



# This Week in the Journal

January 17, 2002

*“Very-low-birth-weight participants had a lower mean IQ and lower academic achievement scores.”*

## **Outcomes in Young Adulthood for Very-Low-Birth-Weight Infants**

Survivors of very low birth weight who were born during the early years of neonatal intensive care are now young adults. This study compared the level of education and other outcomes at 20 years of age among 242 very-low-birth-weight participants and 233 controls with normal birth weight. As compared with the controls, very-low-birth-weight participants had lower educational achievement and IQ scores and higher rates of subnormal height and chronic illness, including neurologic disorders. However, they reported lower rates of alcohol or illicit drug use than normal-birth-weight controls, and the men had lower rates of contact with the police.

*Because the rates of neurodevelopmental sequelae in very-low-birth-weight children have not changed substantially since the 1970s, these findings are likely to be relevant to very-low-birth-weight infants born in recent years.*

**see page 149 (perspective, page 146; editorial, page 197)**

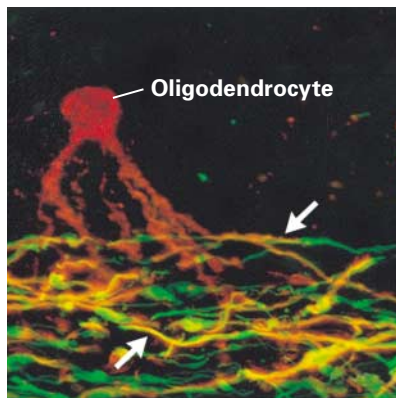
*“Patients with worse clinical outcomes had larger volumes of lesions on MRI at base line and larger increases in lesion volume over time.”*

## **Abnormalities on MRI and Long-Term Disability from Multiple Sclerosis**

Serial T<sub>2</sub>-weighted magnetic resonance imaging (MRI) studies were performed in 71 patients who first presented with optic neuritis or brain-stem or spinal cord syndromes suggestive of multiple sclerosis. After a mean follow-up of 14 years, multiple sclerosis had developed in 88 percent of those in whom the results of the MRI were abnormal at presentation, as compared with 19 percent of those in whom the results of the MRI were normal. The volume of the lesions on MRI correlated with the degree of disability over the course of this longitudinal study.

*Abnormalities on MRI in patients with neurologic syndromes that are the first sign of multiple sclerosis may help in the selection of patients for early disease-modifying therapy.*

**see page 158 (editorial, page 199)**



### Oligodendrocytes in Chronic Lesions of Multiple Sclerosis

Detailed studies were performed on 48 chronic lesions from 10 deceased patients with multiple sclerosis. Most of the lesions contained oligodendrocytes, the cells that produce myelin. The processes of the oligodendrocytes extended along demyelinated axons but had failed to produce myelin. Except in the patients with disease of very long duration, the number of oligodendrocytes appeared adequate.

*This morphologic analysis shows that in multiple sclerosis, most of the chronic lesions contain an adequate number of oligodendrocytes in close association with axons. These findings suggest that the failure of remyelination is due to factors in the microenvironment or in the interactions between the axons and the cells that should be producing new myelin.*

see page 165 (editorial, page 199)

## PERSPECTIVE

### Outcomes of Very Low Birth Weight in Young Adults

Preterm delivery remains the primary public health challenge in obstetrics. Infants who weigh less than 2500 g account for 11 percent of all births in the United States but for more than 90 percent of all neonatal deaths. Very-low-birth-weight infants, weighing between 500 g and 1500 g, account for approximately 1 percent of all live births but more than 60 percent of all neonatal deaths. Forty percent of the very-low-birth-weight children who survive are burdened with long-term sequelae.

The majority of preterm deliveries are spontaneous, caused by premature labor with or without premature rupture of the fetal membranes. About 20 percent of

such deliveries are induced because of the perception that the mother or fetus would be in jeopardy if the pregnancy were to continue. Despite intensive efforts to understand the causes of preterm delivery and to prevent it, the rate has risen over the past two decades. The increase reflects several factors. The rate of multiple births has skyrocketed as infertility treatment has become more common. In addition, increased maternal and fetal surveillance has resulted in more deliveries at earlier gestational ages. Compounding these trends is the fact that we have made no substantial progress toward reducing the rate of preterm delivery that results from premature labor.

#### Methods for Prevention

On the basis of historical risk factors, we are now able to identify women with an increased risk of preterm delivery. Unfortunately, none of the interventions that have been tested among such women — including enhanced prenatal care services, psychosocial support, and nutritional support — have reduced the incidence of preterm

delivery. Many preterm deliveries are induced because of the development of preeclampsia or poor fetal growth (intrauterine growth restriction), and efforts have been made to prevent these complications. However, initial enthusiastic reports of success in small trials of aspirin and calcium supplementation for the prevention of these complications were followed by uniformly disappointing results from large, well-conducted, and adequately powered randomized trials. Other preterm deliveries are precipitated by infection; although limited success has been reported in narrowly targeted high-risk populations, efforts to reduce the rate of preterm delivery by treating infections such as bacterial vaginosis and trichomoniasis have generally been disappointing.

Our ability to stop labor once it has started is also poor. Monitoring women for abnormal uterine contractile activity has very low predictive value for preterm delivery. Once premature labor has been diagnosed, treatment with tocolytic therapy ( $\beta$ -adrenergic agonists and magnesium sulfate) generally pro-

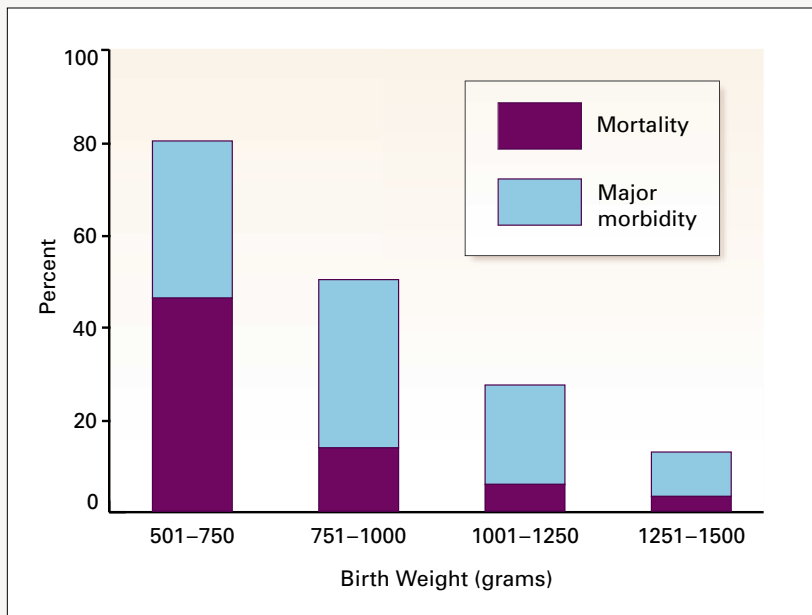


### Clinical Practice: Chronic Urticaria

A 35-year-old woman presents with a three-month history of daily generalized hives. She has also had swelling of her lips and tongue, with associated tightness of the throat. How should she be evaluated and treated?

*This article reviews the approach to chronic urticaria and angioedema. Chronic urticaria consists of hives that persist for more than six weeks. Angioedema occurs in just under half the patients. Various therapies may be beneficial, including histamine-receptor antagonists, leukotriene antagonists, and corticosteroids. The use of cyclosporine in refractory cases is still considered experimental. The article provides practical information about diagnosis and management.*

see page 175



**Figure 1.** Major Morbidity and Mortality in Relation to Birth Weight. Data are from the National Institute of Child Health and Human Development.

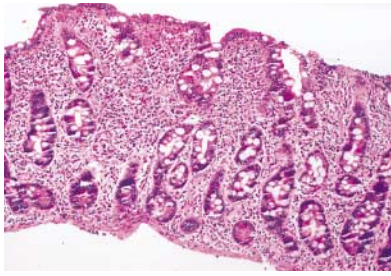
longs pregnancy by no more than 48 to 72 hours. Premature rupture of the fetal membranes usually leads quickly to premature labor and delivery. Prolonged antibiotic therapy may slightly improve perinatal outcomes in some women who do

not deliver promptly. However, undesirable changes in microbial flora and patterns of antibiotic resistance in the newborn nursery may be an unintended consequence that ultimately limits the benefit of this strategy.

Although the results of primary and secondary intervention strategies have been disappointing, some interventions have been effective. Intrapartum antibiotic treatment as prophylaxis against neonatal group B streptococcal infection has effectively reduced the incidence of this potentially devastating complication among women in premature labor. Antenatal treatment with glucocorticoids has reduced the incidence of respiratory distress syndrome and related mortality by about 50 percent among premature infants born at later gestational ages. The willingness of the obstetrician to perform a cesarean delivery because of perceived fetal jeopardy has also been shown to improve perinatal outcomes for infants weighing more than 800 g (those at approximately 25 to 26 weeks of gestation). For infants with lower weight, ironically, the use of cesarean delivery in these circumstances may contribute to an increased rate of survival with handicap.

#### Short- and Long-Term Outcomes

The likelihood that an obstetrician will use any of these interven-



### Current Concepts: Celiac Sprue

Celiac sprue, or gluten-sensitive enteropathy, has a wide spectrum of manifestations and is more common than was previously recognized. New, accurate serologic tests make it easier to diagnose this disease and have led to changes in the strategies for clinical management.

see page 180

*“Medical information is more intimate and more sensitive and therefore merits greater protection.”*

### Personal Privacy in Medical Research

The American people generally support and encourage medical research, but they also place a high priority on the privacy of personal medical information. The Health Insurance Portability and Accountability Act of 1996 imposed new restraints on the use of medical information, with the intent of protecting patients' privacy. A side effect of the act is its application to clinical research. In a Legal Issues in Medicine article, Annas discusses the legal underpinnings and implications of the act, and in a Sounding Board article, Kulynych and Korn argue that the act will make the conduct of clinical research more burdensome and costly.

see pages 201 and 216

tions is clearly influenced by his or her assessment of the ultimate prospects for a successful neonatal outcome. Studies have repeatedly demonstrated that obstetricians routinely underestimate neonatal prospects for survival and survival without handicap. Undoubtedly, this tendency is related in part to the rapid pace of improvement in perinatal outcomes. In 1981, clinicians at a major nursery published a report on their experience with neonatal intensive care under the title “Is intensive care justified for infants weighing less than 801 gm at birth?” The latest data from the neonatal research network of the National Institute of Child Health and Human Development indicate that more than 70 percent of infants weighing between 501 and 1000 g now survive (see Fig. 1). Approximately 9 percent of surviving babies

have severe intracranial hemorrhage, and another 7 percent have periventricular leukomalacia, both of which are strongly associated with the later development of cerebral palsy. Nonetheless, more than half of these very-low-birth-weight babies survive without major neonatal complications. Unfortunately, underestimation by obstetricians of the prospects for success for these very preterm neonates may result in the underuse of effective therapies that could improve perinatal outcomes.

As with all reports of outcomes from the neonatal intensive care unit, the study by Hack et al. reported in this issue of the *Journal* (see pages 149–57) contains both good news and bad news. The bad news is that young adults who were born at very low weights have a higher incidence of neurosensory deficits, a greater burden of illness,

lower IQ scores, and poorer educational achievement than their peers of normal birth weight. The good news is that in the very-low-birth-weight cohort, 51 percent have IQ scores within the normal range, 74 percent have completed high school, and 41 percent are pursuing postsecondary education. Moreover, risk-taking behavior (such as alcohol and illicit-drug use and criminal behavior) is no more common among these young adults than among their normal-birth-weight peers. Obstetricians and pediatricians should use this information to create realistic expectations for outcomes and to plan their treatments accordingly.

MICHAEL F. GREENE, M.D.  
Massachusetts General Hospital  
Boston, MA 02114