liver involvement on an isotope liver scan. Postoperatively he was given chemotherapy (cisplatin, vinblastine, and bleomycin). Tumour markers studied before chemotherapy were α-fetoprotein 919 IU/l and β-subunit of human chorionic gonadotropin 1279 IU/l. He was given four courses of chemotherapy and then two further courses of cisplatin, etoposide, and doxorubicin. Doxorubicin was substituted for bleomycin because of a reducing transfer factor on serial lung function testing. After three courses of chemotherapy tumour markers had returned to normal. However, a chest X-ray at the completion of chemotherapy revealed a persistent right paratracheal mass. Surgical removal was not thought possible. Regular chest X-rays and computerised tomographic (CT) scans for the subsequent 5 years showed no change in this mass. Serial tumour marker levels remained normal. 5 years after receiving chemotherapy the patient was found on routine follow-up to have a raised AFP of 171 IU/l with a normal β-hCG. There were no symptoms or abnormal clinical findings. Chest X-ray and CT scan demonstrated enlargement of the previous paratracheal mass. Salvage chemotherapy was started.

A 5-year interval between treatment and relapse in a patient with non-seminomatous germ cell testicular tumour is to our knowledge the longest yet reported. This and a previous report of late relapse 4 years after chemotherapy[4] emphasise the danger of equating cure with 2 years of disease-free survival in this disease. The natural history of residual tumour after chemotherapy is uncertain. Non-progressive residual tumour cannot be assumed to be benign even after 5 years. The treatment of choice for residual tumours after chemotherapy must be surgical removal if possible.[5,6] Radiotherapy should be given if the tumour is inoperable or if surgical removal is incomplete. Prolonged frequent follow-up with serial tumour marker determination seems worthwhile in this small group of patients.

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LIVER DISEASE IN HAEMOPHILIA

SIR,—Dr Hay and colleagues (June 29, p 1495) found histological signs of chronic active hepatitis (CAH) or cirrhosis in 13 (38%) of 34 multitransfused haemophiliacs who were not carriers of hepatitis B virus (HBV) and who had persistently raised serum aminotransferase (ALT) levels. Moreover, since CAH or cirrhosis did develop during follow-up in some patients with an initial diagnosis of chronic persistent hepatitis, Hay et al concluded that non-A, non-B hepatitis in haemophiliacs often progresses to severe liver disease. These findings contrast with the results of a large retrospective study of 155 unselected liver biopsy or necropsy specimens collected from haemophilia centres worldwide.[1] A panel of pathologists found histological features of severe liver disease (CAH or cirrhosis) in only 22% of cases. Hay's findings also contrast with several reports (cited by Aledort et al[1]) indicating that liver disease is a numerically negligible cause of death in haemophiliacs, and with the results of our prospective study of 10 haemophiliacs with non-A, non-B hepatitis,[2] who have now been followed up for 10 years.

Our study includes only patients who had persistently increased ALT levels on three consecutive annual visits (1975–77). The baseline histological investigation in 1977 revealed chronic persistent hepatitis or chronic lobular hepatitis in 6 patients and CAH in 4. A second liver biopsy, done in 1980 and compared blindly with the first by an independent pathologist, showed persistence of chronic lobular or persistent hepatitis or improvement of CAH to chronic persistent hepatitis.[2] The non-progressive course of non-A, non-B chronic hepatitis in our patients is further confirmed by a third liver biopsy in 1983 (unpublished) which shows continuation of chronic persistent or lobular hepatitis in all cases. Thus, since our patients had similar ALT pattern and length of follow-up as those investigated by Hay et al, we think that other factors must be considered to explain the different courses of liver disease. The fact that our patients were considerably younger than those studied by Hay et al (mean age 12 years, range 3–44 *vs* 32 years, range 3–70) suggests that the degree of liver damage might be inversely related to the age at which patients become infected. Children with chronic hepatitis B tend to have high levels of virus replication in the liver without severe liver disease.[3] So, in view of the many epidemiological similarities between hepatitis B and non-A, non-B hepatitis, it is not surprising that children with non-A, non-B infection tend to have less progressive and more "tolerated" liver disease than adults with the same infection.

In contrast to the non-progressive disease found by us in patients with non-A, non-B hepatitis, we have data indicating that liver disease is progressive and severe in haemophiliacs infected with the hepatitis delta virus. Because our sole haemophiliac patient who died of cirrhosis had delta infection[2] we decided in 1980 to do liver biopsies in HBsAg positive haemophiliacs who had raised ALT levels for at least 2 years. Delta antigen and HBcAg were sought by immunoperoxidase techniques with specific antisera in formalin-fixed sections of the liver of 7 haemophiliacs (mean age 12 years, range 6–39) selected on the above criteria. The 3 delta-positive patients had liver cirrhosis or severe CAH, whereas the 4 delta-negative patients had chronic persistent hepatitis[3] or mild CAH. When children are infected with hepatitis delta agent, which injures the liver through non-immune mechanisms, the liver disease is much more progressive than that in age-matched delta-negative HBsAg carriers without.[4] Our data suggest that this is true for haemophiliacs also.

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FREE RADICALS AND ALCOHOLICS

SIR,—Professor Dormandy and his colleagues have made several contributions to *The Lancet* describing increased "free-radical activity" in various clinical conditions. The latest of these (Aug 10, p 291) recorded increased free-radical activity in alcoholics. The measure of free-radical activity used was the serum level of a diene conjugated non-peroxide isomer of linoleic acid (9,11-LA'). However, only circumstantial evidence indicates that measurement of this isomer is an assay of free-radical activity and our work[1] and theoretical considerations suggest the contrary. We have shown that small rodents (rats, mice, guineapigs) with high metabolic rates and, therefore, with presumably greater fluxes of oxygen radicals in their tissues have insignificant levels of serum 9,11-LA' in comparison with man and large ruminants. Furthermore, exposure of rats to high doses of the red-blood-cell peroxidising agent phenylhydrazine and the liver peroxidising agent bromotrichloromethane failed to increase 9,11-LA' levels in plasma phospholipids.[1] Induction of lipid peroxidation in human or rat blood with either ultraviolet irradiation or phenylhydrazine also fails to increase plasma 9,11-LA' levels. These results indicate that 9,11-LA' is not generated during free-radical-induced injury to liver or blood cells.

There are also several theoretical reasons why 9,11-LA' is unlikely to be derived from free-radical activity. For example,