EDITORIAL

An Epidemic of Non-Hodgkin's Lymphoma: Comments on Time Trends, Possible Etiologies, and the Role of Pathology

Between 1973 and 1988, the incidence of non-Hodgkin's lymphoma (NHL) increased by 57% in the United States, one of the largest increases that occurred for any cancer (1), and exceeded only by lung cancer in females and malignant melanoma. In contrast, the incidence rates of Hodgkin's disease and leukemia were stable during this time period. In 1992, over 37,000 persons will be diagnosed with NHL and approximately 19,000 persons will die of the disease. Although much attention has been devoted to NHL arising in persons with acquired immunodeficiency syndrome (AIDS), most of the recent increase in NHL cannot be attributed to AIDS. By the mid-1990s, AIDS will be a major cause of NHL, accounting for approximately 10 to 15% of all new cases of NHL with some estimates being as high as 27% (2). But whereas AIDS-associated NHL was not noted until the mid-1980s and has occurred largely in young single males, the current epidemic of NHL began in the early 1970s (or earlier) and has occurred primarily in older persons, both males and females. These findings indicate that factors other than AIDS have been contributing to the overall increase in incidence of NHL.

The annual incidence rate of NHL per 100,000 persons in the United States has risen from 5.9 in 1950 to 9.3 in 1975 and to 13.6 in 1988. The increase has occurred in both males and females, and in whites more than blacks, with both age groups over and under 65 years showing increases of over 50% since 1973. The ihcidence rate in 1988 was 50% higher in white males (17.4) than white females (11.6), and the estimated annual percent increase in incidence for 1984 to 1988 was the highest for white males (4%) and black females (5.7%). The largest increases in incidence have occurred in the elderly (Fig. 1). Incidence rates have been increasing more rapidly in rural areas than urban areas, resulting in decrease in the previous urban to rural ratio of 1.4. Histologically, the largest increases have occurred in the diffuse large cell and immunoblastic categories, and there has been a disproportionate increase in extranodal lymphomas (particularly in brain, skin, and stomach). Similar findings have also been reported in other developed countries. However, for the most part, these changes in incidence are unexplained.

An interdisciplinary meeting was held at the National Cancer Institute in October of 1991 to review and discuss this issue in an attempt to determine research strategies for the future. A consensus was reached that the changes in incidence are largely real, rather than artifactual, and not due to changes in the methods of data collection or evaluation, changes in diagnostic criteria or classification, technological advances in diagnostic procedures, or earlier detection. Recent epidemiologic studies have suggested that environmental factors may play an important role in the etiology of NHL. Occupational studied have found that persons with certain types of jobs have an increased risk of NHL, including farniers, pesticide applicators, grain millers, meat workers, wood and forestry workers, chemists, painters, mechanics, machinists, printers, and workers in the petroleum, rubber, plastics, and synthetics industries. Female users of hair coloring products and persons living in close proximity to certain types of factories also appear to have an increased risk of NHL. Thus, chemical exposures of various types pay be etiologic for NHL. Chemicals that have been linked to the development of NHL include a variety of pesticides (2,4-D, organophosphates, chlorophenols), solvents and organic chemicals (benzene, butadiene, carbon tetrachloride, carbon disulfide), wood preservatives) (creosote, pentachlorophenol), drugs (alkylating agents, immunosuppressives, hydantoins), dusts (wood, cotton),

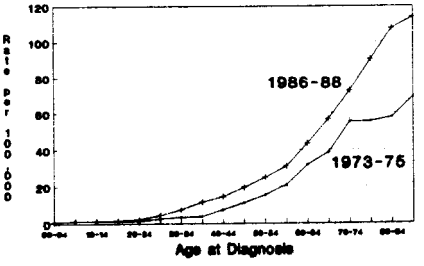

Figure 1. Non-Hodgkin's lymphoma incidence by age for males of all races. Reprinted with permission (1).

and some components in hair dyes. Occupations associated with a higher socioeconomic status, such as professional, technical, and management positions, have also been associated with an increased risk of NHL in some studies. Detailed dietary studies of patients with NHL have not been done, but some studies have found that an increased intake of animal protein is associated with NHL. However, the importance of most of these factors and their role as mediators of genetic change or damage, cancer promotion, or other epigenetic effects, immune suppression, or chronic antigenic stimulation in humans is largely unknown at this time.

Pathologists can play a major role in elucidation of the etiologies and pathogenesis of this epidemic of NHL. Detailed epidemiologic studies of NHL will be performed in the future, and expert pathologists should be an active part of the research team with regard to study design, histologic classification and immunophenotyping of the study cases, and evaluation of the data. Pathologists can also play a major role in the application of molecular biologic techniques in epidemiologic studies, such as the use of polymerase chain reaction technology to detect specific gene rearrangements or the expression of oncogenes in tissue removed from archival tissue blocks. The long-term storage of frozen and paraffin tissue by registries of NHL will play an important role in such studies in the future. Pathologists also have the expertise to pioneer the use of clinical laboratory technology for environmental and biologic monitoring in prospective epidemiologic studies. Pathologists should also conduct basic research addressing the roles of the various factors listed above in the pathogenesis of NHL. Finally, pathologists can serve as a barometers of disease in their communities and service regions, and suggest possible avenues for future study. For example, community pathologists in Nebraska noted an increased incidence and abnormal distribution of NHL in certain areas of the state in the 1970s, thus prompting epidemiologic studies that have pointed toward certain agricultural practices, such as pesticide use, as etiologic factors. Finally, pathologists can play an important role as educators of their fellow physicians and communities with regard to preventative strategies in the future. The epidemic of NHL is already upon us and will accelerate in the years to come. Pathologists should play an important role in turning back the tide of this epidemic in the future.

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REFERENCES

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