# PREMATURITY-INFANT MORTALITY: THE SCOURGE REMAINS

Preterm birth is a common, complex and serious disorder that disproportionately affects African-American families in the United States. In conjunction with low birthweight, prematurity has been the leading cause of neonatal death in African-American newborns for more than a decade and significantly characterizes the continuing racial and ethnic disparities seen in health outcomes today. During the past 20 years, preterm birth rates have increased from 9.5% in 1982 to a rate of 12.3% in 2003, an impressive 30% increase. While the chance of being born premature in 2003 was 1 in 8 for all US infants, the likelihood of being born premature was 1 in 6 for African-American infants.

These factors, in addition to the associated economic cost of providing healthcare resources for vulnerable racial and ethnic populations that are expanding in numbers, has catapulted prematurity and its associated infant mortality to the forefront of public health. Our current challenge is to identify effective interventions through thoughtful social, clinical, and scientific research efforts and expand our approach to achieving improved pregnancy outcomes from a narrow focus on prenatal care to more broadly address the healthcare needs of women well before pregnancy occurs. (*Ethn Dis.* 2006;16[suppl 3]:S3-58–S3-62)

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# INTRODUCTION

The four leading causes of infant death in the United States during 2003 were birth defects, prematurity and low birthweight, sudden infant death syndrome, and maternal pregnancy complications. Of these, prematurity/low birthweight was the second highest cause of infant death after birth defects<sup>1</sup> and is the only cause of infant death that has steadily increased in recent years, from 96.5 deaths per 100,000 live births in 1990<sup>2</sup> to 118.6 deaths per 100,000 live births in 2003.1 Prematurity, defined as birth before 37 completed weeks of gestation, accounted for approximately a half million births in 2003<sup>3</sup> and along with low birthweight, was responsible for 17.3% (n=4849) of all infant deaths in 2003.<sup>3</sup>

# **EPIDEMIOLOGY**

Despite dramatic improvements in other areas of health care, the rate of US preterm births has increased by  $\approx 30\%$  since the early 1980s (Figure 1). In 1982, 9.5% of births were at <37 weeks of gestation, and in 2003 that rate increased to 12.3%.<sup>3</sup> The increase in the rates of multiple births, as a result of assisted reproductive technology techniques and advanced maternal age,<sup>3</sup> has contributed to the current rise seen in preterm birth rates. The *Healthy People 2010* objectives established a goal of 7.6% for preterm births; if this goal is to be reached, much work remains to be done.

Rates of preterm birth/low birthweight also vary substantially by state. Rates are highest in the Southeast (with the exception of Florida), where >13% Diane Ashton, MD, MPH

of live births were preterm in 2003 (compared to a national average of 12.3%). Rates are lowest (<11.6%) in California and the northern United States.<sup>4</sup> The distribution of preterm births follows the racial and ethnic distribution of births for high-risk populations as well as other key socioeconomic factors and distribution patterns seen for other common, complex disorders.

In addition to the tremendous social and emotional costs of preterm birth, it is also associated with substantial economic costs. Average hospital charges for newborn stays without complications were \$1,700; that cost increased to \$77,000 for an infant stay with a principal diagnosis of prematurity/low birthweight.<sup>5</sup> In 2003, the total US hospital costs for prematurity and low birthweight were \$18.1 billion.

# RISK FACTORS FOR PRETERM DELIVERY

The best predictors for preterm delivery are multifetus gestation, a history of preterm delivery, and uterine and/ or cervical abnormalities. Other substantial risk factors include extremes of maternal age, 34- to 36-week gestations (which account for the largest proportion of preterm births), and African-American ethnicity.

### Age

Rates of preterm births increase dramatically at the extremes of maternal age. In 2003, the lowest rate (11.3%) was seen in the 25- to 29-year age group. However, rates increased to >15% in women <18 and  $\geq$ 40 years of age (Figure 2).<sup>4</sup>



Fig 1. Percentage of US births that are preterm: the dashed line represents the *Healthy People 2010* goal of reduction to 7.6% preterm births by 2010

These figures are troubling because the trend in the last two decades has been for women to have children later in life. In 1980, the birth rate for women age 35–39 years was only 19.8 per 100,000 population; by 2003, that figure had climbed to 43.8 births per 100,000 population. For women  $\geq$ 40 years, the numbers are lower but have similarly increased. The 1980 birth rate for women age 40–44 years was 3.9 per 100,000; by 2003, that number had more than doubled to 8.7 per 100,000.<sup>3</sup>

### **Multifetus** Gestation

As noted, gestating twins, triplets, or higher-order multifetal pregnancies dramatically increases the risk for preterm delivery. In 2003, 10.6% of singletons were born prematurely. For twins, this figure was 59.3%. For higher-order gestations (triplets or more), almost all—93.7%—were born before 37 weeks' gestation.<sup>4</sup>

### Duration of Gestation

Perhaps unsurprisingly, most preterm births (71.3%) occur at 34, 35, or 36 weeks. In 2003, 16% of preterm births were at <32 weeks' gestation; 5.1% were born in week 32, 7.7% in week 33, 13% in week 34, 21.2% in week 35, and 37.1% in week 36.<sup>4</sup>

While overall rates of prematurity have increased, rates of very preterm birth (<32 weeks' gestation) have remained stable since 1992 (Fig. 3).<sup>2</sup> This finding is fortunate because very preterm birth is associated with higher rates of illness, death, and long-term sequelae; however, the numbers still fall far short of *Healthy People 2010* goals.

#### Ethnicity

Ethnic minority status is a strong predictor of preterm birth. In 2003, Black women had  $\approx 1.6$  times the rate of preterm birth compared to White women. Native American and Hispanic women also had higher rates, and only Asian/Pacific Islander women had a lower rate of preterm birth (Figure 4).<sup>4</sup>

Similar ethnic disparities exist in infant mortality. In 2002, out of every 1000 live births to Black mothers, 13.9 infants died. The mortality rate per 1000 live births was 8.7 for Native Americans, 5.8 for Whites, 5.6 for Hispanics, and 4.7 for Asians/Pacific Islanders.<sup>6</sup> As shown in Figure 5, the Black/White gap in infant mortality has narrowed slightly since 1990, but the



Fig 2. US preterm births by maternal age, 2003: the dashed line represents the 12.3% of births that were preterm in 2003, across all ages

disparity is still substantial, and both populations are far from *Healthy People* 2010 goals.

Prematurity and low birthweight constitute the cause of infant death with the most substantial ethnic disparity. And while other factors are responsible for a lower proportion of infant deaths, the disparity exists for every cause (Fig. 6). For some causes, such as maternal pregnancy complications and respiratory distress syndrome, the infant mortality rate for Blacks is almost three times that for Whites.<sup>7</sup>

Reasons for the disparities in birth outcomes are often attributed to genetics, but many birth outcomes have no genetic basis. Other hypothesized risks include behavioral, environmental, and socioeconomic factors. Smoking, for example, is hypothesized as an explanation for the disparity, but that relationship appears to be inverse. In 2002, the infant mortality rate for Blacks was more than two times that for Whites, while for Whites the prevalence of cigarette smoking was almost 50% higher.<sup>7</sup> Further, the infant mortality rate for infants of Black nonsmokers was 13.1 per 1000 live births, compared to only 5.3 per 1000 live births for infants of White smokers.<sup>7</sup>

Education and income are also given as potential reasons for the disparity. However, the rate of infant mortality among Black women with a college degree or more education is 9.9 per 1000 live births compared to 6.5 per 1000 live births for White women with a high school education.<sup>7</sup> While rates of preterm birth decrease slightly with education, the overall racial disparity holds. In fact, of women with less than a high school education, Blacks have 1.5 times the risk for preterm birth compared to Whites; when comparing women with more than a high school education, that risk increases slightly to 1.6 times.<sup>6</sup> Nor does income explain the gap-in 1988, Black women earning  $\geq$ \$35,000/year had an infant mortality rate of 16.6 per 1000 live births; for White women



Fig 3. Percentage of US births that are very preterm (<32 weeks' gestation) or preterm (32–37 weeks' gestation), 1992–2003

earning < \$10,000/year, that figure was only 11.2 per 1000 live births.<sup>8</sup>

One hypothesis is the "life-course perspective" proposed by Michael Lu, MD, at the UCLA Schools of Medicine and Public Health, which states that differences in pregnancy outcomes result not only from exposures during pregnancy but from health inequalities experienced by mothers throughout the course of their lives.<sup>9,10</sup> These disparities compound over time and lead to growing gaps in health between Black and White women that ultimately affect fetal health. A version of this hypothesis suggests that altered exposure to stress hormones in utero can cause health disparities later in life, such as susceptibility to infection, impaired inflammatory response, and vascular compromise.<sup>10</sup>

### CONSEQUENCES OF PREMATURITY AND LOW BIRTHWEIGHT

Low birthweight is clearly and directly associated with any number of negative health outcomes. One study found the age-adjusted relative risk for coronary heart disease to be 1.5 for children born at <5 pounds compared to a relative risk of .7 for children born at >10 pounds.<sup>11</sup> Hypertension is also correlated: children born at  $\leq 5.5$ pounds had an average systolic blood pressure of 168 mm Hg compared to 161 mm Hg for children born at >8.5 pounds.<sup>12</sup> Barker et al<sup>13</sup> found that children born at <5.5 lb had 18 times the risk for insulin resistance syndrome when compared to children



Fig 4. Percentage of US births that were preterm by ethnicity, 2003: the dashed line represents the total 2003 rate of preterm births (12.3%)

born at >9.5 pounds, even when adjusting for body mass index.

# PREVENTION AND INTERVENTIONS

No quick fix exists for the problems of prematurity and low birthweight. According to the life-course perspective, disparities in birth outcomes are the consequence of health inequalities experienced during a woman's lifetime. Since negative birth outcomes are associated with poor health later in life and contribute to health disparities, the problem is self-reinforcing. Research must examine differential risk exposures not only during pregnancy but over the life course.<sup>9</sup>

Prevention of prematurity begins with primary prevention. As a component of primary prevention, environmental risks must be identified and managed through preconception and interconception care. Risk-reduction strategies can improve reproductive and overall health. As secondary prevention, preterm delivery should be prevented when possible, and when not possible, tertiary prevention methods should be used to prevent or minimize the complications of prematurity.

Several interventions have been shown to help. Treating folic acid deficiency can reduce the risk for birth defects.<sup>14</sup> Other interventions include encouraging cigarette smokers to quit.<sup>15</sup> Educating women about the signs and symptoms of preterm labor may prompt women to seek early evaluation by their healthcare providers and facilitate early medical intervention when they experience preterm labor. Identifying and treating women who abuse alcohol or other drugs and assessing and intervening in situations of domestic violence prior to pregnancy may also help to decrease women's risk for preterm births and result in improved prenatal outcomes.



Fig 5. Infant mortality rate by maternal race, United States, 1990–2002: the dashed line represents the Healthy People 2010 goal of  $\leq$ 4.5 deaths per 1000 live births

Ongoing research offers some promising directions for preventing prematurity. Two studies of progesterone supplementation in women with a history of preterm delivery have produced encouraging preliminary results. Meis et al<sup>16</sup> showed  $\approx$ 30% decrease in risk for subsequent preterm delivery, and da Fonseca et al<sup>17</sup> showed >50% decrease in risk for subsequent preterm delivery. In addition, a study funded by the Centers for Disease Control and Prevention and the March of Dimes is assessing the role of stress in preterm delivery.

### **CONCLUSIONS**

Ultimately, perhaps the most effective way to improve birth outcomes is to improve overall health, and the best long-term plan to address disparities in birth outcomes is to address disparities in health care. These disparities can only be eliminated by raising public and provider awareness of inequalities in care, expanding insurance coverage, increasing the number and capacity of providers in under-served communities, promoting culturally sensitive services and improving the quality of care.

#### Additional Resources

http://www.cdc.gov/reach2010/ index.htm

CDC program: Reach 2010 - racial and ethnic approaches to community health.

http://raceandhealth.hhs.gov/

DHHS initiative to eliminate racial and ethnic disparities in health.

http://www.omhrc.gov/

DHHS Office of Minority Health home page.

http://bhpr.hrsa.gov/medicine-dentistry/ actpcmd/reports/actpcmdreport.htm

HRSA report on training primary care professionals to eliminate health disparities.



Fig 6. Leading causes of infant death by race, 2002; LBW=low birthweight; SIDS=sudden infant death syndrome; RDS=respiratory distress syndrome

http://www.omhrc.gov/CLAS/

Office of Minority Health - Recommendations for national standards and an outcomes-focused research agenda in cultural competence in health care.

http://www.census.gov/pubinfo/ www/hotlinks.html

U.S. Census Bureau provides racial/ ethnic-specific population data.

http://www.nap.edu/books/ 030908265X/html

Institute of Medicine Report on Unequal Treatment - Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care (March 20, 2002).

http://www.apha.org/NPHW/ solutions/

APHA Health Disparities Community Solution Database. Can search for Health Disparities Projects and Interventions.

http://www.newschool.edu/milano/ Health/cbohealth/disparitiesfin.pdf

Robert Wood Johnson Foundation publication: Addressing Health Disparities In Community Settings: An Analysis of Best Practices in Community-Based Approaches.

http://www.kff.org/whythedifference/ index.htm

Henry J. Kaiser Family Foundation and The Robert Wood Johnson Foundation's initiative to raise physician awareness about disparities in medical care, beginning with cardiac care.

h t t p : / / m c h l i b r a r y . i n f o / KnowledgePaths/kp\_race.html

MCH Library knowledge path on racial and ethnic disparities in health. Provides multiple resources.

http://gucchd.georgetown.edu// nccc/index.html

National Center for Cultural Competence. Provides resources and tools to address health disparities through cultural competence.

http://www.omhrc.gov/summit/ summitoolkit.pdf

Office of Minority Health's community tool kit designed for the national

#### PREMATURITY—INFANT MORTALITY - Ashton

leadership summit on eliminating racial and ethnic disparities in health. Provides data and statistics, information on programs and initiatives, and federal, state and local contact information.

http://www.astho.org/pubs/nabookfull. pdf

ASTHO and NACCHO publication on health department state and local programs addressing ethnic and racial disparities in health.

http://www.cdc.gov/omh/AMH/ factsheets/infant.htm

CDC Office of Minority Health initiative to reduce disparities in infant mortality.

CDC program: Reach 2010 - racial and ethnic approaches to community health.

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