THE EPIDEMIOLOGY OF EPSTEIN-BARR VIRUS-ASSOCIATED MALIGNANCIES

P.H. LEVINE

Clinical Epidemiology Branch
National Cancer Institute
Bethesda, Maryland

SUMMARY

Epidemiologic studies of Epstein-Barr Virus (EBV)-associated malignancies continue to demonstrate the interrelationship of multiple etiologic factors, thereby allowing several opportunities for intervention with the disease process. For the two malignancies most closely linked with EBV, Burkitt's lymphoma (BL) and nasopharyngeal carcinoma (NPC), the risk factors are more readily identified in high-incidence areas than in low-incidence areas. The report of an apparent decline in BL incidence in Africa is in contrast with a reported increase in incidence among young white males in the United States. The search for etiologic factors in BL, in addition to EBV and malaria, is currently focusing on retroviruses. For NPC, evidence continues to support the major roles of genetics and salted fish in southern Chinese, but other etiologic factors appear to be important in non-Chinese. In areas of low incidence for BL and NPC, less homogeneous patterns are seen, suggesting the inclusion of unrelated cases. Precise definition of study groups may be aided by new laboratory assays. The further development and utilization of cancer registry data throughout the world will also increase our knowledge of these diseases.

As noted in the many recent reviews concerning the epidemiology of nasopharyngeal carcinoma (NPC)
P. H. Levine et al. (eds.), Epstein-Barr Virus and Associated Diseases
© Martinus Nijhoff Publishing, Boston 1985
(Shanmugaratnam, 1982; Simons and Shanmugaratnam, 1982; Levine and Connelly, 1985) and Burkitt's lymphoma (BL) (Lenoir et al, 1985), the two malignancies most closely linked with the Epstein-Barr virus (EBV), the interrelationship among a number of etiologic co-factors continues to be an area of active investigation. In the context of prevention, knowledge of multiple etiologic factors offers several approaches to intervening in the chain of events leading to these malignancies. The lack of agreement on disease classification has continued to plague epidemiologic studies, however, and it is to this problem that we and others in this symposium (Magrath, this volume; Bale et al, this volume) will give particular attention. The tendency to consider only tumors which have detectable EBV genomes may be inappropriate since it is not technically feasible to assay more than a small percentage of neoplasms. In addition, it appears that as more sensitive assays are developed the percentage of apparently genome-negative cases declines. The appropriate approach to studying the epidemiology of BL and NPC at the present time, therefore, is to define the disease by clinical/pathologic manifestations and to turn to the laboratory only in specific substudies where a high percentage of cases can be evaluated by standardized laboratory assays.

**Burkitt's Lymphoma**

Definition of BL continues to be a challenging and controversial problem. The majority of cases of BL seen in equatorial Africa appear to be biologically different from most cases seen in low-incidence areas, although there is considerable overlap (Klein, 1974; Lenoir et al, 1985; Levine et al, 1982; Magrath, this volume). At the present time, therefore, investigators should base the diagnosis of BL on the histopathologic criteria as defined by the World Health Organization (Berard et al, 1969). Difficulties encountered in making the diagnosis of BL histopathologically, even for experienced hematopathologists, must be addressed in any studies of BL, particularly in non-endemic areas. The rapid growth of this tumor makes prompt and careful fixation of biopsy material mandatory. The opportunity for a firm diagnosis may be hampered by improper processing of the biopsy. A second problem occurs in the nature of the tumor itself; most cases have the typical morphology allowing full agreement among experienced pathologists but some have atypical features that require a consensus diagnosis. The American Burkitt Lymphoma Registry (ABLR) initially