Donor Transaminase and Recipient Hepatitis

Impact on Blood Transfusion Services

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• To assess the relationship of donor alanine aminotransferase (ALT) level to recipient hepatitis, 283 transfused patients were prospectively followed up after open heart surgery; hepatitis developed in 12.7%, of which 97% was non-A, non-B. The ALT tests on 3,359 donors to these patients indicated that risk of hepatitis was significantly associated with the level of donor ALT; 29% of 52 patients receiving at least 1 unit of blood with an ALT level greater than 53 IU/L had hepatitis develop (20.7 cases per 1,000 units), compared with 9% of 231 recipients of only blood with an ALT level of 53 IU/L or less (7.8 cases per 1,000 units). Calculation of corrected efficacy predicts that, at an exclusion level equivalent to 2.25 SDs above the mean log for normal subjects, ALT testing of donors could prevent 29% of posttransfusion hepatitis at the loss of 1.6% of donor units.

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THE TRANSFUSION Transmitted Virus Study (TTV), a multihospital cooperative study of posttransfusion hepatitis, has recently reported a significant association between donor serum transaminase (ALT, SGPT) and recipient non-A, non-B (NANB) hepatitis.[1] This finding has major implications for blood transfusion services and raises difficult scientific, ethical, and administrative questions. The present study, which was independently conducted, confirms the significant association of an elevated ALT level in donor blood and the development of recipient posttransfusion hepatitis; it suggests that pretransfusion screening of donor blood for ALT level can identify some carriers of the NANB hepatitis virus and possibly prevent approximately 30% of transfusion-related hepatitis.

MATERIALS AND METHODS

The conduct of the study was similar to that reported earlier[1]; 283 consecutive adult patients undergoing open heart surgery and on whom complete donor ALT data were available were entered into the study and followed up for six to nine months.

Blood donors were all volunteers. A serum sample was obtained from each donor at the time of phlebotomy and then sent to a local laboratory for ALT testing. The result of donor ALT testing was generally not known at the time the corresponding blood unit was transfused; moreover, since the implications of the ALT test were still under study, no attempt was made to withhold blood units found to have an elevated ALT level. The recipients of all blood units were followed up from the day of surgery. Weekly or biweekly serum samples were obtained from patients during the first three postoperative months; monthly samples were then obtained for an additional three months and a final sample drawn nine months after surgery. Each sample was tested for ALT, AST (aspartate aminotransferase, SGOT), bilirubin, and hepatitis B surface antigen (HBsAg); (HBsAg was tested by solid-phase radioimmunoassay). In addition, pretransfusion and 3-, 6-, and 9-month posttransfusion samples were tested for antibody to HBsAg (anti-HBs) and pretransfusion, three- and six-month samples were tested for antibody to heptitis B core antigen (anti-HBc). There were 2,952 (88%) donors also tested for anti-HBs. Both anti-HBs and anti-HBc were tested by solid-phase radioimmunoassay.

Criteria for Diagnosis of Posttransfusion Hepatitis

Hepatitis was diagnosed when, between two and 26 weeks after transfusion, a patient with a normal preoperative ALT level demonstrated a rise in the level of ALT to 2.5 times the upper limit of normal (110 IU/L), followed one or more weeks later by an elevation at least two times the upper limit of normal (88 IU/L). Nonviral causes of transaminase elevation, such as drug toxic hepatitis, anesthesia, alcoholism, anoxia, shock, congestive failure, and sepsis, had to be reasonably excluded. When viral hepatitis seemed to be the most likely cause of transaminase abnormalities, serological tests were performed to establish the responsible viral agent. Hepatitis B was diagnosed if the patient showed development of HBsAg during the acute phase of illness, and/or seroconverted for anti-HBs or anti-HBc. Hepatitis A was diagnosed if the development of antibody to the hepatitis A virus (HAV) occurred in temporal relationship to the appearance of transaminase abnormalities. Antibody to HAV was measured by solid-phase radioimmunoassay. Antibody seroconversion to the Epstein-Barr virus (EBV) was sought by immunofluorescence and to the cytomegalovirus (CMV) by indirect hemagglutination. The diagnosis of NANB hepatitis was made only when there was reproducible elevation of the ALT level, as previously described, when nonviral causes of these ALT elevations could be reasonably excluded, and when there was no serological evidence for infection with hepatitis B virus (HBV), HAV, or EBV; five cases with CMV seroconversion were considered as NANB hepatitis for the purpose of this analysis, since the possibility of simultaneous NANB and CMV infection could not be excluded and since a previous study[2] indicated that CMV seroconversions occur with equal frequency among blood recipients who do or do not have development of hepatitis. The statistical associations described in this article were similar whether or not the possible CMV cases were included in the analysis.

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Table 1.—Association of Elevation in ALT Levels in Donors and Hepatitis in Recipients*

Maximum ALT Level Among Donated Units, IU/L (SD)†	Recipients		Donors	
	No. Tested	No. (%) With Hepatitis	No. Tested	No. (%) Associated With Hepatitis in Recipients
≤33 (≤1.5)	162	14 (8.6)	3,179	422 (13.3)
34-53 (>1.5-2.25)	69	7 (10.1)	124	17 (13.7)
54-88 (>2.25-3.0)	38	10 (26.3)	42	11 (26.2)
88 (>3.0)	14	5 (35.7)	14	5 (35.7)
Total				
≤53 (≤2.25)	231	21 (9.1)‡	3,303	439 (13.3)§
>53 (>2.25)	52	15 (28.8)‡	56	16 (28.6)§

*ALT indicates transaminase.
†At least one donor with ALT level in that range; no donor with ALT greater than indicated limit.
‡χ^2=14.9; P<.001.
§χ^2=9.7; P<.01.

Table 2.—Relationship of Donor ALT Level and Transfusion Volume to Recipient Hepatitis*

Maximum Donor ALT Level, IU/L (SD)	No. of Recipients	Average No. of Units Transfused	Recipient Hepatitis	
			No. (%)	No. of Cases per 1,000 Units
≤33 (≤1.5)	162	11.2	14 (8.6)	7.7[A]
34-53 (>1.5≤2.25)	69	12.9	7 (10.1)	7.9[B]
≥54 (≥2.25)	52	14	15 (28.8)	20.7[C]

*ALT indicates transaminase; B vs A, not significant; C vs A or B, P<.001.

Transaminase Testing

Tests for ALT in donor serums were performed by a commercial laboratory, using a kinetic assay on a biochromatic analyzer. A frequency distribution was calculated for 499 consecutive donors in this study and the geometric mean, mean log (base 10), and SD determined. The geometric mean was 12.0 IU/L, the mean log 1.08, and the SD of the mean log, 0.29. The antilog of the mean log plus 2 SDs was 44 IU/L; seven donors (1.4%) exceeded this level. The range of ALT for all 3,359 donors was 1 to 195 IU/L.

Recipient serum samples were tested in the Clinical Chemistry Laboratory, National Institutes of Health (NIH), in a three-point kinetic assay employing a sequential computer-controlled biochemical analyzer. The geometric mean for this assay was 14.6 IU/L, the mean log 1.16, and the SD of the mean log, 0.65. Four of 206 normal control subjects (1.9%) exceeded an ALT of 44 IU/L, and this level was taken as the upper limit of normal for the laboratory.

So the results could be applied to other laboratories, donor transaminase limits in this study are stated in terms of SD from the mean log. The mean log and SD were used because ALT values were found to follow a log normal rather than normal distribution. Equivalent ALT values in international units per liter correspond to the antilog of each log value. The following ALT donor ranges (given as deviations from the mean log value) were examined in this study: ≤1.5 SD (≤33 IU/L); >1.5-2.0 SD (34-44 IU/L); >2.0-2.25 SD (45-53 IU/L); >2.25-2.5 SD (54-63 IU/L); >2.5-3.0 SD (64-88 IU/L); and >3.0 SD (≥89 IU/L).

Statistical Methods

Unless otherwise stated, statistical analyses were based on comparisons in contingency tables and results expressed as χ^2 and its P value.

RESULTS

Relationship of Magnitude of Donor ALT Level to Recipient Hepatitis

Of the 283 recipients in this study, 36 (12.7%) had development of hepatitis. Of the 36 hepatitis cases, 35 (97%) were classified as NANB. Table 1 depicts the risk of recipient hepatitis according to the maximum ALT level of the donated units. The majority of patients (162) received blood with an ALT level of 33 IU/L or less. Of these recipients, 14 (8.6%) had hepatitis develop. Hepatitis incidence did not change appreciably (10.1%) among 69 recipients of blood, in which at least one donor had an ALT level between 34 and 53 IU/L. There was, however, a sharp increase in hepatitis incidence among recipients of blood, in which at least one donor had an ALT level between 54 and 88 IU/L (26.3%), and the incidence increased still further (35.7%) when there was a donor with an ALT level greater than 88 IU/L. The incidence of hepatitis among recipients of blood in which all donor ALT levels were 53 IU/L or less was approximately one third that among recipients of at least 1 unit of blood with an ALT level greater than 53 IU/L (P<.001).

Table 1 also shows the relative frequency of donors associated with a case of hepatitis according to ALT level. Of 3,179 persons with an ALT level of 33 IU/L or less, 422 (13%) donated a unit of blood to a patient who subsequently had hepatitis develop. As the level of donor ALT increased, the frequency with which recipients of that blood had hepatitis develop also increased; donors with an ALT level greater than 53 IU/L were significantly more likely to be involved in a case of posttransfusion hepatitis than donors with an ALT level of 53 IU/L or less (P<.01).

Relationship of Posttransfusion Hepatitis to Transfusion Volume

Since all patients received multiple units of blood, the volume of blood administered introduces a variable that must be distinguished from the effect of donor ALT. Table 2 therefore examines transfusion volume in relation to donor ALT level. Patients who received blood with increasingly higher ALT levels were, on the average, transfused with increasingly larger volumes of blood. To equalize the effect of transfusion volume in each range of donor transaminase, the data are expressed as hepatitis cases per 1,000 units transfused. When transfusion volume was maintained constant in this manner, the number of hepatitis cases per 1,000 units transfused increased from 7.8 to 20.7 for those receiving blood with ALT levels lower and higher than 53 IU/L, respectively (P<.001).

Table 3 indicates that hepatitis incidence increased stepwise as the range of the number of units transfused increased from 1 to 6 up to 10 to 12. Thereafter, the incidence of hepatitis reached a plateau despite increasing transfusion volume. Although the risk of hepatitis did not increase significantly at any of the higher transfusion volumes, the trend suggested that transfusion volume might be a confounding variable in the interpretation of the effect of an elevated ALT level. To evaluate the variable of transfusion number fur-

Table 3.—Impact of Donor ALT Levels at Various Transfusion Volumes*

No. of Transfusions	No. of Recipients	No. of Cases of Recipient Hepatitis (%)
1-6		
ALT ≤53	46	2(4.4)
ALT >53	5	1(20.0)
Total	51	3(5.9)
7-9		
ALT ≤53	44	4(9.1)
ALT >53	5	2(40.0)
Total	49	6(12.2)
10-12		
ALT ≤53	42	4(9.5)
ALT >53	10	5(50.0)
Total	52	9(17.3)
13-15		
ALT ≤53	57	8(14.0)
ALT >53	13	2(15.4)
Total	70	10(14.3)
>15		
ALT ≤53	42	3(7.1)
ALT >53	19	5(26.3)
Total	61	8(13.1)

*ALT indicates transaminase; ALT levels measured in international units per liter; weighted mean difference (see text)=14% ($P<.001$).

Table 4.—Impact of Donor ALT Testing at Various Exclusion Levels*

Exclusion level	Mean Log+Indicated SD				
ALT Equivalent, IU/L	1.5 >33	2.0 >45	2.25 >53	2.5 >63	3.0 >88
χ^2†	5.68	7.85	14.9	4.07	7.01
P Value†	<.02	<.01	<.001	<.05	<.01
Crude efficacy‡	61	44	42	22	14
Corrected efficacy§	32	26	29	12	9
% Blood units excluded	5.3	2.6	1.6	1.0	0.4

*ALT indicates transaminase.

†Significance of association between donor ALT and recipient hepatitis at indicated exclusion level.

‡Maximum prevention based on assumption that unit with elevated ALT level was cause of hepatitis.

§Corrected for hepatitis caused by donors with normal ALT level (see text).

ther, the effect of receiving blood with an ALT level higher or lower than 53 IU/L was examined at each transfusion volume (Table 3). Among patients receiving 1 to 6, 7 to 9, or 10 to 12 units of blood, the incidence of hepatitis was strikingly higher if they received at least 1 unit of blood with an ALT level greater than 53 IU/L. Because of relatively small numbers at each ALT level, a weighted mean difference was calculated.[3] This method uses all the frequency information while preserving the difference in each subset. The weighted mean difference was found to be 14% ($P<.001$), indicating that when transfusion volume is maintained constant and, hence, removed as a variable, there is a highly significant association between donor ALT and recipient hepatitis.

Recipient Susceptibility to Infection

Analysis of demographic and serological characteristics of recipients indicated that patients who had received blood with or without an elevated ALT level did not differ significantly in their sex, age, race, history of hepatitis, history of blood transfusion, or type of cardiac surgery. They did, however, differ significantly in regard to past exposure to the HBV, as assessed by the presence of anti-HBs. Patients who received blood with an elevated ALT level had significantly less evidence of past exposure to HBV ($\chi^2=4.5$, $P<.05$). To distinguish the relative contributions of donor ALT level and recipient susceptibility, as implied by the absence of anti-HBs, the influence of elevated donor ALT level was examined in the 250 patients who did not have anti-HBs in their pretransfusion sample; of these, 199 received only donor blood with an ALT level of 53 IU/L or less. The incidence of hepatitis among the latter was 8.0%; in contrast, 51 patients without pretransfusion anti-HBs who received at least 1 unit of blood with a donor ALT level greater than 53 IU/L had a hepatitis incidence of 27%. The difference in these groups was significant ($P<.001$) and indicates that the level of donor ALT is an important determinant of recipient hepatitis when all recipients have similar susceptibility as judged by the absence of anti-HBs. The data could not be meaningfully analyzed for patients who had anti-HBs before transfusion, since only one of the 32 patients in this group received a unit of blood with an elevated ALT level.

Relationship of Donor ALT to Donor HBV Markers

Of 2,826 donors with an ALT level of 33 IU/L or less, 4.6% had anti-HBs, compared with 15.1% of 86 donors with ALT levels of 34 to 53 IU/L and 10% of 40 donors with ALT levels greater than 53. In composite, donors with an ALT level greater than 33 IU/L (1.5 SD) were significantly more likely to have anti-HBs than donors with an ALT value below this level ($\chi^2=18.6$, $P<.001$), indicating a higher frequency of past HBV exposure in the group with a higher ALT level.

Impact of Donor ALT Testing at Various Exclusion Levels

Table 4 shows the significance of the association between donor ALT and recipient hepatitis at specific ALT exclusion levels and also the percent of hepatitis that might be prevented and the number of donor units that would be sacrificed. Hepatitis prevention is expressed in two ways: (1) crude efficacy based on the assumption that in each hepatitis case where a donor had an elevated ALT level, exclusion of that donor would have prevented the hepatitis; and (2) corrected efficacy in which hepatitis incidence (I) is first calculated in those receiving only normal ALT blood. The number (N) of patients receiving blood with elevated ALT value is then multiplied by I; this establishes the number of cases that would have occurred if only blood with a normal ALT level had been transfused. This product (I×N) is subtracted from the observed number of cases in the group with elevated ALT levels (A) to estimate the number of cases presumably related to the unit with an increased ALT value. Dividing by the total number of observed cases (T) expresses the proportion of cases that might have been prevented by ALT testing: E (corrected efficacy)=100×[A−(I×N)]/T.

Table 4 indicates that as the exclusion level is increased from 1.5 to 2.25 SDs above the mean log, χ^2 increases from 5.68 to 14.9, and that beyond 2.25 SDs, the χ^2 begins to diminish. Thus, the most significant association between donor ALT and recipient hepatitis is achieved at an ALT exclusion level of 2.25 SDs, which in our laboratory was equivalent to an ALT level of 53 IU/L.

Table 5.—Frequency Distribution of ALT Values for 791 Consecutive NIH Donors*

SD	ALT Range, IU/L	No. of Donors With ALT In Range	% In Range
<2.25	0-10	184	23.3
	11-20	400	50.5
	21-30	143	18.1
	31-40	36	4.6
	41-50	17	2.1
Subtotal		780	98.6
>2.25	51-60	6	0.8
	61-70	3	0.4
	>70	2†	0.2
Subtotal		11	1.4

*ALT indicates transaminase; NIH, National Institutes of Health.
†71 and 134.

Table 4 also indicates that although crude efficacy seems distinctly better at low ALT exclusion levels, this is not true for corrected efficacy; there is no meaningful change in corrected efficacy between exclusion levels of 1.5 and 2.25 SDs. Above 2.25 SDs, corrected efficacy markedly diminishes. The number of donor units sacrificed diminishes greatly as one increases the exclusion level from 1.5 to 2.25 SDs.

Application of Donor Exclusion Rule to Other Laboratories

Since completion of the present study, ALT determinations on donor blood have been performed by the Hepatitis Testing Laboratory of the Clinical Center Blood Bank, NIH, rather than at an outside laboratory. This provided an opportunity to see whether the exclusion level chosen on the basis of the data collected in the prospective study could be applied to other laboratories. Using the solid-phase radioimmunoassay method, 791 consecutive NIH donors were tested and a new mean log, SD, and frequency distribution for ALT levels determined (Table 5). The 791 volunteer donors were bled during a single eight-week interval so that no donor was included twice. The vast majority of donors (92%) had ALT values below 30 IU/L, and 98.6% had ALT values below 2.25 SDs from the mean log. This frequency distribution would thus predict a loss of 1.4% of an all-volunteer donor population using an ALT exclusion level of 2.25 SDs. This percent of donors lost agrees closely with the corresponding percent of blood units lost (1.6) previously presented.

COMMENT

Since the sine qua non for the diagnosis of viral hepatitis in transfusion recipients is elevation of serum ALT or AST levels, and since these elevations tend to persist in patients in whom chronic hepatitis develops, it is not unreasonable to assume that some asymptomatic donors who carry a hepatitis virus might also have an abnormally high level of serum transaminase. This concept has been previously investigated,[4] but either because of the simultaneous use of commercial or HBsAg-positive donors or both, or because of insufficient numbers of recipients, incomplete follow-up, or low incidence of hepatitis, none of these studies provided compelling evidence to justify the adoption of routine donor ALT screening.

The most extensive study of the relationship of donor transaminase to recipient hepatitis was conducted by the TTV,[1] a large, prospective study involving four geographically distinct transfusion centers. Composed of more than 1,200 recipients and 4,700 transfused blood units, the TTV study showed that (1) the higher the level of donor ALT, the more likely the donor was to be associated with a case of NANB hepatitis; the relative frequency of association increased progressively from 3.4% in donors with an ALT value of 1 to 14 IU/L to 48.9% in donors with an ALT level greater than 40 IU/L ($P<.01$); (2) the hepatitis attack rate among recipients varied according to the highest donor ALT unit received, ranging from an attack rate of 4.3% in those who received only blood with an ALT level less than 14 IU/L to 50% for those receiving at least 1 unit with an ALT level greater than 60 IU/L; (3) the same relationship between recipient hepatitis and the extent of donor ALT elevation held for 225 patients who received only single-unit transfusions (among such patients, the hepatitis attack rate was ten times higher in those receiving blood with an ALT level greater than 45 IU/L than in those given blood with an ALT level less than 45 IU/L); and (4) the hepatitis risk increased dramatically if more than 1 unit of blood with an elevated ALT level was administered; ten of 11 patients receiving 2 units of blood with an ALT value greater than 45 IU/L showed development of hepatitis.

The results presented here confirm those of the TTV report, except that we could not analyze the effect of elevated ALT level in respect to single-unit transfusion. As in the TTV study, our recipients were increasingly liable to have hepatitis develop the higher the ALT level of the donor and, conversely, the higher the donor ALT level, the more likely that donor was to be associated with a case of posttransfusion hepatitis. The incidence of hepatitis among recipients of at least 1 unit of blood with an ALT value greater than 53 IU/L (2.25 SDs) was strikingly greater than the incidence among recipients of blood in which all ALT levels were less than 53 IU/L ($P<.001$).

To exclude the possibility that the observed relationship between donor ALT and recipient hepatitis was coincidental, a number of donor and recipient variables were assessed. In addition to donor ALT level, only the volume of blood transfused and the hepatitis B immune status of the recipient showed a possible relationship to recipient hepatitis. Since the more blood received, the greater the probability that at least 1 unit would have an elevated ALT value, the possibility existed that the observed association of donor ALT with hepatitis was coincidental to increased transfusion volume and the likelihood of receiving an infectious unit irrespective of donor ALT. However, this does not seem to be the case; when transfusion volume was equalized among recipient groups by expressing hepatitis risk as cases per 1,000 units received (Table 2), or by examining the level of ALT as a variable at each transfusion level (Table 3), there remained a significant increased hepatitis risk in those recipients of blood with an elevated ALT level ($P<.001$).

In the absence of specific serological tests for the agent or agents of NANB, there is no way to assess directly the hepatitis susceptibility of transfusion recipients. If, however, populations or persons with increased exposure to HBV also have increased exposure to NANB, then the presence of antibody to HBV might be used as an indirect measurement of immunity to NANB. This is of relevance to the

current study, since recipients of blood with normal ALT levels had an increased prevalence of anti-HBs in their pretransfusion sample ($P<.05$), suggesting they may have been less susceptible to both HBV and NANB hepatitis viruses than recipients of blood with an elevated ALT level. The importance of donor ALT as a hepatitis risk factor was, however, distinguished from the variable of recipient susceptibility by examining the influence of ALT only in recipients with similar pretransfusion anti-HBs status.

The essence of this study is summarized in Table 4, where hepatitis association, hepatitis prevention, and donor loss are calculated at various donor ALT exclusion levels. It can be seen that the most significant, and presumably specific, association between donor ALT and recipient hepatitis is achieved at a donor exclusion level of 2.25 SDs above the mean log ALT level. The considerably higher χ^2 is a compelling reason to choose 2.25 SDs as the appropriate exclusion level; this is further emphasized when both efficacy and donor loss are considered. When one corrects for hepatitis caused by blood units with a normal ALT level (corrected efficacy—see "Results"), the percent of hepatitis prevented does not differ appreciably using cutoffs of 1.5, 2.0, and 2.25 SDs. Beyond 2.25 SDs, there is a striking decrease in corrected efficacy, suggesting that exclusion levels above 2.25 SDs have little practical value even though they have the enticing feature of reduced donor loss. Exclusion levels below 2.25 SDs do not offer a significant advantage in corrected efficacy but result in the loss of considerably more donor units. In this study then, an exclusion level of 2.25 SDs is the most advantageous in that it correlates highly with the development of posttransfusion hepatitis (PTH) ($P<.001$), in that it potentially prevents 29% of PTH, and in that it results in the loss of only 1.6% of blood units.

The TTV study predicted that exclusion at a donor ALT level of 45 IU/L would prevent approximately 40% of PTH; however, this prediction is based on the crude, rather than the corrected, efficacy and, hence, is probably too high. Using the TTV data on single-unit transfusions, where no correction is necessary, four of the observed hepatitis cases might have been prevented if donors with elevated ALT levels were excluded. This represents a 28.5% hepatitis reduction, a figure virtually identical to the 29% derived in our study.

It is important to emphasize the negative aspect of the donor ALT-recipient hepatitis relationship, namely, that 70% of PTH will not be prevented by screening donors for ALT. In addition, 40 (72%) of the 56 donors with elevated ALT levels were not associated with a case of PTH. While some of these elevated ALT units were undoubtedly transfused to patients who were not susceptible to the NANB virus, and others may have resulted in hepatitis too mild to meet the criteria of our study, it is probable that many donors with elevated ALT levels were not, in fact, carriers of a hepatitis virus. These imperfect correlations reflect the nonspecific nature of the ALT test and emphasize that adoption of donor ALT screening will, at best, be an interim measure. Continued vigorous pursuit of a specific serological test for the agent or agents of NANB is mandatory.

The NIH and TTV studies combined provide data on more than 8,000 donors and 1,500 recipients and have important implications for blood transfusion services, raising many difficult ethical and practical issues. Paramount among these is the question of whether the findings now available are sufficient to require that routine donor screening for ALT be instituted or whether a randomized, controlled, prospective study is needed to confirm that the predicted reduction in PTH can actually be achieved. Many of the current considerations are similar to those raised by the introduction of tests for HBsAg. Indeed, even the projected extent of hepatitis prevention (30%) is similar to that predicted and then confirmed for HBsAg testing. There are, however, two major differences. First, the ALT test does not identify a specific viral marker but is a nonspecific test identifying a variety of nonviral as well as viral disorders. Second, donor loss will amount to 15 to 30 per 1,000 instead of the one to three per 1,000 that occurred with HBsAg testing.

For the blood recipient, the ALT test offers new hope for hepatitis prevention; for the donor, it offers new information, but perhaps information that is not really desired; for the blood supplier, it increases the complexity and cost of blood delivery and reduces the available amount of a product already in critically short supply. The ALT testing of donors is thus in a tenuous balance between risk and benefit. The balance shifts toward testing when one considers that approximately 30% of PTH might be prevented (90,000 cases per year in the United States), but this is tempered by the realization that 70% will not be prevented and that even the prevention of 30% is in some doubt unless confirmed by a randomized clinical trial. The balance also shifts away from testing when one considers the estimated additional $20 million in the annual cost of blood in the United States alone and the potential national loss of 45,000 donors and more than 90,000 blood units. It is a difficult equation, whose solution will require thought and planning.

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References

1. Aach RD, Szmuness W, Mosley JW, et al: The transfusion-transmitted virus study: Serum alanine aminotransferase of donors in relation to the risk of non-A, non-B hepatitis in recipients. *N Engl J Med* 1981; 304:989-994.

2. Alter HJ, Purcell RH, Feinstone SM, et al: Non-A/non-B hepatitis: A review and interim report of an ongoing prospective study, in Vyas GN, Cohen SN, Schmid R (eds): *Viral Hepatitis*. Philadelphia, Franklin Institute Press, 1978, pp 359-369.

3. Cochran WG: Some methods for strengthening the common χ^2 tests. *Biometrics* 1954; 10:417-451.

4. Norris RF, Potter HP, Reinhold JG: Present status of hepatic function tests in the detection of carriers of viral hepatitis. *Transfusion* 1963; 3:202-210.

5. Bang NV, Ruegsegger P, Ley AB, et al: Detection of hepatitis carriers by serum glutamic oxalacetic transaminase activity. *JAMA* 1959;171:2303-2306.

6. Brandt KH, Meulendijk PN, Pauli NJ, et al: Data on the determination of SGOT and SGPT activity in donor blood for the possible prevention of post-transfusion hepatitis. *Acta Med Scand* 1965;177:321-325.

7. Miller WV, Watson LE, Holland PV, et al: Evaluation of the effectiveness of hepatitis screening tests. *Vox Sang* 1971;21:1-10.

8. Otto-Servais M, Plomteux G, Brocteur J, et al: Interest of enzymatic determinations: OCT, GOT, GPT and observations of the presence of Australia antigen relating to viral hepatitis in blood donors. *Vox Sang* 1970;19:338-344.