

BACKGROUND INFORMATION FOR:

**PRIMARY PREVENTION:
AVOIDING NON COMMUNICABLE DISEASES BY REDUCING EARLY LIFE EXPOSURES**

Developmental Origins of Health and Non-Communicable Diseases

The Global Burden of Non-Communicable Diseases (NCDs)

More than 35 million deaths per year—60 percent of all global deaths—are attributed to NCDs, including diabetes, cardiovascular disease, metabolic syndrome, and chronic lung diseases.¹ Approximately 80 percent of these deaths are recorded in low to middle income countries; over the next decade, some of these countries will experience an increase in NCDs that is measurably higher than the anticipated 17 percent average increase worldwide. NCDs create an immense burden, affecting not only individuals and their families, but also economies and health care services. The United Nations General Assembly, in recognition of the impact of NCDs, recently held an international summit to devise strategies to control the risk of NCDs.

Developmental Origins of NCDs



It is now well established that NCDs in adulthood are influenced not only by genetic and adult lifestyle factors but also by environmental factors acting in early life. Indeed, this dramatic increase over the last few decades precludes a genetic origin. This concept, which has been termed the Developmental Origins of Health and Disease (DOHaD) hypothesis, is based on extensive

human epidemiologic data and experimental animal models. These data and models demonstrate that the risk of poor adult health is associated with environmental influences during fetal development and infancy, as well as influences affecting ancestral development.

Phenotypic adaptations in response to environmental pressures during development have potential adaptive value and may confer an immediate survival advantage when the stressor is nutrition-related. For example, David Barker and colleagues observed that a fetus in a malnourished environment could adapt its metabolism to survive until birth, but these adaptations then increased the risk of cardiovascular disease.^{2,3} The impact of fetal adaptations to either over- or under-nutrition is detrimental when the fetal environment differs from the adult environment. This so-called “mismatch” may help to explain why NCD increases are especially pronounced in countries undergoing rapid socioeconomic and cultural transformations.

Critical Environmental Exposures During Early Development

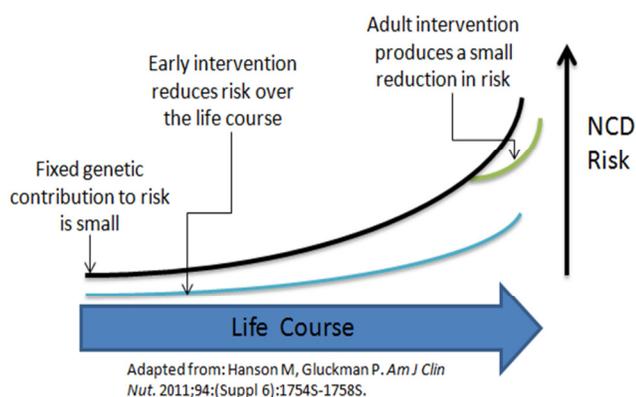
We are living in a rapidly changing environment that is markedly different from past human experience. Modern environments include not only poor nutrition but also energy-dense nutrition, increased caloric intake, widely varying diets, more sedentary lifestyle, altered physical environments, social stress, and new/increased environmental chemical exposures. Even minimal exposure during development to these environmental factors, singly or in combinations, can contribute to an increased risk of disease and general ill health in later life.

Developmental Mechanism of NCDs

The developmental environment induces phenotypes with increased disease risk through an interaction of genetic, physiological, and epigenetic mechanisms. The term “epigenetics” refers to heritable changes in gene expression or cellular phenotype that are not transmitted through changes in the underlying DNA sequence. Epigenetic changes including altered DNA methylation, a modification of histones, and non-coding RNAs have recently been shown to underlie many complex diseases.

Taking a Life Course Perspective for NCD Prevention

Since the risk of NCDs increases with age, strategies to address risk have historically focused on adult interventions, such as lifestyle modification. Although healthier adult behaviors are clearly important, adult intervention alone has been only partially effective in reducing NCDs. Under the DOHaD hypothesis, environmental conditions (nutrition, stress, drugs, infections, and environmental chemical exposures) in fetal development and/or early childhood, or even the environments of an individual's parents and grandparents, establish the trajectory of NCD risk. Consequently, intervention during development holds the greatest promise for reducing the occurrence of NCDs in future generations.



NIEHS Research in the Developmental Origins of Adult Disease

NIEHS is committed to understanding the link between environmental exposures and disease risk across the lifespan. NIEHS has a specific program examining developmental exposures to environmental chemicals (and how they interact with nutrition, drugs, stress, and infections) and the risk of NCDs. NIEHS-supported research has shown that developmental exposure to a wide variety of environmental chemicals can lead to increased risk of NCD later in life in animal models. Indeed, the list includes the major human burden today: early puberty, infertility, asthma, cardiovascular disease, attention-deficit hyperactivity disorder/learning disabilities, increased infections, neurodegenerative diseases, endocrine

cancers, obesity, and diabetes. For example, researchers have found that there are chemicals, now called “obesogens,” that result in weight gain, glucose intolerance, and metabolic syndrome after developmental exposures in animal models—a finding that is beginning to be supported by epidemiologic studies. While the exposures in these animal studies are limited to a short time during development, there is a latency for the effect, as the diseases show up across the lifespan.

The following publications provide additional information on the developmental origins of NCDs

OVERVIEW:

1. Gluckman, P.D., Hanson, M.A., and Mitchell, M.D. *Genome Medicine*. 2010;2:14.
2. Hanson, M., Godfrey, K.M., et al. *Prog Biophys Mol Biol*. 2011;106(1):272–280.
3. Hanson, M.A., and Gluckman, P.D. *Int J Gynecol Obstet*. 2011;115(Suppl 1):S3–S5.
4. Jirtle, R.L., and Skinner, M.K. *Nature Reviews Genetics*. 2007;8:253–262.
5. Perera, F., and Herbstman, J. *Reprod Toxicol*. 2011;31(3):363–373.

CANCER:

6. Stein, R. *J Epidemiol Community Health*. 2012;66(1):8–13.
7. Weidman, J., Dolinoy, D., et al. *Cancer J*. 2007;13(1):9–16.

CARDIOVASCULAR DISEASE:

8. Singhal, A., and Lucas, A. *Lancet*. 2004;363(9421):1642–1645.

METABOLIC DISEASE:

9. Godfrey, K.M., Gluckman, P.D., and Hanson, M.A. *Trends Endocrinol Metab*. 2010;21(4):199–205.

OBESITY:

10. Janesick, A., and Blumberg, B. *Int J Androl*. 2012. In press.

RESPIRATORY DISEASES:

11. Ho, S.M. *J Allergy Clin Immunol*. 2010;126(3):453–465.
12. Martino, D., and Prescott, S. *Chest*. 2011;139(3):640–647.

¹Alwan, A., Geneva, Switzerland: World Health Organization. 2008.

²Barker, D.J., Gluckman, P.D., et al. *Lancet*. 1993;341(8850):938–94.

³Barker, D.J., Winter, P.D., et al. *Lancet*. 1989;ii:577–80.