Review Article

Effect of Low Birth Weight on Women's Health

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ABSTRACT

Purpose: The theory of the developmental origins of health and disease hypothesizes that low birth weight ($\leq$5.5 lb) indicative of poor fetal growth is associated with an increased risk of chronic, noncommunicable disease in later life, including hypertension, type 2 diabetes mellitus, and osteoporosis. Whether women are at greater risk than men is not clear. Experimental studies that mimic the cause of slow fetal growth are being used to examine the underlying mechanisms that link a poor fetal environment with later chronic disease and investigate how sex and age affect programmed risk. Thus, the aims of this review are to summarize the current literature related to the effect of low birth weight on women's health and provide insight into potential mechanisms that program increased risk of chronic disease across the lifespan.

Methods: A search of PubMed was performed with the keywords low birth weight, women's health, female, and sex differences; additional terms included blood pressure, hypertension, renal, cardiovascular, obesity, glucose intolerance, type 2 diabetes, osteoporosis, bone health, reproductive senescence, menopause, and aging.

Findings: The major chronic diseases associated with low birth weight include high blood pressure and cardiovascular disease, impaired glucose homeostasis and type 2 diabetes, impaired bone mass and osteoporosis, and early reproductive aging.

Implications: Low birth weight increases the risk of chronic disease in men and women. Low birth weight is also associated with increased risk of early menopause. Further studies are needed to fully address the effect of sex and age on the developmental programming of adult health and disease in women across their lifespan. (*Clin Ther*. 2014;36:1913–1923)

Key words: blood pressure, early menopause, low birth weight, osteoporosis, type 2 diabetes, women's health.

INTRODUCTION

The theory of the developmental origins of adult health and disease was first proposed by Barker et al, who noted a geographic association between deaths from coronary heart disease and infant mortality.[1] Low birth weight (LBW) indicative of slow growth during fetal life contributes to infant mortality and morbidity. Thus, they proposed that events during fetal life that slow fetal growth may increase cardiovascular (CV) risk in individuals who survive a complicated pregnancy.[2] To further their investigation, Barker et al[3] examined the association between high blood pressure, a risk factor for CV disease, and LBW, a marker of poor fetal growth, and noted an inverse association between birth weight and blood pressure, supporting their original hypothesis. Since these initial observations, numerous epidemiologic studies have investigated the inverse association between birth weight and blood pressure[4] and substantiated the findings of Barker et al.[3] Furthermore, additional studies indicate that birth weight is inversely associated with an increased risk for type 2 diabetes (T2D)[5,6] and osteoporosis[7] (**Figure**); LBW also increases the risk of early menopause (**Figure**).[8–10] Experimental models are providing proof of principle, and use of exper-

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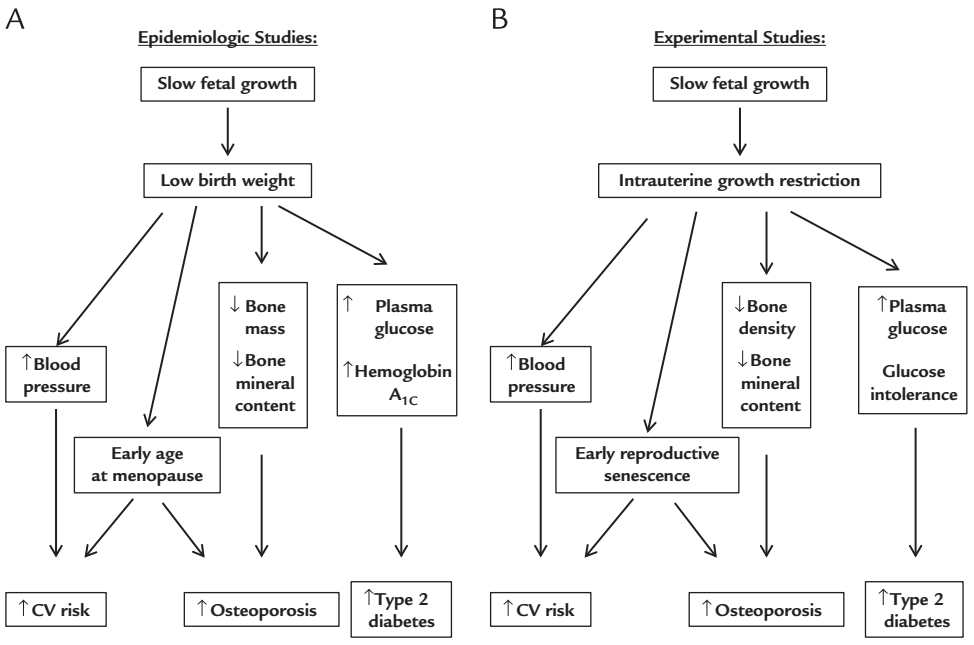

Figure. (A) Epidemiologic studies indicate that slow growth during fetal life programs an increased risk of cardiovascular (CV) disease, Type 2 diabetes, osteoporosis, and earlier age at menopause in low birth weight women. (B) Experimental models that mimic slow fetal growth are providing proof of concept and are also allowing investigation in the mechanisms that link low birth weight with later chronic disease in women.

imental models that mimic the pathophysiologic and environmental conditions that slow fetal growth are being use to investigate the underlying mechanisms that link fetal life and chronic disease in later life (Figure).[11–15] Thus, the goals of this review are to summarize the current literature related to the effect of LBW on women's health and provide insight into potential mechanisms that program increased risk of chronic disease across the lifespan.

METHODS

An electronic search was conducted via PubMed related to the effect of LBW on chronic health in women and in experimental models of developmental programming of CV disease, T2D, and osteoporosis.

RESULTS

LBW and Experimental Models of Developmental Programming

LBW results from a number of different factors, including maternal complications, such as preeclampsia or gestational diabetes, improper nutrition, poor prenatal care, smoking, and age.[16,17] Teenagers and women older than 40 years are at greater risk for having a LBW infant.[18] Race also affects the risk of LBW, with African American woman having a 2-fold increased risk compared with American women of European descent.[18] Maternal smoking also increases the risk of having a LBW infant by 2-fold,[19] and maternal infection and placental abruption are also causative factors.[16] Numerous studies indicate that complications during pregnancy increase the risk of chronic disease in later life of the offspring.[20–24] Preeclampsia is associated with an increased risk of LBW and the development of hypertension and CV complications in the offspring.[22,23] Children born to mothers whose pregnancies were complicated by gestational diabetes also have an increased risk of hypertension, CV disease[20,24] and metabolic disturbances, including T2D.[21] Experimental models that mimic the origin of LBW are being used to explore the underlying mechanisms that link a poor fetal environment with later increased chronic disease. Poor fetal nutrition is associated with hypertension in later life,[25]