CONCISE REPORT

Screening Tests for Blood Donors Presumed to Have Transmitted the Acquired Immunodeficiency Syndrome

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We investigated 18 sets of blood donors from 12 to 50 months after they donated blood to recipients who subsequently developed the acquired immunodeficiency syndrome (AIDS). Within each donor set, only one donor was suspected of having transmitted the disease (ie, member of an AIDS risk group). The other donors (n = 189) were not risk group members and served as controls. A number of suspected donors were homosexual men; three were intravenous drug patients; median, nine). Donors were identified as suspected transmitters if they were members of an AIDS risk group. Fourteen donor investigations had been completed,2 (2) a single donor per case was identified as the likely transmitter, and (3) donor blood 12 to 50 months postdonation was available for testing. Seventeen cases qualified. These AIDS patients received blood products from 206 donors (two to 34 donors per patient; median, nine). Donors were identified as suspected transmitters if they were members of an AIDS risk group. Fourteen suspected donors were homosexual men; three were intravenous drug abusers. Of these, three had lymphadenopathy and one had developed AIDS. An additional donor is added to this set of 17. He gave blood to a patient who developed AIDS, and he subsequently developed AIDS himself; the other donors, however, could not be investigated.

Laboratory Methods

We applied three measures shown to have the highest rate of positivity with AIDS or lymphadenopathy patients, intermediate rates with AIDS risk-group controls, and low rates with the general population. They were selected for study because they are simple tests and because they are positive in a high percentage of AIDS patients exist, but it remains to be seen how these tests perform in so-called AIDS carriers, many of whom may be asymptomatic, or how effective they would be for screening donor blood. The ultimate validation of any AIDS screening test will require a large-scale prospective study. Short of this, we have retrospectively studied donors who had given blood products to patients who subsequently developed AIDS, in order to evaluate these tests for their ability to detect “AIDS carriers.”

MATERIALS AND METHODS

Epidemiologic Methods

Methods for investigating transfusion-associated cases of AIDS have been reported.1 As of December 1984, 79 cases of transfusion-associated AIDS had been reported, ie, AIDS patients for whom the receipt of blood products was the sole identified risk factor. We selected for study those cases in which (1) donor investigations had been completed,2 (2) a single donor per case was identified as the likely transmitter, and (3) donor blood 12 to 50 months postdonation was available for testing. Seventeen cases qualified. These AIDS patients received blood products from 206 donors (two to 34 donors per patient; median, nine). Donors were identified as suspected transmitters if they were members of an AIDS risk group. Fourteen suspected donors were homosexual men; three were intravenous drug abusers. Of these, three had lymphadenopathy and one had developed AIDS. An additional donor is added to this set of 17. He gave blood to a patient who developed AIDS, and he subsequently developed AIDS himself; the other donors, however, could not be investigated.

Laboratory Methods

We applied three measures shown to have the highest rate of positivity with AIDS or lymphadenopathy patients, intermediate rates with AIDS risk-group controls, and low rates with the general population. These included antibody to hepatitis B core antigen (a-HBc) (Abbott Laboratories, N Chicago), the T helper/T suppressor cell ratio, antibody to hepatitis B core antigen, and immune complexes, but none of these was as sensitive and specific as tests for antibody to the human retrovirus, HTLV-III/LAV.

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RESULTS

Table 1 presents tests results from specimens of donors of blood products that had been given to recipients who subsequently developed AIDS. The cutoff value for distinguishing a positive from negative (or abnormal from normal) test result was predetermined on the basis of results with independent control groups. With one exception, none of the tests differed significantly in sensitivity (positivity rate in suspected donors). The a-HTLV-III/LAV blot tests were significantly more sensitive than the a-HBc test (P = .006, Fisher's exact test).

Alternatively, as some of the tests are (or can be) expressed as a quantitative value, we used a sliding cutoff value and plotted the rates of positivity (or abnormality) for suspected donors (sensitivity) v non-suspected donors (100% − specificity) (Fig 1). This allows a comparison of test sensitivity when matched for specificity (or vice versa). With few exceptions, the tests were not significantly different from each other over the range of specificities. There were three exceptions: at 100% specificity (0% false-positive rate),
Because the numbers are small, we could not ascertain any bias or trends that would favor one test over another, such as suspected donor groupings (ie, AIDS, lymphadenopathy, risk group, symptomatic or asymptomatic), the interval between original blood donation and specimen acquisition, or incomplete testing on some donors. Finally, there was complete concordance between the α-HTLV-III/LAV blot tests. One suspected donor whose serum was negative in the α-LAV p25 RIP assay had detectable antibodies to p24/p2S in the blot assays; the remaining suspected donor sera, which were negative in the α-LAV p25 RIP assay, had antibodies to p41 in the blot assays. This result is not unexpected. One nonsuspected donor serum was positive in all four retrovirus antibody assays. One and two additional nonsuspected donor sera were registered as positives in the α-HTLV-III ELISA and α-LAV p25 assays, respectively (Table 1).

DISCUSSION

Several tests with high positivity rates for AIDS were run on specimens from 18 sets of donors, each set having contributed blood products to a recipient who subsequently developed AIDS. Within each set, one donor was suspected of having transmitted the disease by criteria independent of laboratory test results. The other donors were considered nonsuspected and served as a control group. This control group is appropriate because it allows a comparison between the tests (as in Fig 1), rather than relying on separate control groups for each test (as in Table 1), because specimen processing and transport were the same for the suspected donors, and because the group reflects the context in which screening tests for AIDS would be applied. The only drawback occurs if any of the suspected or other donors are misidentified. This, however, would tend to underestimate sensitivity and specificity, and the results presented here may, therefore, represent a conservative estimate of test efficacy. The presentation of data as a sensitivity-specificity plot (Fig 1) allows a comparison of test performance over a range of specificities or false-positive rates. Public health considerations or blood banking economics may dictate the level of detection required (sensitivity) or the level of rejection of normal donors that can be tolerated (100% specificity). Given one of these, the other can be estimated from the plot.

These data offer an initial indication of what the likely efficacy would be of a screening program to detect high-risk donors, in relation to the impact on the normal blood donor pool. To interpret the study in this way, it is critical to keep in mind three assumptions that underlie its design and that have not been firmly established. First, we assume that AIDS is an infec-

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### Table 1. Screening Tests for Donors of Blood Products to Transfusion-Associated AIDS

<table>
<thead>
<tr>
<th>Test</th>
<th>Suspected Donors (n = 18)*</th>
<th>Nonsuspected Donors (n = 189)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Positive/</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td>No. Tested</td>
<td></td>
</tr>
<tr>
<td>Low T4/T8 ratio</td>
<td>15/18</td>
<td>83.3</td>
</tr>
<tr>
<td>α-HBc</td>
<td>10/16</td>
<td>62.5</td>
</tr>
<tr>
<td>SBA</td>
<td>15/18</td>
<td>83.3</td>
</tr>
<tr>
<td>α-LAV p25 RIP</td>
<td>14/18</td>
<td>77.8</td>
</tr>
<tr>
<td>α-HTLV-III ELISA</td>
<td>15/16</td>
<td>93.8</td>
</tr>
<tr>
<td>α-HTLV-III blot</td>
<td>18/18</td>
<td>100.0</td>
</tr>
<tr>
<td>α-LAV blot</td>
<td>18/18</td>
<td>100.0</td>
</tr>
</tbody>
</table>

*Positivity rates with the two blot tests are significantly higher than with the α-HBc test \( P = .015 \), and the p25 RIP test \( P = .035 \); at a 1% false-positive rate, the blot tests outperformed the SBA \( P = .003 \); and at a 2% false-positive rate, the α-HTLV-III ELISA test outperformed the SBA \( P = .043 \).

†Positivity rates with the two blot tests are significantly lower than with the SBA and α-HBc tests \( P < .05 \). All other comparisons are not significant.
tious disease and can be transmitted by blood products. Second, we assume that the identification of suspected donors is accurate. This identification was based on membership in an epidemiologically recognized risk group, the presence of an AIDS-associated syndrome (unexplained lymphadenopathy), or the development of AIDS. We reasoned that because 94% of AIDS patients belong to one of several risk groups, which represent a minority of the US population, probability favors transmission by a donor who is a member of such a risk group over a donor who is not. We presume that a donor who develops AIDS or an AIDS-associated illness is (or was) infective. The third assumption is that the test results obtained on specimens collected 12 to 50 months postdonation reflect the results that would have been obtained at the initial donation. The question really is: If donors were to donate again, would they be detected?

For a number of reasons, the HTLV-III or LAV virus is considered the etiologic agent of AIDS, whereas low T4/T8 ratios and immune complexes presumably reflect the immune defect, and α-HBc positivity may be a coincidental phenomenon. A specific test that indicates infection with the etiologic agent is most appealing, and three of the retrovirus antibody tests performed better than the others. With our data set, a 30% to 40% difference in test sensitivity would be required to establish a statistical advantage of one test over another. This degree of difference was not found; however, it is found in another context, which supports the use of screening tests. The rates of positivity in suspected donors with the T4/T8 ratio, SBA, and α-HTLV/α-LAV tests are considerably higher than the positivity rate for patients with AIDS or the AIDS-associated syndrome, lymphadenopathy (references 4, 6, 10, and CDC unpublished data). Finally, it is worth noting that the sensitivities obtained are within the range of those obtained with the hepatitis B surface antigen test for detecting blood products that transmit hepatitis B.11

Sensitivity/specificity data are essential, but are only one factor in determining the effectiveness of a screening program. Decisions must also take into account the positive and negative predictive value of the tests (a function of prevalence or pretest probability of disease), the cost of implementing and maintaining a screening program, the cost of loss of blood from the normal donor pool, the margin of benefit over existing screening programs (voluntary abstention), social and legal ramifications, and some estimate of benefit (ie, reductions in human suffering or death, disease incidence, or patient care costs). While the cost–benefit calculations are straightforward, some of the variables are unknown, are a matter of dispute, differ in different population groups or geographic areas, or are subject to value judgments regarding their relative importance. We estimated sensitivity/specificity in a select setting in which we felt “AIDS carriers” could be reasonably (albeit presumptively and retrospectively) identified. While by no means definitive, the data are relatively quickly obtained and support the concept of screening.

ACKNOWLEDGMENT

We are grateful to Drs W. Dowdle and J. Bennett for reviewing the manuscript; to F. Porcher for editorial assistance; to B. Broome for typing the manuscript; to M.S. Kennedy, B.M. Jones, G.D. Cross, S. Loskoski, M. Hubbard, and N. de la Torre for technical assistance; to R. Holman for statistical assistance; and to M. Parvin and staff, CDC serum bank, for specimen acquisition, coding, and distribution.

REFERENCES


*Toto be 80% confident (β-error probability of .2) that a difference of 15% in detection rates is significant (α-error probability of .05), data from about 150 suspected donors would be required.

10. Centers for Disease Control: Antibodies to a retrovirus etiologically associated with acquired immunodeficiency syndrome (AIDS) in populations with increased incidences of the syndrome. MMWR 33:377, 1984

Screening tests for blood donors presumed to have transmitted the acquired immunodeficiency syndrome

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