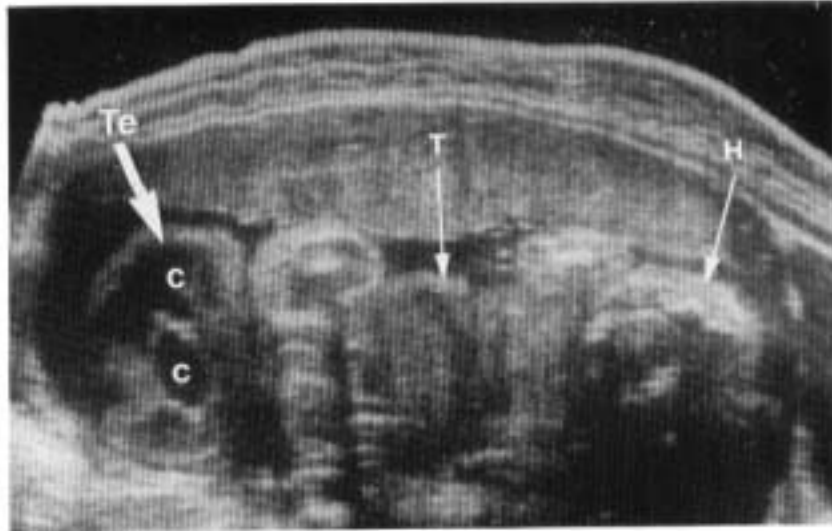
### Pathology

The American Academy of Pediatrics<sup>1</sup> classifies SCTs into four types: type I, a predominant external lesion protruding from the perineal region and covered by skin with a minimal presacral component; type II, a predominant external tumor with a significant presacral component; type III, a tumor with a predominant sacral component and external extension; type IV, a presacral tumor with no external component. Types I and II account for more than 80 percent of cases.<sup>10,21</sup> In 15 percent of patients, the lesion is entirely cystic. In the remaining patients, it is either solid or mixed.<sup>7</sup> A histopathologic classification similar to that used for ovarian teratomas has been suggested.<sup>10,27</sup> Three types of SCT can thus be distinguished. (1) Mature (or benign) teratomas consist of tissues markedly similar to normal, well-developed structures. A variety of tissues, usually derived from all three germ layers, can be found in these cases. Glia, bowel, pancreas, bronchial mucosa, skin appendages, and striated and smooth muscle have been described.<sup>5,10,27</sup> Fully formed organs may be present. Bowel loops,<sup>12</sup> limb components, such as metacarpal

bones and digits,<sup>20</sup> and well-formed teeth<sup>5</sup> have been documented. Choroid plexus structures are frequently found, and their production of cerebrospinal fluid is responsible for the cysts within the tumor. (2) Immature teratomas are usually graded from 0 to 3



**Figure 12-19.** Longitudinal scan demonstrating a cystic lesion (Te) arising from the sacrum (Sa). The integrity of the sacrum and the intraabdominal extension of the lesion (\*) allow a diagnosis of sacrococcygeal teratoma.



**Figure 12-20.** Longitudinal scan passing through the head (H) and trunk (T) of a fetus affected by a large, partly cystic (c), partly solid teratoma (Te).

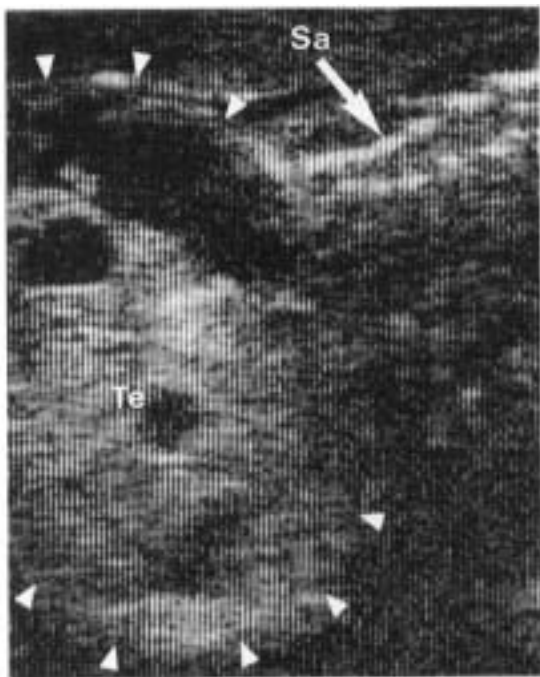
depending upon the proportion of immature or embryonal tissues. The immature component is almost exclusively of neuroepithelial origin or, less frequently, of renal origin.<sup>10,27</sup> (3) Malignant teratomas are of the yolk sac or endodermal sinus tumor type

and are characterized by production of alphafetoprotein.

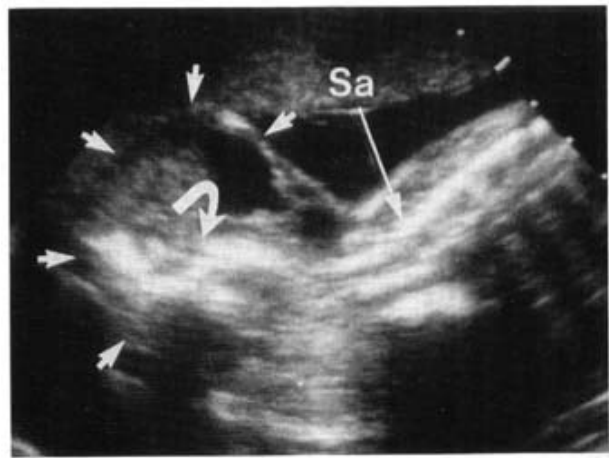
Mature, immature, and malignant forms account for 55 to 75 percent, 11 to 28 percent, and 7 to 13 percent of all SCTS, respectively.<sup>27</sup> Mature and immature forms are frequently cystic (72 percent and 62 percent, respectively). Malignant forms are predominantly solid.<sup>27</sup> Hypervascularity is a frequent finding<sup>26</sup> and may result in severe spontaneous and intraoperative hemorrhage.

#### Associated Anomalies

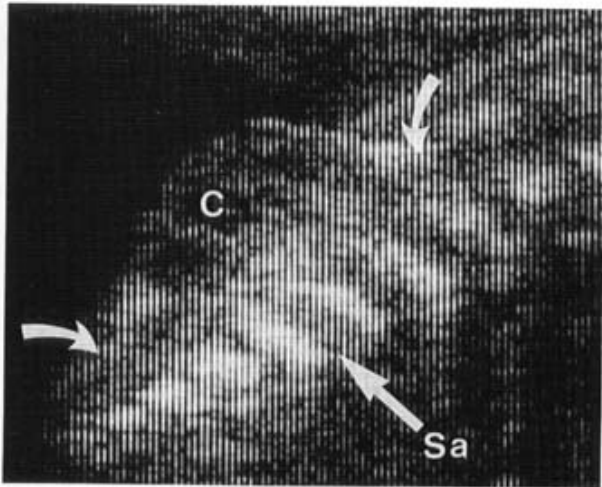
The frequency of associated anomalies ranges from 5 to 25 percent in different series.<sup>1,3,7,10,11</sup> No specific pattern has been identified. Anomalies have included



**Figure 12-21.** Longitudinal scan passing through the sacrum (Sa) of a fetus with very large, mixed sacrococcygeal teratoma (Te, arrowheads).



**Figure 12-22.** Longitudinal scan passing through the sacrum (Sa) in a midtrimester fetus with a large, predominantly solid sacrococcygeal teratoma. Calcifications are seen within the tumor (arrowheads). At necropsy, a well-formed foot was found inside the mass.



**Figure 12-23.** Myelomeningocele. A cystic lesion (c) with internal septa is seen arising from the posterior aspect of the sacrum (Sa). Note the defect of the vertebrae below the cystic structure (curved arrows).

spina bifida, obstructive uropathy, cleft palate, and calcaneus valgus deformity. Severe hemorrhage inside the tumor leading to anemia and NIH has been reported in a fetus.<sup>9</sup>

### Prenatal Diagnosis

The experience in prenatal diagnosis of SCT has been reviewed recently.<sup>14</sup> A total of 20 cases<sup>4,6,8,9,13-15,17,19,22,25,28,29</sup> has been reported, to which we can add 7 cases from our own experience.

The diagnosis of types I, II, and III is easy and depends on demonstration of a mass arising from the sacral area and protruding through the perineum. The mass may be either cystic (Fig. 12-19), solid, or mixed (Figs. 12-20, 12-21). Calcifications are present in 36 percent of cases<sup>7</sup> (Fig. 12-22). Identification of type IV SCT appears difficult, since this type occurs as intraabdominal masses, and establishing their origin may be impossible. A careful investigation of the intraabdominal cavity in search of tumor extension is critical for the assessment of the type of SCT. Evaluation of fetal bladder function has been suggested, in an effort to identify involvement of the pelvic nerves.<sup>14</sup> The accuracy of ultrasound in recognizing such dysfunction remains to be established.

In some patients, an elevation of the amniotic fluid alphafetoprotein level and the presence of acetylcholinesterase have been reported.<sup>13,14</sup> Polyhydramnios has been found in association with SCT.

In the fetus, a large myelomeningocele may closely mimic SCT. However, a distinction can be made by demonstrating in the latter that the spine is intact, the tumor has intraabdominal or perineal extensions, and derives from the anterior portion of the sacrum (Fig. 12-23). Alphafetoprotein and acetylcholinesterase may have limited value in the differential diagnosis between a neural tube defect and SCT. A differentiation between SCT and more rare conditions, such as neuroenteric cysts and tumors of various origins (e.g., chordoma, sarcoma, ependymoma), may be impossible in prenatal ultrasound studies.



**Figure 12-24.** Newborn with a large sacrococcygeal teratoma.



**Figure 12-25.** The same infant as in Figure 12-24. This mass was resected with no difficulties in the immediate neonatal period.

### Prognosis

The prognosis is related to the histology and size of the tumor. The histologic type predicts the likelihood of malignancies, and the size of the tumor relates to the occurrence of complications during surgical extirpation (Figs. 12-24, 12-25). According to Altman et al.,<sup>1</sup> no patient with type I tumor had metastasis, whereas types II, III, and IV were associated with spread in 6 percent, 20 percent, and 76 percent, respectively. Malignant tumors are uniformly and rapidly fatal. The average time of survival after diagnosis is 8.9 months,<sup>27</sup> with only one reported case of long-term survival.<sup>18</sup> Malignancies should be differentiated from local recurrences of benign SCT after extirpation.<sup>3</sup> The mortality rate of patients with immature SCT varies between 55 percent<sup>10</sup> and 37 percent.<sup>27</sup> Benign SCT carries a good prognosis and its mortality rate varies between 3 percent<sup>5</sup> and 12 percent.<sup>7</sup> The main cause of death in these patients is uncontrolled hemorrhage at the time of surgery. Even though entire cystic lesions and those with calcifications are likely to be benign, such correlation is not always correct.<sup>7</sup> The size of the tumor does not seem to predict malignancy. However, very large SCT may be associated with significant intraoperative morbidity. There is limited experience with the intrauterine growth of these lesions. We have seen one rapidly growing tumor that was benign in nature. A review of the prenatally diagnosed cases indicates a much higher mortality rate than that expected from the pediatric series. Of a total of 27 patients, an elective termination was performed in 7. The perinatal mortality rate in the remaining patients was 45 percent (9/20). It is remarkable that in the 7

fatalities for which histopathologic examination was available, the SCT was benign in 6 and immature in 1.

### Obstetrical Management

Before viability, the option of pregnancy termination should be offered to the parents. A careful search for associated anomalies is indicated. In continuing pregnancies, serial scans are indicated to evaluate the growth of the tumor and to detect the appearance of hydrops. SCT can vary greatly in size. Dystocia has complicated 6 to 13 percent of labors. With a large tumor, a cesarean section would seem prudent. Aspiration of a massive cystic lesion to permit cesarean delivery has been reported.<sup>19</sup>

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