The "Family Study" Approach to Investigating the Role of Genetic Factors in Nasopharyngeal Carcinoma

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SUMMARY

A number of reports strongly indicate the importance of genetics in determining the outcome of EBV infection, the most apparent example being the X-linked recessive lymphoproliferative syndrome. In a cancer such as nasopharyngeal carcinoma (NPC), where genetic factors may modify the effect of environmental influences, emphasis to date has been placed on laboratory studies in defining the genetic component. Since these cancers frequently occur in areas where logistic considerations prevent application of many laboratory assays, particular attention should be given to utilizing epidemiologic techniques which have proven satisfactory for other neoplasms. In this report, we describe the "family study" approach, including the collection, analysis and interpretation of the data. These methods could be utilized in a hospital setting where such patients are seen, thereby improving our knowledge of the relative contributions of genetics and environment in the etiology of these diseases.

INTRODUCTION

Several lines of evidence suggest that there is a genetic component to nasopharyngeal carcinoma (NPC) susceptibility. Demographic studies of the Southern Chinese indicate a factor apparently determined by ethnicity (Menck
and Henderson, 1979). HLA typing of affected and unaffected Singapore Chinese has shown that individuals with the HLA-B type Bw46 have an increased risk for the disease (Simons, et al., 1978), and familial clustering has been reported (Nevo, et al., 1971; Ho, 1972; Williams and de Thé, 1974; Lanier, et al., 1979). However a simple dominant, recessive, or X-linked model for inheritance is probably not consistent with observed data. Some proportion of cases may be attributable entirely to the effect of a single gene, but probably most cases result from the interaction of a single gene or multiple genes with environmental factors, especially the Epstein-Barr virus, which is thought to be etiologically important in some forms of this malignancy (de Thé, 1980).

Carefully planned family studies are one approach to clarifying the genetics of NPC and may be the most practical. In this report we suggest a plan that can be carried out in a clinic or hospital setting where NPC is frequently seen. This approach can be used to provide information on the relative role of genetic and environmental factors in the etiology of this malignancy. This "how to" proposal is divided into several sections according to the following outline:

I. DATA COLLECTION

A. Defining the disease
B. Collection of pedigrees

II. Data Analysis

A. Evaluating the contribution of genetic and environmental factors and determining an inheritance pattern (segregation analysis)
B. Gene mapping/identification of family members at high risk (linkage analysis).

I. DATA COLLECTION

A. Defining the Disease

The first step in family studies must be establishment of diagnostic criteria likely to identify all carriers of the NPC gene (or genes). Those individuals with biopsy proven NPC would clearly be considered to carry the gene;