



Published in final edited form as:

*Am J Nurs.* 2009 January ; 109(1): 60–63. doi:10.1097/01.NAJ.0000344041.49768.ec.

## Solving the Puzzle of Prematurity:

### Healthy infancy starts with a healthy woman

**Barbara Louise McFarlin [research assistant professor]**

*Department of Women, Children, and Family Health Science at the University of Illinois at Chicago.*

The birth of a healthy, full-term infant is the hope of all prospective parents. But preterm birth, which carries an increased risk of infant death<sup>1, 2</sup> and often both medical and financial complications,<sup>3, 4</sup> is on the rise. In 2005 more than 500,000 infants in the United States—one in every eight—were born prematurely (before 37 weeks' gestation). That's 12.7% of all U.S. births that year, representing a 20% increase in preterm births since 1990, when 10.6% of U.S. infants were born prematurely.<sup>5</sup> (See Figure 1, page 61.) According to preliminary 2006 data, 18.4% of non-Hispanic black infants, 14.2% of American Indian and Alaska Native infants, and 12.2% of Hispanic infants were born prematurely, compared with 11.7% of non-Hispanic white infants.<sup>6</sup>

A study of the connection between preterm birth and infant mortality examined 27,970 records from 2002 linking U.S. infant death and birth certificates and found that preterm birth was the primary cause of infant death,<sup>7</sup> not the secondary cause (after congenital anomalies) as previously reported.<sup>1</sup> Preterm infants made up 68.6% of all U.S. infants who died in 2005.<sup>8</sup> Of the 4 million infants world-wide who die each year within the first four weeks of life, 1.1 million (28%) die because they're premature.<sup>9</sup>

Recent increases in multiple births have contributed to the rise in the incidence of preterm births, but premature births have also increased among singleton deliveries.<sup>5, 10</sup> The greatest increase in preterm births has occurred in "late-preterm" infants—those between 34 and 36 weeks' gestation.<sup>11</sup> In fact, the gestational age of spontaneous singleton births in the United States is now significantly younger: in 1992 most infants were born at 40 weeks' gestation; most were born at 39 weeks' gestation 10 years later.<sup>12</sup> Medical intervention has been implicated in the shift toward earlier gestational age at birth. In 1992, 29% of births required a cesarean delivery or induction of labor, but by 2005, 30.3% of infants were being delivered by cesarean section, whether medically necessary or elective, and 22.3% of women giving birth had their labor induced, more than twice the 1990 rate of 9.5%.<sup>5</sup> In 2005 late-preterm births accounted for 71.6% of all preterm births in the United States.<sup>5</sup> And late-preterm infants have a mortality rate that's three times that of full-term infants.<sup>13</sup>

Advances in neonatal care have improved preterm infant survival, particularly among extremely low-birth-weight infants.<sup>3</sup> But among infant survivors of preterm birth and extremely low birth weight from 2000 to 2002, 23% suffered a major neurologic disability.<sup>3</sup> A 2000 study by St. John and colleagues estimated that for all neonates born between 1989 and 1992 in the United States, initial postdelivery, in-hospital care alone cost \$10 billion annually.<sup>14</sup> Infants born full-term at 37 weeks' gestation or later were responsible for 42.7% of those costs, and infants born at 32 weeks' gestation or earlier for 11.9%, but the authors noted that the latter percentage was low only because few infants were born so early. A 2005 study in *AJN* showed that mean hospital charges for infants born in 2001 at 26 to 28 weeks' gestation were \$239,749 compared with only \$4,788 for infants born at 37 weeks' gestation or later.<sup>4</sup> Delaying the birth of an infant from less than 29 weeks' gestation to full-term is estimated to save at least \$122,000 per case.<sup>15</sup>

In response to the increased incidence of preterm births in the United States, the March of Dimes has released its first annual Premature Birth Report Card, in which the organization grades each state according to how its rates of preterm births compare to the goals of the Healthy People 2010 initiative. In its first report card issued last November, the nation as a whole received a D; Vermont received the highest grade, a B; and 18 states received an F. The report card is the organization's attempt to raise public awareness about this issue. (For more information, go to [www.marchofdimes.com](http://www.marchofdimes.com).) Although the Healthy People 2010 initiative recommends reducing preterm births to 7.6% of all births,<sup>16</sup> that goal can be achieved only with greater understanding of the many factors involved.

## WHY HAVE PREVENTIVE EFFORTS FAILED?

Even though tocolytics (medications used to stop uterine contractions) have been available for more than 40 years, such “myocentric”<sup>17</sup> strategies haven't reduced the rate of preterm births. Tocolytics can prolong pregnancy for up to 48 hours<sup>18</sup> to allow steroids, used to stimulate fetal lung maturation, to be administered.<sup>19</sup> Clearly, preventive strategies must be started earlier in pregnancy, *before preterm labor begins*.

Both full-term labor and preterm labor involve activation of the decidua (membranes lining the uterus), cervical ripening, and uterine contractions. In full-term labor this process is physiologic; in preterm labor and birth it's pathologic.<sup>20</sup> Romero and colleagues have hypothesized a preterm parturition syndrome that includes the following<sup>20</sup>:

- intrauterine infection or inflammation
- uterine ischemia
- uterine overdistention
- abnormal allograft reaction, when the woman's body tries to reject the fetus as foreign tissue
- allergy
- cervical insufficiency
- hormonal disorders

Future directions for treatment —such as the administration of progesterone to women with a history of premature delivery<sup>20</sup>— will need to focus not only on stopping contractions, but also on treating the pathologic stimuli of preterm labor.

## NEW RESEARCH DIRECTIONS

The research my colleagues and I are conducting at the University of Illinois at Chicago concerns one factor: keeping the cervix closed during pregnancy. Although the uterus and cervix are sometimes seen as one structure, they actually have distinct functions throughout pregnancy and birth. The body (corpus) of the uterus is composed mainly of smooth muscle, which must expand and remain supple to accommodate the growing fetus and then start to contract only at the right time. Meanwhile, the cervix, composed mainly of connective tissue (collagen), must remain strong and closed until labor. It starts to soften early in pregnancy, then ripens without losing its strength, and finally dilates. During the process of cervical ripening, the collagen fibrils become disorganized so that more space is created between them, allowing the cervix to dilate in preparation for labor and birth.

My colleagues and I have developed a new ultrasound method that detects the changes in collagen organization that occur with cervical ripening before the cervix effaces (shortens and

thins) or dilates.<sup>21</sup> Presently, these early changes in the cervix can't be detected noninvasively. We've been conducting this work in an animal model, but we plan to translate it to humans. Noninvasive detection and monitoring of early cervical changes at the microscopic level will lead to a better understanding of cervical ripening.

## WHAT CAN NURSES DO?

### Educate women before they plan a pregnancy

The first prenatal visit is too late to prepare for a healthy pregnancy. And once pregnancy begins, healthy tissues require more than prenatal vitamins. The incidence of neural tube defects in the United States decreased by 25% to 30% after folic acid fortification of grain products was mandated by the Food and Drug Administration in 1998.<sup>22</sup> But more than folic acid is needed for a healthy pregnancy. The third National Health and Nutrition Examination Survey found significantly lower serum levels of vitamins A, C, and E in black and Hispanic participants than in white participants, who had the highest serum levels.<sup>23</sup> These findings suggest that many black and Hispanic women's diets lack the nutrients necessary for healthy tissues, which can be found in fresh fruits and vegetables<sup>23</sup>—foods that aren't always available or affordable in low-income neighborhoods.

To understand the importance of prenatal diet, consider the functions of the uterus and cervix. Collagen is the most abundant protein in the body, and it keeps the fetal membranes and the cervix strong.<sup>24</sup> Vitamin C plays an important role in the formation, strengthening, and stabilization of collagen; it's a water-soluble vitamin that humans can't synthesize, so steady dietary intake is required to maintain necessary amounts in the tissues. Women who smoke have lower serum vitamin C levels.<sup>25</sup> As pregnancy advances, serum levels of vitamin C are higher in the fetus and decline in the mother until the third trimester.<sup>24</sup> An association has been found between premature rupture of the uterine membranes and low maternal serum vitamin C levels.<sup>26</sup>

Also, in in vitro studies, cigarette smoking has been found to increase the sensitivity of the myometrium (muscular wall of the uterus) to oxytocin,<sup>27</sup> thus setting up a contractile state and increasing the risk of preterm birth. We know that black women<sup>28</sup> and women who smoke cigarettes<sup>5</sup> have the highest rates of preterm birth. Nurses can counsel women to stop smoking and to eat foods high in vitamin C in order to prepare their tissues before they attempt to conceive.

Nurses can also advise women to keep a record of their menstrual periods. Many women don't understand that gestational age and therefore due date are calculated from the *first* day of the last normal menstrual period. By being aware of the earliest signs of pregnancy, a woman can take precautions to limit exposure to drugs, alcohol, and toxins that could place the fetus at risk.

Reproductive technologies, such as in vitro fertilization, have contributed to the high preterm birth rates in the United States.<sup>29</sup> In 2005 the incidence of preterm birth among pregnancies conceived through such technologies was 14.9% for singletons, 66.3% for twins, and 97.1% for triplets and higher-order multiples.<sup>30</sup> It's important that families know the risks of having a multiple pregnancy, and nurses can educate women on the risks, benefits, consequences, and safe uses of reproductive technologies. For example, limiting the number of embryos implanted has been effective in reducing the risk of multiple births.<sup>30</sup>

### Normal pregnancy, normal delivery

Women should know that elective cesarean section and induction of labor carry a risk of premature birth, because estimated due dates may be inaccurate. Spontaneous labor is best for

normal, uncomplicated pregnancies. In a “normal” pregnancy, the fetus is part of the process of signaling the onset of labor; labor begins when the fetus is mature and ready to be born. According to Fuchs and Wapner, the American College of Obstetricians and Gynecologists “recommends that elective delivery should not be performed before 39 weeks’ gestation.”<sup>31</sup> Patients, nurses, and physicians must carefully consider the risks and benefits of an elective induction or cesarean.<sup>12, 31, 32</sup>

Often we tell our patients to take care of themselves and follow a healthful diet. The message is much more powerful when we back our advice with data on the consequences. With knowledge of the physiologic and epidemiologic effects of diet and other lifestyle choices, nurses can help women of childbearing age optimize their health—and that of their future children. Until providers better understand the specific pathways leading to preterm labor and birth, we can’t solve the puzzle of prematurity. In the meantime, we can help families sort through the evidence to live healthier lives and choose beneficial interventions.

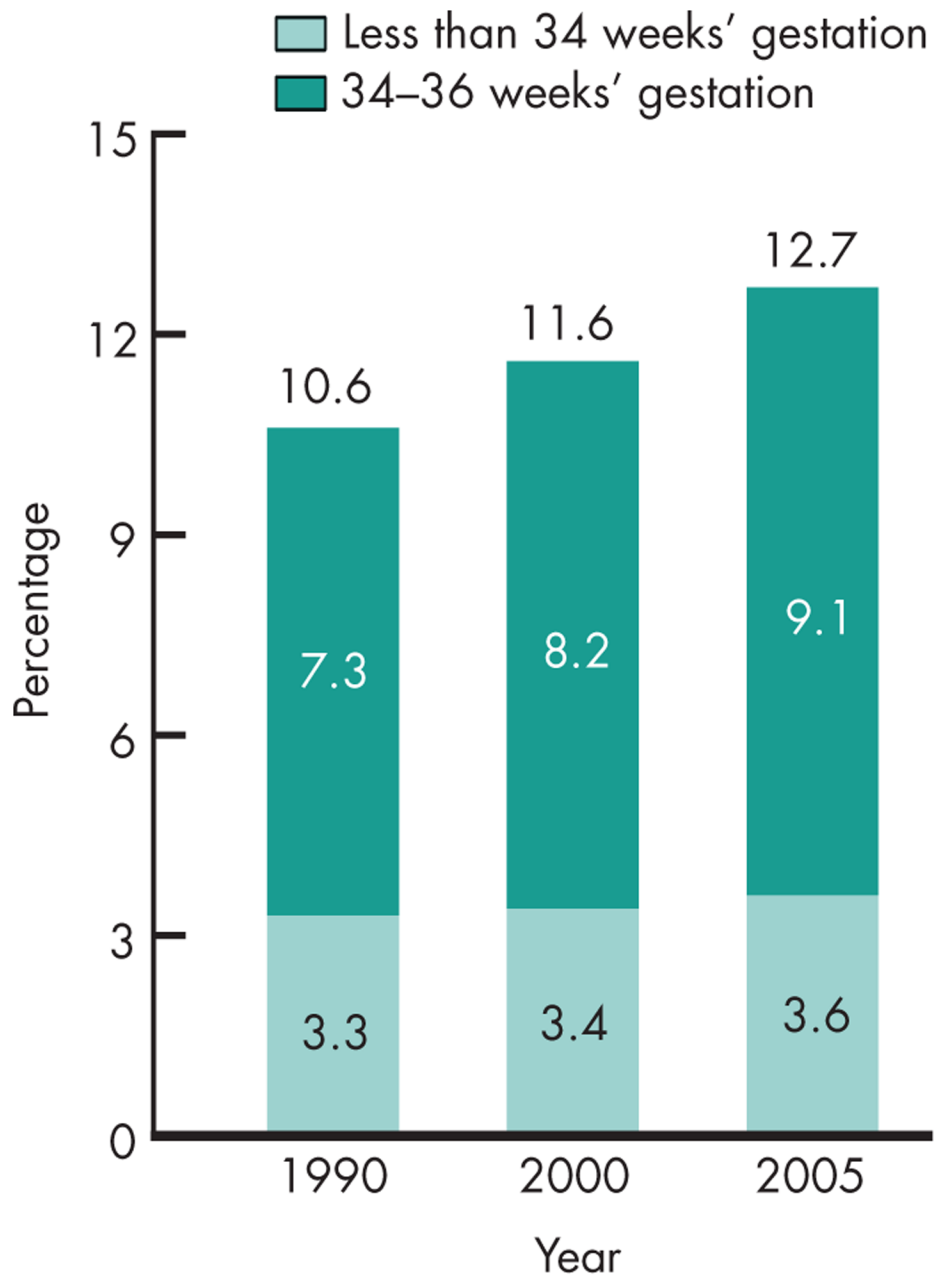
## Acknowledgements

Manuscript preparation was supported by the Center for Reducing Risk in Vulnerable Populations, Grant # P30 NR009014, National Institute of Nursing Research, National Institutes of Health. Reducing Risk is coordinated by Julie Johnson Zerwic, PhD, RN: juljohns@uic.edu.

## REFERENCES

1. Minino AM, et al. Deaths: preliminary data for 2004. *Natl Vital Stat Rep* 2006;54(19):1–49.
2. Swamy GK, et al. Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. *JAMA* 2008;299(12):1429–1436. [PubMed: 18364485]
3. Wilson-Costello D, et al. Improved neurodevelopmental outcomes for extremely low birth weight infants in 2000–2002. *Pediatrics* 2007;119(1):37–45. [PubMed: 17200269]
4. Cuevas KD, et al. The cost of prematurity: hospital charges at birth and frequency of rehospitalizations and acute care visits over the first year of life: a comparison by gestational age and birth weight. *Am J Nurs* 2005;105(7):56–64. [PubMed: 15995395]
5. Martin JA, et al. Births: final data for 2005. *Natl Vital Stat Rep* 2007;56(6):1–103. [PubMed: 18277471]
6. Hamilton BE, et al. Births: preliminary data for 2006. *Natl Vital Stat Rep* 2007;56(7):1–18. [PubMed: 18277471]
7. Callaghan WM, et al. The contribution of preterm birth to infant mortality rates in the United States. *Pediatrics* 2006;118(4):1566–1573. [PubMed: 17015548]
8. MacDorman, MF.; Mathews, TJ. Recent trends in infant mortality in the United States. Hyattsville, MD: National Center for Health Statistics; NCHS Data Brief; 2008 Oct 9. <http://www.cdc.gov/nchs/data/databriefs/db09.pdf>
9. Lawn JE, et al. 4 million neonatal deaths: when? Where? Why? *Lancet* 2005;365(9462):891–900. [PubMed: 15752534]
10. Blondel B, et al. Preterm birth and multiple pregnancy in European countries participating in the PERISTAT project. *BJOG* 2006;113(5):528–535. [PubMed: 16637897]
11. Hamilton BE, et al. Births: preliminary data for 2005. *Natl Vital Stat Rep* 2006;55(11):1–18.
12. Davidoff MJ, et al. Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. *Semin Perinatol* 2006;30(1):8–15. [PubMed: 16549207]
13. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2005 period linked birth/infant death data set. *Natl Vital Stat Rep* 2008;57(2):1–32. [PubMed: 18972721]
14. St. John EB, et al. Cost of neonatal care according to gestational age at birth and survival status. *Am J Obstet Gynecol* 2000;182(1 Pt 1):170–175. [PubMed: 10649175]
15. Phibbs CS, Schmitt SK. Estimates of the cost and length of stay changes that can be attributed to one-week increases in gestational age for premature infants. *Early Hum Dev* 2006;82(2):85–95. [PubMed: 16459031]

16. U.S. Department of Health and Human Services. Healthy People 2010: understanding and improving health. 2nd ed. Washington, DC: U.S. Government Printing Office; 2000. Maternal, infant, and child health. <http://www.healthypeople.gov/document/HTML/Volume2/16MICH.htm>.
17. Clark K, et al. Mifepristone-induced cervical ripening: structural, biomechanical, and molecular events. *Am J Obstet Gynecol* 2006;194(5):1391–1398. [PubMed: 16647925]
18. Simhan HN, Caritis SN. Prevention of preterm delivery. *N Engl J Med* 2007;357(5):477–487. [PubMed: 17671256]
19. Caritis S. Adverse effects of tocolytic therapy. *BJOG* 2005;112:74–78. [PubMed: 15715600]
20. Romero R, et al. The preterm parturition syndrome. *BJOG* 2006;113:17–42. [PubMed: 17206962]
21. McFarlin BL, et al. Quantitative ultrasound assessment of the rat cervix. *J Ultrasound Med* 2006;25(8):1031–1040. [PubMed: 16870896]
22. Pitkin RM. Folate and neural tube defects. *Am J Clin Nutr* 2007;85(1):285S–288S. [PubMed: 17209211]
23. Chen J, et al. Relationship of serum antioxidant vitamins to serum creatinine in the US population. *Am J Kidney Dis* 2002;39(3):460–468. [PubMed: 11877564]
24. Woods JR Jr, et al. Vitamins C and E: missing links in preventing preterm premature rupture of membranes? *Am J Obstet Gynecol* 2001;185(1):5–10. [PubMed: 11483896]
25. Galan P, et al. Serum concentrations of beta-carotene, vitamins C and E, zinc and selenium are influenced by sex, age, diet, smoking status, alcohol consumption and corpulence in a general French adult population. *Eur J Clin Nutr* 2005;59(10):1181–1190. [PubMed: 16034362]
26. Casanueva E, et al. Vitamin C supplementation to prevent premature rupture of the chorioamniotic membranes: a randomized trial. *Am J Clin Nutr* 2005;81(4):859–863. [PubMed: 15817864]
27. Nakamoto T, et al. Cigarette smoke extract enhances oxytocin-induced rhythmic contractions of rat and human preterm myometrium. *Reproduction* 2006;132(2):343–353. [PubMed: 16885542]
28. Orr ST, et al. Race, clinical factors and pre-term birth in a low-income urban setting. *Ethn Dis* 2000;10(3):411–417. [PubMed: 11110358]
29. Wright VC, et al. Assisted reproductive technology surveillance—United States, 2003. *MMWR Surveill Summ* 2006;55(4):1–22. [PubMed: 16723970]
30. Wright VC, et al. Assisted reproductive technology surveillance—United States, 2005. *MMWR Surveill Summ* 2008;57(5):1–23. [PubMed: 18566567]
31. Fuchs K, Wapner R. Elective cesarean section and induction and their impact on late preterm births. *Clin Perinatol* 2006;33(4):793–801. [PubMed: 17148005]
32. McFarlin BL. Elective cesarean birth: issues and ethics of an informed decision. *J Midwifery Womens Health* 2004;49(5):421–429. [PubMed: 15351332]



**Figure 1.**  
Preterm Birth Rates in the United States: 1990, 2000, and 2005  
Adapted from Martin JA, et al. *Natl Vital Stat Rep* 2007; 56(6):1-103.