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## **Identifying Lymphoma Risks**

Little is known about the causes of lymphoma. A case-control study conducted by Professor Nikolaus Becker and Dr. Alexandra Nieters, Division of Clinical Epidemiology at the Deutsches Krebsforschungszentrum (German Cancer Research Center, DKFZ), is looking closely at possible risk factors. First results of this German lymphoma study suggest immunological factors associated with lifestyle and environment. Too few challenges for the immune system during early childhood may possibly promote not only allergies, but also leukemias and lymphomas.

Lymphoma are divided into two general types: Hodgkin's disease and non-Hodgkin's lymphomas. The latter are among the few cancers whose incidence and mortality have both increased steadily over the past 20 years. Similar to allergies, scientists are discussing a possible effect of early childhood events. According to a notion called hygiene hypothesis, reduced exposure to infectious agents early in life, typical of today's small family environment, may alter immune responsiveness in a direction which favors allergies, lymphomas or diseases. If this hypothesis is right, then growing up "on a farm" should offer a certain protection.

The case-control study compared the data of over 700 patients, collected between 1999 and 2003, suffering from lymphomas (both Hodgkin's and non-Hodgkin's lymphomas) with those of 700 non-affected individuals matched for age, gender and place of residence. In detailed interviews, the investigators posed questions about demographic characteristics, lifestyle factors, medical history and occupational environment. Every study participant was requested to provide a blood sample. A first evaluation of data was restricted to demographic characteristics, exposures to animals, childhood diseases and vaccinations.

Several factors were indeed found to be associated positively or negatively with the risk of lymphoma. Thus, the chance of developing lymphoma was reduced for childhood exposures to animals (such as sheep, goats, rabbits and hares). Close contact to cattle, however, was associated with a higher risk. The positive association in the case of cattle exposure seems to be specific for this species and has been reported in previous studies from other countries.

The risk of lymphoma was also reduced when participants had experienced childhood diseases (e.g. measles or pertussis) or received vaccinations (e.g. against tetanus) during childhood. In the case of tuberculosis vaccinations, however, the risk was elevated. Several previous studies on infections during childhood with respect to the lymphoma risk have yielded contradictory results. However, a reduced risk after measle infection, in particular, has been repeatedly observed. The fact that the disease is also associated with an increased allergy risk might indicate immunological commonalities in disease development.

Other indicators of a rural environment and, thereby, strong microbial exposure remained negative, however. Thus, no association with the intake of raw milk was apparent. Nor was a relation to the number of people living in the household or the number of siblings (as an indicator of frequent infections during early childhood) observed.

Nikolaus Becker interprets the results as follows: "The results are only partly in agreement with the so-called hygiene hypothesis. This can mean that these factors really are not pivotal in the development of lymphomas or that the indicators studied (such as the number of siblings) are inadequate. Nevertheless, environmental conditions during early childhood appear to have a long-lasting effect on the immune system, which can indeed be associated with the development of lymphomas."

A second phase of data evaluation will now analyze further potential risks.

Nikolaus Becker, Evelin Deeg, Alexandra Nieters: Population-based study of lymphoma in Germany: rationale, study design and first results. Leukemia Research 28 (2004), 713-724.

Hodgkin's disease:

Every year, more than 1,800 people in Germany are diagnosed with Hodgkin's disease. The average age at diagnosis is 41 years.

Non-Hodgkin's lymphoma:

Every year, about 6,000 men and 6,500 women in Germany are diagnosed with non-Hodgkin's lymphomas. The average age at diagnosis is 61 or 66 years, respectively.

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).

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Dr. Julia Rautenstrauch
Division of Press and Public Relations
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg

T: +49 6221 42 2854 F: +49 6221 42 2968