Fetal Basis of Childhood and Adult Disease: Role of the Environment

It is recognized that between 2% and 5% of all live-born infants have a structural (birth) defect. Approximately 40% of these defects, although of unknown etiology, are thought to be due to the effects of adverse exposure(s) of the embryo/fetus to intrauterine environmental factors. In addition, 10% of all births occur prematurely, accounting for 75% of early postnatal death and 50% of all long-term handicaps. Exposure to environmental agents during development can result not only in the death of the embryo/fetus, structural (birth) defects, and altered growth but also in functional changes in tissues and organ systems that appear normal but have altered functional potential. A growing body of evidence indicates that such subtle functional defects can lead to childhood–adult morbidity and/or mortality because of the altered fetal programming of tissues, organs, and/or systems during development. Although the mechanism of permanent fetal programming is unknown, evidence suggests that the induced effect can be transgenerational. The advent of the powerful new technologies of genomics, proteomics, and bioinformatics has opened the avenue to detailed explorations of the underlying mechanism(s) of the fetal programming process from initial exposure(s) to the consequent health outcome.

Epidemiologic studies have shown that low birth weight at term and, more specifically, intrauterine growth retardation are associated with insulin resistance, type 2 diabetes mellitus, hypertension, coronary artery disease, and lowered cognitive performance. In these studies, low birth weight at term was due to severe malnutrition during pregnancy. Preliminary data show that functional changes similar to those seen with severe malnutrition may occur with *in utero* exposures to environmental agents. Indeed, exposure to environmental agents *in utero* can alter gene expression, and some of these changes are permanent. Thus, altered genetic programming may have the potential to lead to increased susceptibility to reproductive, cardiovascular, or nervous system diseases.

In February 2002, the National Advisory Environmental Health Sciences Council approved a concept for initiative development in the area of the fetal origin of adult disease. The NIEHS is developing a program that recognizes the growing concern that exposures to environmental factors, either *in utero* alone or in combination with childhood exposures, may predispose individuals to childhood- or adult-onset diseases. Initiatives coming out of this program may be found at http://www.niehs.nih.gov/dert/home.htm. Elucidating the underlying mechanism of such susceptibilities may allow risk reduction via public health intervention/prevention efforts.

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