Mr Macpherson

Copies to: Dr Scott
Dr Young
Dr McIntyre
Dr Covell
Dr Bell
Mr Boe, Solicitor's Office
Mr Liddle

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

The passage of time has necessitated a few minor changes in the blood transfusion portion of the draft PS minute on this subject. I therefore attach, on behalf of medical interests and myself, appropriately reworked paragraphs. I also attach a copy of the Lancet letter referred to.

It would seem desirable to bring into the last paragraph your recommendations relating to notification. I had not attempted to do this. I think we have agreed that, as the minute is effectively in response to PS/Mr MacKay's minute of 29 January, you will sign it.

GRO-C

J G DAVIES
21 March 1985

Room 115
Division IVD
Ext: GRO-C

ENCS

Blood Transfusion

6. It is known that AIDS can be transmitted through transfusions of blood or blood products fro m an infected donor. Ministers will recall the discovery of antibodies to HTLV III, the virus implicated in AIDS, in a number of Scottish haemophiliacs towards the end of last year. All Scottish produced Factor VIII, in which Scotland is self-sufficient, is now heat treated to counter HTLV III and hence greatly reduce the risk of transmission to haemophiliacs.

7. Tests are becoming commercially available for the screening of blood donations for the presence of HTLV III antibodies. The first of these tests, from the USA, was marketed in the UK at the beginning of March. DHSS Ministers have agreed in principle that, in England, all blood donations should be screened and that Regional Health Authorities should meet the costs. Regional Blood Transfusion Directors throughout the UK have written to the Lancet (copy attached) strongly supporting the screening of all blood donors, but advising that such a screening programme should be delayed until the available test systems have been evaluated and until alternative testing facilities are made available to individuals who may be at high risk of transmitting AIDS.

8. We consider these views of the Transfusion Directors to be sensible and responsible, and support them, particularly in the Scottish context. As noted above, all Scottish Factor VIII is heat treated; the risk from ordinary blood transfusions is believed to be very small; as far as is known, in Scotland where 280,000 donations are collected each year, there has only ~~ever~~ been one infected donation of blood (the one which corrupted the batch of Factor VIII); there is other evidence that blood donated in Scotland is "clean"; and donors are now required before giving blood to sign a statement that they are not in a group at risk of contracting AIDS.

9. The tests becoming available from United States Companies are likely to give a high rate of false positive results - ~~as much as~~ maybe ~~about~~ 4%. On that basis about 10,000 Scottish blood donors could be identified as having antibodies to HTLV III who are in fact quite free of them, the implications for the individuals concerned, and for the resources required for further testing and counselling, would be profound and substantial. The tests also have an unpredictable false negative rate, so that an infected person might not be identified; and since the test is for antibody and not antigen it will not in any case identify a person who has been infected with the antigen but not yet developed antibodies.

10. Antibody testing is at present expensive, at approximately £2 per test. This figure, which would suggest an overall expenditure on such testing of about £600,000 pa in Scotland, has to be set against a total cost per donation for all other tests, including blood grouping, also of £2. Nevertheless, we should not wish to stand in the way of testing solely on financial grounds. However a test is being developed in England, partially using NHS resources, which it is hoped will be cheaper and more accurate. A UK Evaluation Panel has been set up to test the validity and reliability of the commercial test kits coming on to the market, and the English test will be included in these evaluations.

11. A further problem has been highlighted by recent experience of a pilot testing facility for AIDS associated with a regional transfusion centre in England, when homosexual men travelled to the centre concerned, ostensibly to give blood, but in reality to determine their antibody status. Thus, having regard to the possibility of false negative tests, the risk of infected blood being donated could be increased rather than the reverse. We therefore propose that testing facilities should be made available by the Health Service, possibly associated with sexually-transmitted disease (STD) ~~D~~departments, prior to the introduction of general screening by the transfusion service, so that people considering themselves to be at risk ~~to~~ of AIDS can have access to the antibody test without presenting themselves as blood donors.

Recommendation

12. No doubt there will be public pressure for routine screening of blood donations once it is known that commercial tests are readily available. However having regard to (i) the limitations of currently available tests, (ii) the disproportionate effects of a high rate of false positive findings and (iii) the need to provide alternative screening facilities to divert at risk individuals from the blood transfusion service; we recommend to Ministers the adoption of a phased policy leading to the routine screening of blood donors, which would take into account a comparative evaluation of the tests available, the need for ready access to testing facilities outwith the transfusion service, and a recognition of the considerable requirement for additional testing, monitoring and counselling of donors with positive tests.

RESULTS OF ELISA SCREENING FOR ANTIBODIES TO HTLV-III IN 1014 HEALTHY BLOOD DONORS FROM NORTHERN CALIFORNIA

ELISA P/N ratio*					
<2	2-3·9	4-5·9	6-7·9	8-9·9	>10
921	75†	12	4	2	0

*Median P/N ratio = 0·7, mean ± SD = 0·95 ± 0·99
†Single true positive serum (P/N ratio 2·7).

development of a screening test to detect antibodies to AIDS-related retroviruses. The US Public Health Service has recommended excluding blood donors known to be at high risk of AIDS. With the introduction of an enzyme-linked immunosorbent assay (ELISA) for antibody to human T-lymphotropic virus type III (HTLV-III) regulations will soon require the screening of all blood donors. As with any screening test, the problem lies with false positives which will have a significant impact both on blood supplies and on blood donors since seropositive blood will be discarded and donors will be notified of their test result. The definition of "positivity" is thus an important issue. The positive detection limit is best established by comparison of the ELISA P/N ratio with reference methods: the ELISA P/N ratio is calculated as the optical density of a test specimen divided by that of the background or a negative sample. To establish performance standards we compared results by ELISA with those obtained by immunofluorescent assay (IFA) and western blot procedure. The target antigen was gradient purified, disrupted HTLV-III for ELISA and western blot and productively infected cells for IFA. The HTLV-III infected cell line was provided by Dr R. C. Gallo.

We screened 1014 consecutive anonymous blood donor sera by ELISA and retested all specimens with P/N ratios of 2 or more by IFA and western blot (table). Our regional blood centre serves a population of 1·5 million and draws 77 000 units a year from about 50 000 individuals in twelve counties of northern California, excluding San Francisco County. A large percentage of the blood is drawn in Sacramento County where 13 cases of AIDS have been reported since 1982. 2 additional cases have been reported in the other eleven counties. The general donor population thus appears to be at low risk of AIDS.

93 specimens (9·2%) had P/N ratios of 2 or more by ELISA. These were re-examined by IFA and western blot and 1 serum was found (P/N ratio 2·7) which contained antibodies to HTLV-III. Virus specificity was confirmed in the western blot by reactivity with HTLV-III polypeptides (p61, p54, p41, p24).[2] The remaining 92 sera were negative by IFA and western blot. This included 18 specimens with an ELISA P/N ratio of 4·0 or more. None of 48 selected samples with P/N ratios below 2 contained HTLV-III antibodies as identified by IFA or western blot.

Blood banks want to be able to identify all true-positive results without jeopardising the blood supply by unnecessarily deferring blood donors or alarming donors by mentioning a "positive" test that does not represent true infection. In a recent study of a blood donor population, a P/N ratio of 5·0 was established as the cut-off for true positives.[3] However, none of the specimens with a P/N ratio ⩽4·0 were examined by confirmatory methods. Therefore, according to our findings true positives may have been missed in that study. Our results indicate that use of the more sensitive P/N ratio of 2 as a cut-off point without confirmatory testing would have resulted in 9·2% of blood units being discarded. However, only a single unit would have been discarded if ELISA screening had been used in combination with a confirmatory test.

We conclude that it is necessary to use the most sensitive ELISA P/N value possible to detect all antibody-positive sera in the healthy blood donor population. When used in combination with a confirmatory test, either IFA or western blot, this strategy will not result in a major disruption in the procurement of blood or in the significant loss of future blood donors. Further, we recommend that only individuals who are positive by both ELISA and a confirmatory test be placed on a deferred donor list and informed about their AIDS serology results.

A few symptomless virus-positive individuals without antibody will be missed by even the most sensitive HTLV-III antibody screening methods.[4] The resolution of this problem depends on HTLV-III antigen detection tests yet to be developed.

J. CARLSON

Department of Pathology, School of Medicine, University of California, Davis, Davis, California 95616, USA
S. HENRICHS, M. BRYANT, M. LEVY, J. YAMAMOTO, J. YEE, M. GARDNER

School of Veterinary Medicine, University of California, Davis
J. HIGGINS, N. PETERSON

Sacramento Medical Foundation Blood Center
P. HOLLAND

1. CDC. Provisional Public Health Service interagency recommendations for screening donated blood and plasma for antibody to the virus causing acquired immunodeficiency syndrome. *MMWR* 1985; **34**: 1–5.
2. Saxinadharan MG, Popovic M, Bruch L, et al. Antibodies reactive with human T-cell leukemia retroviruses (HTLV-III) in the serum of patients with AIDS. *Science* 1984; **224**: 506–08.
3. Weiss SH, Goedert JJ, Saxinadharan MG, et al. Screening test for HTLV-III (AIDS agent) antibodies. *JAMA* 1985; **253**: 221–25.
4. Salahuddin SZ, Groopman JE, Markham PD, et al. HTLV-III in symptom-free seronegative persons. *Lancet* 1984; i: 1418–20.

SIR,—We believe that current commercial kits for HTLV-III antibody tests are likely to give a high rate of false-positive results. We would therefore recommend that careful consideration be given before they are introduced for the screening of all voluntary blood donors, for the amount and degree of unnecessary stress and hardship that a fair number of our donors and their families would thus have to undergo is unacceptable. This in turn could lead to a sizeable drop in the supply of blood and blood products. Of no less importance, for the safety of transfused patients, is the need to ensure that the first priority for the introduction of any HTLV-III antibody tests into a community is given to patients attending special (venereal disease) clinics and other members of the general public who wish to have access to these tests. If this is not done, many high-risk people, from a blood-transfusion point of view, may present themselves at blood-donation sessions simply to find out their HTLV-III antibody status.

We do support, strongly, the screening of all blood donors for HTLV-III antibody testing, but we would advise that this is delayed until test systems have been appropriately evaluated and efforts have been made to give all members of the public access to HTLV-III antibody testing.

National Blood Transfusion Service, Birmingham, Newcastle upon Tyne, Edgware, Oxford, Bristol, Brentwood, Lancaster, Cardiff, Southampton, Leeds, and Sheffield; Scottish National Blood Transfusion, Dundee, Edinburgh, Glasgow, Aberdeen, and Edinburgh, and Protein Fractionation Centre, Edinburgh

F. A. ALA, A. K. COLLINS, M. CONTRERAS, C. C. ENTWISTLE, I. D. FRASER, J. F. HARRISON, D. LEE, J. A. F. NAPIER, D. S. SMITH, L. A. D. TOVEY, W. WAGSTAFF, E. BROOKES, D. B. L. MCCLELLAND, R. MITCHELL, S. J. URBANIAK, W. WHITROW, R. J. PERRY, J. D. CASH

HTLV-III ANTIBODY IN SEQUENTIAL PLASMA SAMPLES: FROM HAEMOPHILIACS 1974–84

SIR,—In an earlier report[1] we showed that seropositivity for antibody to human T-lymphotropic virus type III (HTLV-III) among Scottish and Danish haemophiliacs was related to their use of factor concentrate products made from United States donor material. We here present the HTLV-III antibody results on