

Early-life risk factors for non-Hodgkin lymphoma

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Factors influencing early life non-Hodgkin lymphoma (NHL) incidence include family characteristics, high fetal growth, older maternal age, low birth order, and male gender, according to a study published May 22 in the *Journal of the National Cancer Institute*.

Over the last 50 years, NHL incidence increased substantially, although the overall incidence started to stabilize in the 1990s, at least among adults. But incidence has continued to climb in children, adolescents, and young adults. Perinatal factors have been thought to increase NHL risk, but previous studies of those factors were limited due to small sample sizes, wide variability in adjustment for confounding, and possible selection bias such as socioeconomic circumstances.

In order to determine the cause of NHL incidence in children, adolescents, and young adults, Casey Crump, M.D., Ph.D., of the Department of Medicine at Stanford University and colleagues, conducted a national cohort study of more than 3.5 million people born in Sweden between 1973-2008 who were followed for NHL incidence through 2009. Information on perinatal and family characteristics and NHL diagnoses were attained through linkage of national birth and cancer registries, and Cox proportional hazard models were used to assess association of those characteristics with the risk of NHL.

The researchers found that genetics and in utero conditions contributed to the incidence of NHL in adolescents. The strongest link was a family history of NHL in either a sibling or parent. A high fetal growth rate,



older maternal age, and low birth order also played a key role in incidence rates. Male gender was linked with NHL incidence in children younger than age 15, but not with later onset of NHL. "These findings suggest several heterogeneous mechanisms including possible growth factor pathways in utero, immunologic effects of delayed infectious exposures, as well as other unmeasured environmental and genetic factors," the authors write. "Further elucidation of these risk factors may facilitate the identification of high-risk individuals at young ages and potentially enable earlier detection and treatment."

In an accompanying editorial, William F. Anderson, M.D., M.P.H., and Benjamin Emmanuel, MPH, of the National Cancer Institute at the Division of Cancer Epidemiology and Genetics, write that this is a "well-performed national cohort study," but point out certain limitations, including: the unavailability of host and environmental risk factors such as radiation and environmental contaminants. They also point out the small number of case patients. However, they conclude that the study's, "large-scale and population-based design minimized selection bias and maximized generalizable conclusions for associations between NHL in early life and family history, high fetal growth weight, older maternal age, low birth order, and male sex."

Provided by Journal of the National Cancer Institute

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