Localization of Hepatitis B Antigen in Liver Organ Cultures

Sir,—Hepatitis B antigen has been produced in organ cultures of human embryo liver inoculated with a limited number of known infective sera.1 One serum, referred to as G.C., was obtained from a young healthy volunteer blood donor whose blood recently caused two deaths from hepatitis in transfused recipients. Examination by electron microscopy of ultrathin sections of a liver organ culture inoculated with 0·1 ml of this serum revealed the presence of spherical particles measuring 20-22 nm in diameter in both the cytoplasm and nucleus of hepatocytes (see figure). The particles were detected four and seven days after inoculation of the organ culture. These particles were present in many of the cells, principally at the rim of the culture. Such particles were not found in control organ culture preparations inoculated with normal human serum.

These particles are very similar to the hepatitis B antigen particles described in antigen-positive liver biopsy material by a number of other investigators.2,3 Nowoslawski et al.4 demonstrated by immunofluorescence the presence of hepatitis B antigen in the cytoplasm as well as the nucleus of hepatocytes of six patients with lymphoproliferative disorders; but by electron microscopy only intranuclear particles were found. These particles were identical to those we describe now. Specific fluorescence was demonstrated in many of the hepatocytes by the direct immunofluorescent antibody technique5 in 5-7 μm sections of the same liver organ culture preparation inoculated with serum G.C. No fluorescence was detected in the control organ cultures.—We are, etc.,

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Severely Malformed Children

Sir,—In the tape-recorded discussion on malformed children (5 May, p. 284) Mr. H. B. Eckstein draws attention to a strange anomaly—namely, that untreated babies in first-class centres of baby care have all died “within a month,”’ within eight months,” or similar figures, and yet surgeons are seeing a number of untreated cases for salvage from other hospitals.

The “100% success” rate for the no-treatment policy contrasts with my own personal experience 25 years ago, when no patients received primary surgery and most of them received ordinary home care. The survival of quite a number of the latter makes me wonder whether the ordinary standards of care of baby care are worse than 25 years ago— or is there some other factor in their management?

Another impression which comes over in the discussion—perhaps wrongfully—is the apparent lack of concern for the maximum fulfilment and the happiness of these severely affected children during their life of a few years or so that may be expected. One is particularly concerned about the psychiatrist in the discussion does not even hint at the feelings of contentment and security which at this age are important factors if the child and which come from knowing and being loved by one person (usually the mother).

A severely disabled child needs this personal affection and attachment, perhaps even more than an able-bodied child and if this poses a heavy burden in the mother and the family, I should have thought that the psychiatrist would be the very one to propose support for the family rather than the isolation of the child from the family environment.—I am, etc.,

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Multiple Factors in Leukaemogenesis

Sir,—In their study of children with leukaemia Bross and Natarajan investigated the association between irradiation in utero and some “indicators of susceptibility” (viral infection, bacterial infection, and allergy) shown by the leukaemic child from birth up to a time six months before diagnosis. They and you, in a leading article (21 October, 1972, p. 128), interpreted their results as showing that “the apparently harmful effects of antenatal irradiation are greatly increased in those at risk with congenital anomalies.”

However, these findings may be interpreted as showing that children with leukaemia are simply more prone to viral and bacterial infections and allergies before clinical onset of the disease (or are more likely to report such conditions in a retrospective study) and that irradiation is a red herring in this argument.

If this is correct, the relative risk of irradiation (that is, the ratio of the risk of a child irradiated in utero developing leukaemia to the risk of a child not so irradiated developing leukaemia) would be the same in children reporting such conditions as those who do not.

Bross and Natarajan kindly supplied us with the data on their leukaemic patients and controls tabulated by age at diagnosis, intrauterine radiation history, and susceptibility indicators of infections or allergies (tables I and II). Table III shows the relative risks of irradiation in each age group for those reporting viral or bacterial infections or allergies (R) and those not reporting such diseases (R0). For example, in the first row of table III the relative risk of irradiation in children 1-4 years old reporting viral infections—R = (15 × 43)/(32 × 12) = 1.68. Similarly the relative risk of irradiation

Virus-like particles of hepatitis B antigen in the cytoplasm of a hepatocyte from an inoculated human embryo liver organ culture at day 7 × 100,000.