Special Report

Report of the ad hoc committee on ALT testing*

Two recent studies1,2 have shown convincingly a relationship between elevated levels of serum alanine aminotransferase (ALT) in blood donors and elevated levels of the same enzyme in the recipients of their blood. Since the elevated levels of ALT in the recipient group have been equated with the diagnosis of transfusion-associated hepatitis, it has been suggested that elimination of donors with elevated aminotransferase levels will lead to a substantial reduction of posttransfusion non-A, non-B hepatitis. While we share the desire of the entire medical community to reduce the incidence of transfusion-associated hepatitis, we believe that currently available evidence does not justify either universal testing of donor blood for ALT or the rejection of donors who have elevated levels. Therefore, at this time we do not advise routine donor testing for ALT as a means of reducing the incidence of non-A, non-B hepatitis. Furthermore, we strongly advise that any testing that is undertaken be done in a way that will increase our information concerning the significance and natural course of elevated levels of ALT in donors and its relationship to the transmission of non-A, non-B hepatitis. Some of our more salient concerns include the following:

1. The measurement of ALT, although a test for one aspect of liver function, is not a specific test for non-A, non-B hepatitis. Between one and one-half and seven per cent of otherwise acceptable donors have elevated levels of ALT for unknown reasons. Exercise, alcohol, and use of many common medications may lead to elevated ALT levels. Males have higher levels than females, and there are differences in normal ranges between various parts of the country. This lack of specificity will result in an intolerably high rate of unnecessary rejections; 70 percent of donors who would have been excluded due to high levels of ALT in one of the studies were not implicated in the transmission of disease. The same study implies that elimination of donors with an elevated ALT might reduce the incidence of non-A, non-B hepatitis by no more than 30 per cent. The test thus fails to detect seven out of ten carriers of non-A, non-B hepatitis viruses while rejecting seven noncarriers for each three it does detect.

2. No study has shown that the actual elimination of donors with elevated levels of ALT will reduce the incidence of elevated levels of ALT posttransfusion, much less hepatitis. Current studies correlate donor levels of ALT with posttransfusion levels in the recipient. It is essential to show that elimination of donors with high levels of ALT will, as postulated, reduce the number of recipients who also have high levels. Such studies must be done before drastic changes in donor qualifications can be justified. A decision to test all donors will preclude these essential studies.

3. The significance of elevations of ALT after transfusion is unknown. Further evaluation of the long-term health implication of both the transient and persistent elevations of ALT seen after transfusion is needed. In one-half of such individuals serum enzyme levels spontaneously revert to normal.2 In those whose transaminase elevations persist beyond one year, the associated liver pathology is mild and the long-term significance is unknown.2 Continued study of this problem is essential before donor requirements are modified.

4. There is insufficient information to establish a cut-off level that will separate acceptable from non-acceptable donors. Cut-off levels based on statistical analysis of a local donor population will require the application of different cut-off levels in different geographic areas. Thus, donors acceptable in one geographic area may not be acceptable in another. On the other hand, a single cut-off level used nationwide will eliminate too many donors in one region and too few in another.

5. The methods for ALT testing need to be evaluated. The proper methods for ALT testing must be evaluated in the setting of a busy blood center. Appropriate quality control and proficiency standards must be established. Precision of results within a laboratory, as well as between laboratories, must be high if cut-off levels are to be meaningful.

6. The effect on the donor base is unknown. The loss of an estimated three per cent of current blood donations may seriously stress the nation's already precarious donor supply. Studies on the effect of

* JOSEPH R. BOYE, M.D. (Chairman), Professor, Laboratory Medicine, Yale University School of Medicine; HAROLD A. OBERMAN, M.D. (Vice Chairman), Professor, Pathology, Director of Laboratories and Blood Bank, University of Michigan Hospital and Medical School; PAUL V. HOLLAND, M.D., Director, Blood Bank, National Institutes of Health; KAMAL G. ISHAT, M.D. (Chairman, Hepatic Pathology Branch, Armed Forces Institute of Pathology; CARL. PECK, M.D., Professor, Clinical Pharmacology, Uniformed Services University of Health Sciences; and JAMES SHOREY, M.D., VA Medical Center/Dallas.
such reduction should be available to ensure that severe blood shortages do not cause more morbidity and mortality than might be prevented by universal testing. The loss of healthy donors and the long-term effect of increased rejections on donor recruitment must be evaluated. For example, will transfusion of blood drawn from those donors recruited to replace those rejected pose a greater hazard to recipients than not universally testing donors? More information is needed about the long- and short-term effects of an elevated ALT in otherwise healthy donors so that they and their physicians can be counseled appropriately. At present, there is insufficient information to make a decision about whether the rejection should be temporary or permanent. Before embarking on widespread testing we must have more information about its impact on the blood banking system and on the donor. As was stated in a recent editorial in Lancet,4

"We should be very much aware of the risks of creating a new and much larger group of donors who are rejected because of a new 'hepatitis' test which does not necessarily signify infectivity, and which may be detecting a form of infection whose natural history we know very little about."

These are the major, but not the only, reasons that have led our Committee, as well as The Ad Hoc Committee on Alanine Aminotransferase Testing and the ARC Blood Services Directors' Council to advise that widespread ALT testing not be recommended at present. Many important questions have been raised and some appropriate studies are underway. Until more data are available, we believe that the best interests of the many patients who depend on a reliable supply of blood are best served by continued investigation rather than a change in donor eligibility standards.

REFERENCES