Lymphocyte subset ratios and factor VIII usage in haemophilia

Commentary

J S LILLEYMAN
Children’s Hospital, Sheffield

At the time this paper goes to press the haemophiliac’s world is in turmoil. After the widespread introduction of large pool, freeze dried factor VIII concentrate over 10 years ago, replacement treatment in haemophilia has become relatively simple and efficient. Many patients are now on home treatment and there is little doubt that the quality of life for them has improved enormously as a result. But at what price? First there was (and still is) a high incidence of transmission related chronic hepatitis, but now that problem, serious enough one might think, has been totally eclipsed by the more dramatic prospect of transmission transmitted acquired immune deficiency syndrome (AIDS). AIDS was first described in a haemophiliac from the United States in 1982 and by the close of 1984 had been noted in a further 51. At the time of writing, however, only three—all adults—have developed the disease so far in the United Kingdom. The apparently higher incidence in the United States has been supposed to be due to a higher infection rate in the paid donors giving plasma for American factor VIII. If this is so, any difference is likely to be temporary, as much of the American product has been (and still is) used in the United Kingdom despite a large increase in home produced material. Furthermore at least one batch of UK concentrate has proved to be contaminated.

Almost as worrying as the small numbers who have developed the full blown syndrome is the greater prevalence of what might be described as AIDS related phenomena. Some of these are clinically symptomatic disorders with lymphadenopathy, weight loss, fever, or diarrhoea and are generally referred to as AIDS related complex (ARC) syndromes. Others are merely laboratory abnormalities, and include the lymphopenia, T4 lymphocyte reduction, reversed T4:T8 ratios, and thrombocytopenia described here by Beddall et al. Though not previously shown so clearly, as might be expected these abnormalities seemingly correlate with the degree of exposure to factor VIII concentrate, and over three quarters of the heaviest consumers in this study have been found to have some objective immune disturbance. A worrying statistic indeed as the report deals only with children.

At the same time as studies of non-specific haematological and immunological abnormalities have been carried out, over the last few months it
has also been discovered that a large number of UK haemophiliacs (currently around a third) have antibodies to a putative causative virus of AIDS, human T lymphotropic virus type III, HTLV III. In the United States the figure may be as high as 90%. Not only that, but evidence from retrospective studies would suggest that HTLV III seroconversion is a fairly recent event, at least in Europe where most haemophiliacs were HTLV III antibody negative before 1981. It is less clear whether the non-specific immunological and haematological abnormalities described in this paper are similarly recently acquired, or indeed whether they are AIDS specific. Unlike those based on serology, retrospective studies cannot be done, so the clinical importance of lymphopenia, reversed T4:T8 ratios, and thrombocytopenia must await the passage of time, as the authors point out. So must the significance of HTLV III seropositivity, it has to be stressed, for it is not yet apparent how many patients with it will develop any overt disease.

In the meantime for the treatment of childhood bleeding disorders it would seem prudent to avoid large pool blood products where possible, and to use heat treated factor VIII concentrate (heat is thought to inactivate the AIDS virus) in those haemophiliacs without antibodies to HTLV III. It should also be remembered, however, that severe haemophilia is itself a life threatening problem as well as a potentially crippling disability.

References