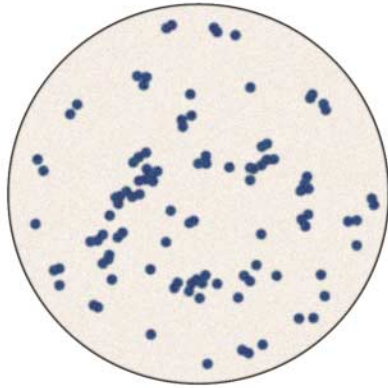




This Week in the Journal

July 25, 2002

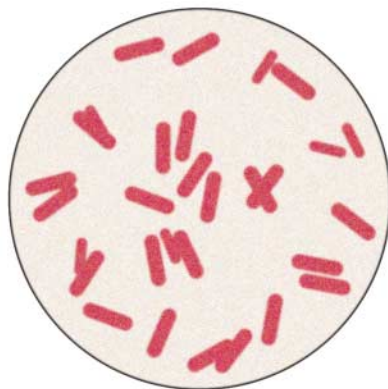


Prevention of Early-Onset Group B Streptococcal Disease

Current U.S. guidelines for reducing the incidence of early-onset group B streptococcal disease in neonates recommend either screening pregnant women for infection or using the presence of clinical risk factors to identify candidates for intrapartum antibiotic prophylaxis. This multicenter, retrospective study compared the rates of early-onset group B streptococcal disease among infants born to mothers who had a documented culture for group B streptococcus during pregnancy (screened group) and those born to women with no screening documented (presumed “risk-based” group). The risk of early-onset disease in the screened group was half that in the risk-based group. Potential misclassification in the risk-based group of women whose providers had no defined strategy did not explain the observed results, since the lower risk persisted after the exclusion of women who had clinical risk factors warranting prophylaxis but did not receive it.

Universal prenatal screening for group B streptococcal colonization appears to be more effective in reducing the incidence of early-onset group B streptococcal disease than the use of clinical risk factors to identify candidates for intrapartum antibiotic prophylaxis. These findings suggest the need to reconsider current recommendations endorsing both approaches.

see page 233 (editorial, page 280)



Pathogens Causing Early-Onset Sepsis in Very-Low-Birth-Weight Infants

In this study, to assess whether the increasing use of intrapartum antibiotics to reduce neonatal group B streptococcal infection has been associated with changes in the rate and causes of early-onset sepsis in very-low-birth-weight infants, the authors compared the incidence of early-onset sepsis (that occurring within 72 hours of birth) among infants weighing 401 to 1500 g who were born between 1998 and 2000 with an earlier cohort of very-low-birth-weight infants born between 1991 and 1993. As compared with the 1991–1993 cohort, there was a marked reduction in group B streptococcal sepsis in the 1998–2000 cohort but an increase in *Escherichia coli* sepsis, such that the overall rate of early-onset sepsis was not significantly changed. Infants with early-onset sepsis were more likely to die than uninfected infants.

The change in causes of early-onset sepsis over time, from predominantly gram-positive to gram-negative organisms, requires confirmation, but this finding arouses concern about a possible adverse effect of broader use of antibiotics during labor and delivery.

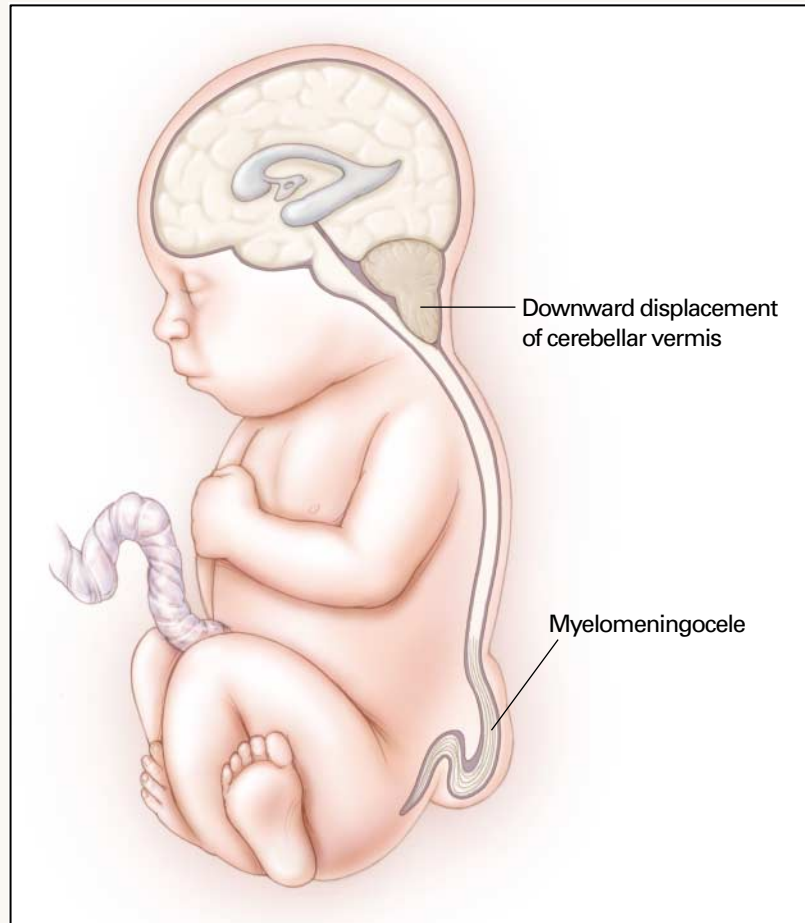
see page 240 (editorial, page 280)

PERSPECTIVE

Fetal Surgery for Myelomeningocele

The most common nonlethal malformation in the spectrum of neural-tube defects is myelomeningocele. This defect, caused by failure of the neural tube to close completely at about four weeks of gestation, occurs in approximately 1 in 2000 births. The extent and severity of the neurologic deficits (which include motor dysfunction in the legs and lack of bladder and bowel control) depend on the location of the lesion along the neuroaxis; the cord below the lesion is dysplastic. Myelomeningocele is often associated with the type II Chiari hindbrain malformation, a downward displacement of the cerebellar vermis into the cervical spinal canal, causing elongation of the brain stem and obliteration of the fourth ventricle. In about 90 percent of cases, the resulting obstruction leads to the development of hydrocephalus late in gestation or after postnatal closure of the spinal defect. Surgical closure of myelomeningocele (see Figure) is usually performed soon after birth, with the goals of preventing infection and minimizing any further loss of function. However, if the neurologic deficits persist, brain-stem dysfunction may occur, and shunt-related problems are virtually inevitable.

Much progress has been made in dealing with this severe congenital anomaly. A key advance has been made in prevention. Folic acid supplementation before conception and during the first month of pregnancy can prevent up to 70 percent of cases of neural-tube defects. The introduction of enriched-grain products (such as cereals, bread, and pasta), which are supplemented with 140 μg of folic acid per 100 g

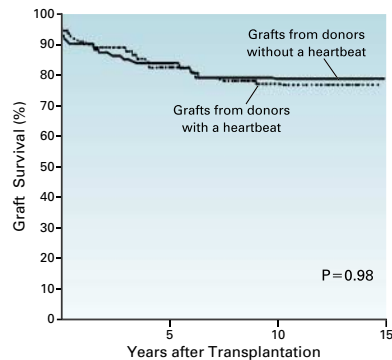


Myelomeningocele with Associated Downward Displacement of the Cerebellar Vermis.

of grain, has been linked directly to a decrease in neural-tube defects. Prenatal screening of maternal blood at 16 to 18 weeks of gestation for elevated alpha-fetoprotein levels and fetal ultrasonography have facilitated early diagnosis of severe neural-tube defects. Until recently, the parents of a fetus with myelomeningocele had two options: either make the difficult decision to terminate the pregnancy or anticipate the birth of a child with lifelong defects.

The new option is fetal surgery to repair the myelomeningocele. Is there reason to think this approach will result in a better outcome? If the myelomeningocele is simply the

most obvious anatomical manifestation of a generalized neurodevelopmental syndrome, then closing the defect at 20 to 28 weeks of gestation will not alter the clinical course. However, fetuses with myelomeningocele have leg movement early in gestation that is often absent after birth at term, suggesting loss of function in utero. Experimental surgery, primarily in fetal sheep, has shown that closure of the exposed spinal cord can decrease cord dysplasia and preserve function, presumably by protecting the spinal cord from trauma and amniotic fluid. More surprising is the finding that closure of the defect can prevent the development of the



Kidney Transplantation from Donors without a Heartbeat

The shortage of renal allografts has led to interest in sources of organs other than living donors and cadaveric donors with a heartbeat. Accumulating data suggest that the short-term survival of cadaveric kidneys from donors without a heartbeat is similar to that of kidneys from donors with a heartbeat. This report describes a single-center study of 122 patients who received kidney transplants from donors without a heartbeat and 122 matched patients who received transplants from donors with a heartbeat. Recipients were followed for up to 15 years. Although there was a significantly higher incidence of initial delay in graft function among those who received kidneys from donors without a heartbeat, long-term graft survival was similar in the two groups.

Renal allografts from cadaveric donors without a heartbeat may be transplanted safely and with an acceptable outcome.

see page 248 (editorial, page 281)

type II Chiari brain-stem malformation. This preventive effect is thought to result from a restoration of normal cerebrospinal fluid dynamics, which is reminiscent of the need for blood flow for normal fetal vascular and cardiac development. These experimental findings, which suggest that many of the deficits associated with myelomeningocele may be mitigated by early closure of the defect, point to the potential for a tremendous benefit of fetal surgery for this condition.

The question of whether fetal surgery for myelomeningocele is beneficial in humans is not easily answered. In fetal surgery, there are two patients: the mother and the fetus. The lumbar or sacral myelomeningoceles selected for fetal repair are not lethal lesions. Fetal surgery puts both the mother and the fetus at risk for complications, including a high risk of preterm delivery. The

newborn with myelomeningocele has a long list of complications. The newborn who has undergone in utero repair may have a different list of complications.

The possibility of unforeseen complications is raised by a report in this issue of the *Journal*. Mazzola et al. describe loss of neurologic function in the first year of life in three children who underwent in utero repair of myelomeningocele (see pages 256–259). All three had dermoid inclusion cysts and spinal cord tethering. For fetal surgery to be warranted, its benefits for neurologic function must outweigh its complications and risks.

In utero surgery for myelomeningocele has been performed more than 220 times, primarily at four centers in the United States, yet its benefits and risks remain uncertain. Fortunately, the three centers that have the most experience with this

type of surgery have agreed to enroll all eligible patients in a randomized clinical trial comparing fetal surgery with routine management. Children will be followed closely for two years after birth. The fetal-surgery community is to be congratulated for formally studying a procedure with great potential and high risk.

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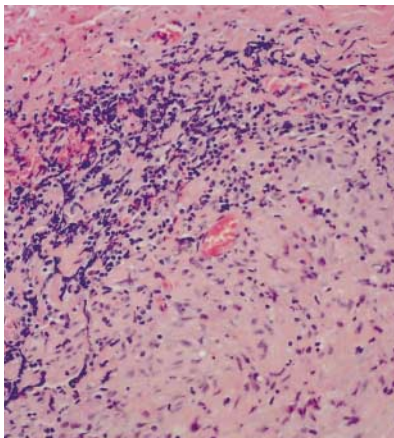


Dermoid Inclusion Cysts and Early Spinal Cord Tethering after in Utero Surgery for Myelomeningocele

In utero surgery for myelomeningocele has been proposed to reduce neurologic dysfunction that may result from exposure of the spinal cord to amniotic fluid; approximately 220 such surgeries have been performed to date. The authors report on three girls under one year of age who had loss of motor function in the legs or loss of bladder function after in utero repair of myelomeningocele at 22 to 24 weeks of gestation. All three had dermoid cysts with associated spinal cord tethering, which required surgery.

Although in utero surgery for myelomeningocele holds promise for improving the neurologic outcome, these cases of early spinal cord tethering and dermoid-cyst formation sound a note of caution. There is a need for long-term assessment of children who undergo closure of myelomeningocele in utero, as compared with those in whom closure is performed after birth.

see page 256 (Perspective, page 230)



Medical Progress: Polymyalgia Rheumatica and Giant-Cell Arteritis

Polymyalgia rheumatica is an inflammatory disorder manifested principally by stiffness of the neck, shoulder girdle, and pelvic girdle; giant-cell (or temporal) arteritis affects the cranial branches of arteries arising from the aortic arch. The two conditions are believed to be linked and may occur together. Giant-cell arteritis is a serious disorder that can cause blindness as a result of ischemia of the optic nerve or retina. Both disorders respond to corticosteroid therapy. This comprehensive article reviews the clinical manifestations, pathophysiology, and treatment of these disorders.

see page 261

“Both overt and covert barriers to transplantation (in healthy HIV-positive patients) remain.”

Sounding Board: Solid-Organ Transplantation in HIV-Infected Patients

Many centers do not consider asymptomatic HIV-positive patients to be candidates for solid-organ transplantation, although there are no data to indicate that the outcome of transplantation is worse among these patients than among other transplant recipients. This Sounding Board reviews the ethical arguments for considering transplantation in patients with HIV infection as similar to transplantation in patients with other chronic illnesses.

see page 284