characteristic acid-phosphatase reaction, and a higher incidence of meningeal leukæmia and probably a worse prognosis than in A.L.L. negative for B or T markers.[4-6]

We prefer to use the term "T-A.L.L." rather than "acid-phosphatase-positive A.L.L.", as suggested by Ritter et al., for the following reasons: (1) the positive acid-phosphatase reaction is only relevant in the context of A.L.L., because early myeloid cells may also contain the enzyme (as well as myeloperoxidase) in the primary granules; (2) a positive reaction seems to be a general characteristic of the T-lymphocyte-rich areas of lymph-nodes [7] and of T-lymphocytes after mitogenic stimulation in vitro [8] or in vivo during viral infections; (3) the reaction is positive also in morphologically "mature" (non-blastic) lymphoproliferative disorders such as T-C.L.L.[4] Sezary's syndrome,[9] and T-prolymphocytic leukæmia (see table); and (4) T-A.L.L. denotes more specifically the nature as well as origin of the leukæmic cells.

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PROTHROMBIN-COMPLEX CONCENTRATES IN LIVER DISEASE

SIR,—We wish to clarify some points raised by Dr Blatt and Dr Roberts (July 26, p. 189). Firstly, there was no intention on our part to suggest that the presence of factor VII in the Oxford concentrate we used prevented the induction of disseminated intravascular coagulation (D.I.C.). Our investigation was undertaken largely because we were aware of the possibility of D.I.C. induction by certain prothrombin-complex concentrates. We were gratified that the Oxford concentrate did not produce any clinical or laboratory evidence of intravascular clotting. The presence or absence of factor VII does not therefore appear to determine whether or not concentrate preparations are thrombogenic. Since our article (June 14, p. 1311) appeared a further 8 patients with liver disease have received this concentrate without evidence of intravascular clotting. In the 21 patients we have now studied, the material was derived from three different batches supplied to us by Dr E. Bidwell.

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SIR,—Concern has been expressed by workers in the United States regarding the risks of thromboembolism in patients receiving clotting-factor concentrates.[10,11] It is known that prothrombin activation may occur as an unwanted byproduct in the preparation of factor concentrates [12] and, since the liver normally removes activated procoagulant substances from the circulation, hepatic dysfunction may be associated with delayed clearance from the blood.[13] The risk of induced thromboembolism is thus theoretically greater in patients with liver disease.

We have shown that factor VIII and other clotting factors are significantly reduced in patients with Christmas disease receiving non-heparinised factor-IX concentrates.[14] The therapeutic value of this material for this group of patients is undoubted, and to our knowledge there have been no reported cases of thromboembolism following its use. Nevertheless, we share the concern of Dr Blatt and Dr Roberts [15] "that caution needs to be exerted before this material is broadly used in patients with liver disease".

Two groups [16,17] have reported that infusion of clotting-factor concentrates in patients with liver disease has been unaccompanied by signs of activation of the coagulation system. We believe that the data should be interpreted with some caution. In our experience, induced changes do not always occur immediately after infusion. For example, factor VIII fell significantly in each of the five subjects studied by us.[14] Lowest values were observed within one hour in four subjects, but not until two hours in the fifth. Similar results were observed with other clotting factors.

We believe, therefore, that before factor concentrates are considered safe for patients with liver disease, frequent post-infusion sampling should be undertaken in order to exclude delayed activation of the coagulation system.

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FACTOR-VIII CONCENTRATE AND HEPATITIS

SIR,—In July last year we tested three batches of commercial factor-VIII concentrate for HBsAg using our own solid phase radioimmunoassay test (R.I.A.). We found that all three were HBsAg positive. The Department of Health and Social Security was informed, because these batches had been found HBsAg negative by the manufacturer. One of these three batches was referred to by Dr Craske and his colleagues (Aug. 2, p. 221). A recipient developed hepatitis B. We understand from Dr Craske that the other two batches have also been associated with cases of hepatitis B.

During the past year we have had the opportunity of testing eleven batches of factor-VIII concentrate from two manufacturers. We found five to be HBsAg positive, but because the amount of antigen detected in the positive batches was near to the detection limits of our test we believe that more sensitive testing might have revealed additional positive batches. Both manufacturers had been using counter-migration electrophoresis (C.E.P.) for screening donations and R.I.A. for testing the final product. It appears that the final R.I.A. testing contributed little to safety because of the dilution factor involved in a large-pool product.

If donations were screened by R.I.A. we believe that the final product would be much more likely to be safe. The use of the comparatively insensitive C.E.P. method for screening original donations virtually ensures that some batches will contain hepatitis-B virus in concentrations which are likely to be infectious. The proportion of batches which are contaminated will depend on the type of donor panel used. At least one of the manufacturers

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involved is now changing to R.I.A. screening of original donations—this seems the least that can be done to offset the disadvantage of having to use large pools in the preparation of factor-VIII concentrates.

In spite of the hepatitis-B risk to hæmophiliacs and the much smaller risk to their families and medical attendants, the only contraindication to the use of such concentrates should be when cryoprecipitate can be used as an alternative treatment.

We agree with Dr Craske and his colleagues that the prevention of factor-VIII-induced viral hepatitis in hæmophiliacs by passive immunisation is well worth a trial.

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BLOOD-TRANSFUSION AND PROPHYLAXIS AGAINST HEPATITIS

SIR,—Many data collected during recent years show the complexity of the epidemiology of hepatitis. Knowledge of this field, however, is still sparse. This undoubtedly explains why the role of blood-transfusions in hepatitis has been overemphasised in the past.[1-3]

Accumulating evidence shows that blood-transfusions play only a minor role in the spread of hepatitis.[3,4] Thus, demands for extensive tests, which are more or less indicative of hepatitis infectivity, on transfusion blood only seem to disregard recent knowledge as well as the need for a general prophylaxis for the disease, when similar demands are not applied to other epidemiologically far more important sources of infection.

With regard to hospitals, the role played by patients and staff as well as hospital procedures and instruments in propagating and disseminating hepatitis must be considered.[5,6] We would strongly advise that, for all future hepatitis cases related to hospital surroundings, the same epidemiological methods of investigation are employed as on blood-donors, hospital patients, and hospital staff. These methods of investigation should include clinical, biochemical, histological, serological, and general epidemiological aspects of the propagation and dissemination of the disease.[5]

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NEURAL AND MUSCULAR INVOLVEMENT IN DYSTROPHIA MYOTONICA

SIR,—The inherited disorder of dystrophia myotonica is classified as a muscular dystrophy[1] because electromyography and muscle biopsy demonstrate mainly "myopathic" features. However, it has been suggested that muscle changes in the disease are primarily neurogenic.[2-4] Roses and Appel found abnormal muscle and red blood-cell membranes in patients with dystrophia myotonica, and speculated that "even if nerve involvement is firmly established, the myopathic involvement need not be secondary but may be a separate expression of the disease process".[5] The results of our clinical and electrophysiological study[6] of 22 patients with dystrophia myotonica and 39 matched healthy subjects support this view.

We found unequivocal electrophysiological evidence of peripheral-nerve involvement in the disease. This was indicated by (a) prolongation of the terminal latencies and slowing of the motor conduction of the deep peroneal nerve ($P < 0.001$), (b) delayed conduction of the F wave along the proximal portions of the nerves ($P < 0.01$–0.02), (c) a reduced number of motor axons innervating the extensor digitorum brevis (E.D.B.) muscle ($P < 0.001$), and (d) high-amplitude motor-unit potentials (M.U.P.) and discrete E.M.G. activity on the maximal volitional contraction in one patient with no obvious muscle wasting and weakness.

However, the most interesting finding was that the muscles and nerves seemed to be independently affected by the disease. Thus, whilst in some patients, with little or no obvious muscle wasting, there was clear electrophysiological evidence of peripheral neuropathy, in other patients, with pronounced muscle wasting and weakness, no such evidence could be demonstrated. Cases intermediate between these extremes were more commonly seen. Furthermore, the mean amplitude of the motor-axon potentials (M.A.P.) of the E.D.B. muscle did not differ significantly from that of controls, but in two patients the mean M.A.P. amplitude was smaller than the smallest value for control subjects (as expected in myopathies), and in one patient it was greatly in excess of the highest control value (as expected in neuropathies). Our results are consistent with and can explain the "puzzling clinical finding" of loss or reduction of tendon reflexes in some patients who were only slightly affected and normal tendon reflexes in severely affected cases.[1]

If the muscle changes were secondary to the nerve involvement, one would expect that the electrophysiological findings indicative of peripheral neuropathy would become more evident with increasing severity of the muscle involvement. However, this was not borne out by our results in patients with dystrophia myotonica. Therefore, our data suggest that the muscles and the nerves are independently affected by the pleiotropic gene of the disease and that a combined lesion of the two systems, with a varied and unequal degree of involvement in different patients, is responsible for the muscle changes in dystrophia myotonica.

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