Genetic Susceptibility and Variability of Human Malformations

According to the *National Vital Statistics Reports* from the National Center for Health Statistics of the Centers for Disease Control and Prevention for 1993–1995, congenital anomalies are the leading cause of death in children under the age of one, the second-leading cause (after unintentional injuries) in ages one through four, and the third-leading cause in ages five through nine. Birth defects to many organ systems require surgical, medical, nutritional, dental, speech, and behavioral interventions over a child's lifetime and impose a substantial economic burden on society. Most congenital malformations have a complex etiology involving both genetic and environmental influences. Genetic processes that control development may go awry during pregnancy, causing a child to be born with a congenital malformation. Factors during pregnancy including nutrition and exposure to pharmaceuticals and environmental toxicants may also interfere with the development of the offspring. Understanding the interaction between genetics and the environment in the development of birth defects is key to preventing them.

The NIEHS recently joined with the National Institute of Child Health and Human Development, the National Institute of Dental and Craniofacial Research, and the U.S. Environmental Protection Agency to develop a new research program focusing on the role of genetic susceptibility in the etiology of birth defects. This initiative was designed to encourage innovative studies that integrate the latest advances in developmental genetics, functional genomics, and high throughput biotechnology with epidemiologic methods in diverse populations. Investigators will explore multiple gene interactions and genetic factors working in concert with environmental factors such as nutrition and exposures to chemicals.

Ten new studies will begin in 2000. These studies will focus on neural tube defects, heart defects, urogenital defects, and other malformations. Investigators will search the genome to identify new polymorphisms that may confer risk. The role of maternal nutrition will be emphasized as scientists use new techniques to understand the precise role of dietary folate and other nutrients in high-risk populations. Exposures to over-the-counter and prescription drugs and to chemicals in the workplace and in the environment will also be explored in concert with genetic factors associated with the metabolism of these agents in the body.

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