

Final Report
Environmental Exposures and Lymphoid Neoplasms (EpiLymph)

Contract number: QLK4-1999-01470

Start project: January 1st 2001, duration: 42 months

Coordinator and partners

The partners in this project include the project coordinator and the case-control recruiting centers.

The partners involved in the contract

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Summary.

Objectives of the project

The objective of the study is to recruit 2500 cases of lymphoid neoplasms and a group of comparable controls, to test specific hypotheses related to the causes of lymphomas in the European population and to investigate the reasons behind the continuing increase in the incidence of this group of neoplasms. More specifically it aims to obtain information on environmental and lifestyle exposures including sources of ultraviolet radiation, use of hair dyes, family history, previous medical history and a detailed job history. The job history information is gathered by a specialized questionnaire. This job history is coded by industrial hygienists using the 5-digit 1968 International Labour Office International Standard Classification of Occupations (ISCO) and the 4-digit 1996 EEC Classification of Economic Activities, revision 1 (NACE, rev. 1) coding systems. Also blood and serum samples are collected from all subjects to examine serum levels of organochlorines. All lymphoma cases are classified under the Revised European-American Lymphoma (REAL) classification. An expert group of pathologists aims to review 20% of all lymphoma cases. This study is conducted in seven EU countries (Czech Republic, Finland, France, Germany, Ireland, Italy and Spain) characterized by wide environmental, social and occupational diversity.

Results

A total of 2480 cases and 2540 controls have been recruited in the study. The controls are matched on sex, gender and country. The controls are hospital-based in France, Italy, Ireland, Finland and population-based in Germany and Spain. Incident cases were histologically or cytologically confirmed lymphoid neoplasms, encompassing 281 multiple myelomas, 1842 non-Hodgkin lymphomas (NHL) and 357 Hodgkin lymphomas (HL). Further classification of NHL revealed 146 T-cell NHL and 1696 B-cell NHL, of which 584 diffuse large B-cell lymphomas (DLCL), 270 follicular lymphomas (FL), and 418 chronic lymphocytic leukemias (CLL).

For organochlorine measurements, 663 serum samples from 325 cases and 338 controls have been analyzed. Samples that were above detection limit were divided in four equal groups over the total study population, and the subjects with the undetectable values were used as the reference, when that was more than 10% of the total study population. When 90% or more of the study subjects had a measurable amount of organochlorine in their plasma, subjects with undetected values were added to the lowest quartile to form the reference group. Subjects classified in the highest quartile of serum level of polychlorinated biphenyl (PCB)-28 (odds ratio [OR]2.6, 95% confidence interval [CI] 1.5-4.5) and PCB-138 (OR 4.5, 95% CI 2.3-9.0), but not total PCBs (OR 1.1, 95% CI 0.7-1.8) showed an increased risk of NHL.

An average of 4 jobs occurred in the working history of study subjects, ranging from 2.4 jobs to 5.0 by country. This revealed in an increased risk for all lymphoma in men for professional nurses (OR 2.1, 95% CI 1.0-4.1) and sale supervisors (OR 2.6,

95%CI 1.0-6.7). In women, lymphoma risk was increased for women that do material handling and related equipment operators, dockers and freight handlers (OR 1.5, 95% CI 1.0-2.2). When using the industry codes, men that work in the manufacture of office machinery and computers industry (OR 4.9, 95% CI 1.1-22) and in education (OR 1.3, 95% CI 1.0-1.6) had an increased lymphoma risk. Women that work in hotels and restaurants had an increased lymphoma risk (OR 1.5, 95%CI 1.1-2.0).

Analyzing exposure to specific occupational agents, which were assessed by local teams of experts, revealed an increased lymphoma risk for subjects that were in contact with meat (OR 1.2, 95% CI 1.0-1.4), and in particular beef (OR 1.3, 95% CI 1.0-1.7). This risk was more pronounced in women than in men. Another occupational exposure that showed an increased risk of lymphoma was the group of inorganic pesticides (OR 1.3, 95% CI 1.0-1.8).

One agent that was of specific interest is ultraviolet (UV) radiation. Occupational exposure to UV radiation was divided by artificial and natural source. The risk of DLCL and FL was decreased when comparing subjects that had ever a job with natural UV radiation with subject that had never had natural UV radiation during work. No association was found between occupational artificial UV radiation exposure and lymphoma risk. There was also information on recreational UV exposure. Being outside in the sun during childhood was associated with a statistically significantly increased risk of NHL. The OR for exposure for more than 6 hours in the sun during childhood compared to subjects with less than 1 hour of exposure was 1.7 (95% CI 1.2-2.4). Frequent use of sunlamps was associated with a reduced risk of NHL (OR 0.7, 95% CI 0.5-0.9). Furthermore, hazel or green eye color as well as blue or grey eye color were associated with an increased risk of HL, (OR 1.7, 95% CI 1.1-2.5, and OR 1.7, 95% CI 1.1-2.7, respectively). Red hair color conferred an increased NHL risk (OR 1.6, 95% CI 1.0-2.7).

Looking at the results for medical history, we found a decreased risk of lymphoma for repeated diarrhoea (OR 0.8, 95% CI 0.7-1.0) and an elevated risk for hepatitis B (OR 2.0, 95% CI 1.3-3.0) and mononucleosis (OR 1.5, 95% CI 1.1-2.2). Among non-infectious diseases, we observed a decreased risk of lymphoma for diabetes (OR=0.7, 95% CI 0.6-0.9), hypertension (OR 0.8, 95% CI 0.7-0.9), asthma (OR 0.7, 95% CI 0.6-0.9), and arthrosis (OR 0.7, 95% CI 0.6-0.8). A significant decrease of lymphoma risk was also observed for history of food allergy (OR 0.7, 95% CI 0.5-0.9). Subjects were asked about their health status at school time in comparison to schoolmates and siblings. The findings indicated an inverse relationship, i.e. a healthier childhood was related to an increased risk of lymphoma.

A total of 916 cases and 945 controls have ever used hair dyes, resulting in an OR of all lymphomas of 1.2 (95% CI 1.0-1.4). No clear dose-response was detected although there was a slight increase in lymphoma risk among those women whose mean number of hair dye applications per year was higher than 11 (OR 1.3, 95% CI 1.0-1.7).

Use of medications was evaluated on the basis of the answers to the lifetime questionnaire, after exclusion of use during the year prior to the enrolment in the study. Chronic use was defined as usage once per week during a year or more. Five different groups of drugs were examined; oral antidiabetic agents, insulin, statins, fibrates and non-steroidal anti inflammatory agents. Regular statin use was associated with a lymphoma risk reduction (OR 0.62, 95% CI 0.5-0.8), and a trend was suggested according to duration of statin use (OR for less than 2 years 1.0, 95%

CI 0.5-2.2; OR for 2-7 years 0.7, 95% CI 0.4-1.1; OR for more than 7 years 0.5, 95% CI 0.2-1.0, p for trend 0.08).

The investigation of tobacco smoking did not reveal any association with the risk of NHL, HL or histological subtypes. Similarly, there was no association between alcohol drinking and the risk of NHL or histological subtypes. However, subjects that ever drunk alcohol showed a decreased HL risk (OR 0.7, 95% CI 0.45-0.9) compared to subjects that never drunk alcohol.

Summary

Testing of the specific hypothesis related to the causes of lymphomas resulted in the identification of the following suspected environmental risk factors: a high serum level of PCB-28 and PCB-138; meat contact, occupational exposure to inorganic pesticides, use of hair dyes and exposure in the sun for more than 6 hours in childhood. In contrast, some medical conditions decreased the lymphoma risk, including diarrhoea, diabetes, hypertension, asthma, arthrosis and food allergy.