T CELLS AND THE HEPATITIS OF INFECTIOUS MONONUCLEOSIS

To the Editor: The Epstein–Barr virus (EBV) provides a good example of direct interference by a virus with human B-cell and T-cell function. The main target of this virus is the B lymphocyte. It induces an antigenic alteration in the B cell’s chromosomal protein, producing EBV-specific B-cell antigens. The virus alters B cells into permanently growing cell lines. T-cell function is markedly depressed as measured by in vitro tests, although T-cell numbers are increased. Many investigators believe that during the acute phase of infectious mononucleosis, there is an acute rejection reaction by T lymphocytes against B lymphocytes expressing viral antigens.

It has been suggested that T cells may be the effector cells in the pathogenesis of the hepatitis associated with hepatitis B virus infection, and, since we have shown that T cells predominate markedly in the hepatic infiltrate of patients with hepatitis B, it was of interest to determine whether the lymphocytes infiltrating the liver in a patient with mononucleosis hepatitis were T or B cells. If the EBV is expressed in hepatocytes, a fact about which there is currently no information, an analogy could exist between the pathogenesis of liver injury in hepatitis B and infectious mononucleosis. A five-year-old boy was admitted to the hospital with a seven-week history of fever, weakness and a transient maculopapular rash. The white-cell count was 10,000, with 66 percent lymphocytes including 35 percent atypical lymphocytes. Serum glutamic oxaloacetic transaminase was 1400 Karmen units per 100 ml, and bilirubin 2.2 mg per 100 ml. HB, Ag, anti-HB, toxoplasmas and cytomegalovirus were all negative by virus-specific antibody titers. In mononucleosis, the antibody titers to 1:56, in mononucleosis ox-hemolysin titer to 1:128, and in EBV antibody to 1:40 during a 10-day period. Liver biopsy showed severe acute hepatitis, with a granulomatous reaction. Approximately 1 cm (one third) of the liver-biopsy core was homogenized in a small tissue-grinder (Micro-metric Instrument Company, Cleveland, Ohio), the homogenate layered on Ficoll-Isoaque, and lymphocytes removed by density-gradient centrifugation. T cells were enumerated after E-rosette formation, and B cells were assayed with use of their receptor for Co3. Similar assays were done on peripheral blood obtained at the time of liver biopsy. The results of peripheral blood assays showed 70 per cent T cells (6216 per cubic millimeter) and 22 per cent B cells (1367 per cubic millimeter). The lymphocytes obtained from the liver tissue contained 76 per cent T cells and 5 per cent B cells.

The marked predominance of T cells in this patient’s hepatic infiltrate suggests a possible role for the T cell in the pathogenesis of the hepatic injury during infectious mononucleosis, analogous to this lymphocyte’s alleged role in hepatitis B.

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MELANOMA AFTER EXPOSURE TO PCB'S

To the Editor: We wish to report a possible new carcinogenic hazard. Arochlor 1254, one of the polychlorinated biphenyls (PCB’s), was used by a petrochemical plant in the Northeast in certain processes during a nine-year period ending in the late 1950’s. A preliminary analysis of the incidence of malignant neoplasms among workers who handled this compound, based upon information provided by the medical director of the plant, has been made (this preliminary report would not have been possible without the prompt attention to this potential problem and the research co-operation given by the company).

Of a total of 31 men believed to have been heavily exposed to this agent, two malignant melanomas are known. On the basis of a person-year analysis and with use of the second National Cancer Survey incidence rates as the standard only 0.04 malignant melanomas would be expected. These data are significant at the 0.001 level, given the assumptions of our statistical model. An additional malignant melanoma is also known for one of 41 employees in another group believed to have had less exposure.

Although the data are based on small numbers and the study is still in progress, there are biologic grounds for assuming an association between PCB and malignant melanoma: chloracne dermatitis upon industrial exposure to PCB’s; and aceneform eruptions of Japanese women and pigmentation of the skin of these women and their offspring due to accidental ingestion of rice oil contaminated with a PCB compound (Kanechlor 400).

PCB’s have had widespread industrial use in the manufacture of capacitors and transformers. PCB’s have been used in industry in fluids for hydraulic and heat transfer systems, for retardants, plasticizers, wax additives for investment castings, electrical components, adhesives and food-packaging materials. They are a known pollutant of certain water-supply systems, and their persistence in the environment is of widespread concern.

Further study of this possible carcinogenic association is warranted. Because early detection of malignant melanoma may markedly affect survival rates, surveillance for melanoma among those exposed should be considered. The experience with this small case series demonstrates the value of incidence as well as mortality rates in historical prospective studies designed to search for occupational cancers.

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