The rapidly growing number of adult survivors of preterm birth has necessitated and made possible for the first time large-scale investigations of long-term outcomes of preterm birth. Large epidemiologic studies have shown that the long-term sequelae are wide-ranging, including metabolic disorders, cardiovascular and respiratory disease, psychiatric disorders, and increased mortality risk. Clinicians should now recognize preterm birth as a long-term, multidisease risk factor in adults. These research findings contribute to a growing body of evidence of early life programming for chronic disease, which in turn supports a “life course” paradigm for patient care. Family medicine is an ideally conceived discipline for this paradigm because of its unique role in caring for patients across the entire life span. As our understanding of early life influences on long-term health continues to advance, family physicians are ideally positioned to incorporate this knowledge into clinical practice. (J Am Board Fam Med 2015; 28:121–123.)

Keywords: Birth, Chronic Disease, Epidemiology, Longitudinal Studies

Preterm birth (<37 weeks of gestation completed) has become more prevalent over the past four decades and now accounts for nearly 12% of all US births (~500,000 births annually).¹ It is the leading cause of perinatal morbidity and mortality in the United States and other developed countries.¹ Its health outcomes during infancy and early childhood, including respiratory complications and increased mortality, have been widely studied.²,³ Until recently, the available evidence suggested that these health risks wane during and after childhood and thereafter begin to approach similar levels as the general population.²,⁴ Data on longer-term outcomes have been more scarce. However, starting with neonatal care advances in the 1970s and 1980s, early survival among preterm infants improved dramatically, and the first generation to benefit from those advances has now reached young adulthood. The rapidly growing number of adult survivors of preterm birth now necessitates and has made possible, for the first time, large-scale investigations of longer-term outcomes into adulthood.

Large epidemiologic studies subsequently found that preterm birth has wide-ranging sequelae that persist into adulthood,³ including increased risks of diabetes,⁵,⁶ hypertension,⁷,⁸ venous thromboembolism,⁹ asthma,¹⁰ infections,¹¹ thyroid disorders,¹² epilepsy,¹³ and psychiatric disorders.¹⁴ These health sequelae also carry increased mortality risks in adulthood. A large national cohort study in Sweden found that among all people who survived to young adulthood, those who were born preterm had a ~40% increased risk of dying during young adulthood (ages 18–36 years) compared with those who were born at full term (adjusted hazard ratio for all-cause mortality, 1.4; 95% confidence interval, 1.2–1.6).¹⁵,¹⁶ This risk increased by earlier gesta-
tional ages and was ~2-fold among young adults who were born extremely preterm (<28 weeks).\textsuperscript{15} This increased mortality had multiple causes, including diabetes, cardiovascular disease, and respiratory disease, and was not explained by sociodemographic differences or birth defects that are more common with preterm birth. Although longer follow-up into later adulthood is needed, other studies of diabetes and cardiovascular disease have suggested that the risks associated with preterm birth persist at older ages. The continued high prevalence of preterm birth means that the long-term health effects will have a growing clinical and public health impact, reinforcing the need for better prevention of preterm birth.

These research discoveries contribute to a growing body of evidence of the origins of chronic disease in early life. According to the “developmental origins hypothesis,” variations in fetal or postnatal nutrition may permanently alter gene expression, resulting in early life programming for the onset of chronic disease in later life.\textsuperscript{17,18} The underlying mechanisms involve a complex interplay of hormonal and immunologic processes that are still being delineated and may be commonly associated with preterm birth. The cumulative evidence from this research shows that factors in early life can have important long-term health effects throughout the life span.\textsuperscript{3,17,18}

These findings have important implications for clinical practice and family medicine in particular. First, preterm birth should now be recognized as a long-term multidisease risk factor in adults.\textsuperscript{19} Despite the substantial research evidence of long-term sequelae, clinical standards of care do not yet reflect this knowledge. For example, relatively few physicians ascertain birth history in patients beyond childhood. A UK survey of respiratory specialists found that only a small minority (\textless25\%, mostly hospital pediatricians) asked “most respiratory patients” about birth history such as preterm birth, birth weight, or perinatal complications, and a large proportion did not ask patients about birth history at all.\textsuperscript{20} In primary care settings, ascertainment of birth history among adult patients is not well studied but is likely to be even less common, despite the fact that the reported mortality risks associated with preterm birth\textsuperscript{15,6} are higher than those of other factors commonly elicited by medical history, such as physical inactivity, poor nutrition, or heavy alcohol use.\textsuperscript{21,22} Although birth history (unlike lifestyle factors) is not modifiable, better awareness of the associated risks can help motivate healthy behavior change to reduce other common risk factors.

Ascertaining a history of preterm birth among adults is now supported by the substantial evidence of long-term health risks. The medical history of adults, such as that taken during a periodic health evaluation, should encompass birth history including gestational age (or preterm birth [yes/no]), birth weight, and perinatal complications, when available.\textsuperscript{19} International Classification of Diseases (ICD) codes can be used to denote preterm birth (765 in ICD-9, P05 in ICD-10) or small for gestational age (764 in ICD-9, P05 in ICD-10) in the medical record, and further subclassifications can indicate birth weight. Such information can enable physicians and patients to be better aware of the potential health risks (such as metabolic disorders and cardiovascular disease) throughout life, consider more intensive screening for such risks, motivate healthy behavior change to reduce other modifiable risk factors, and better understand the context of chronic diseases when they occur.\textsuperscript{19} Additional research is needed to determine the predictive significance of preterm birth for specific clinical profiles. Nonetheless, birth history can provide important context for understanding a patient’s health.

Systematic tracking of birth history information should be developed in health care systems in which it does not currently exist to facilitate better long-term patient care, as well as additional research on health outcomes. When birth records are unavailable, maternal recall of gestational age (or birth weight) has been reported to be sufficiently accurate for clinical use,\textsuperscript{23} but self-reported birth history among adult patients has not been well studied. The accuracy of self-reported birth information would, however, be expected to improve as public and media awareness of its long-term relevance also improves.

These research findings have further implications for family medicine in particular. The substantial and growing evidence for early life origins of chronic disease supports a “life course” paradigm for patient care. In such a paradigm, health and illness are conceived not primarily in terms of episodic events marked by health care encounters, but within the longitudinal trajectory of an entire life span.\textsuperscript{24} This perspective is consistent with family medicine’s traditional emphasis on a highly contex-
tual approach to patient care, seeking to understand individual health in the context of relationships and function within family and community. However, the life course paradigm also adds to this contextual background a temporal dimension that is critically important for integrating knowledge about health risks that often originate before birth and continue to develop into adulthood. Family medicine is an ideally conceived discipline for this approach because of its unique role in caring for patients across the entire life span. As our understanding of early life influences on long-term health continues to advance, family physicians are ideally positioned to incorporate this new knowledge into clinical practice.

References

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