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Safety of blood transfusion: the Japanese experience

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There are eight million blood donors in Japan. Blood is donated in units of 200 ml or 400 ml and by haemapheresis. The major problems are concerned with the transmission of infection, particularly with HIV and HTL-1 viral infections, and this leads to rejection of about 8% of donated blood. Recent emphasis has been placed on the automated screening of blood at the time of donation and the more widespread use of patient records to eliminate infected blood.

Au Japon, huit millions de personnes donnent de leur sang que l'on prélève par hémophérèse à raison de 200 ou 400 ml. On s'inquiète des risques de transmission infectieuse et plus particulièrement du HIV et du HTL-1, ce qui entraîne le rejet de 8% des unités. On a récemment mis l'accent sur le dépistage automatique lors du don de sang et sur un plus grand recours aux dossiers des patients afin réduire le risque d'infection.

The Japanese blood program

In 1988, about eight million people (6.5% of Japanese population) donated blood. Of the three types of blood donation (200 ml, 400 ml and haemapheresis), 200 ml is the most common. The 400 ml and haemapheresis donations began in 1986, and are increasing (Table I). Japan is self-sufficient for red cells which are supplied exclusively through the Japanese Red Cross but many plasma products are imported. Imported virus-contaminated anti-haemophilic factor (AHF) concentrates have caused HIV in Japanese haemophiliacs, and the Government and the Red Cross have decided that AHF concentrates will be made from blood donated here so that Japan will be self-sufficient by 1992.

Predonation testing

Serological tests before donation to exclude virus carriers may be beneficial to avoid inappropriate blood collection. The tests should be simple and reliable as donors should not be kept for a long time at collection sites awaiting results. For transfusion safety, however, all collected blood units should be examined. Inappropriate blood collection may also be reduced by referral to the previous records of donors 80% of whom are repeat donors. Direct computer access to these records from donation sites will help to avoid collection from hepatitis B virus (HBV), human T-cell lymphotrophic virus (HTLV-I), hepatitis C virus (HCV) or human immunodeficiency virus (HIV-1) carriers.

Serological tests are not performed before donation to exclude virus carriers although predonation tests for haemapheresis donors would help because haemapheresis is time-consuming and expensive. This would be particularly advantageous for HLA-matched or cytomegalovirus (CMV) free platelets which must be supplied rapidly, and where alternative registered donors must be contacted as soon as possible.

Blood donor screening

About 8% of donated blood units are rejected in our blood center (Table II). The main reason is virus infection particularly with HBV and HTLV-I infection.

The HBV carrier rate of the general population is estimated to be higher than that of blood donors. The major route of the HBV transmission in Japanese is mother to infant.[1] Since vaccination of affected infants is highly effective, the carrier rate should decrease in the future. Residual cases of transfusion-associated hepatitis B are probably due to the low sensitivity of the screening method of hepatitis B surface antigen (HBsAg). They should decrease following the recent adoption of anti-hepatitis B core antigen (HBc) screening.

Japan is an endemic area for HTLV-I infection. The Japanese Red Cross started HTLV-I seroscreening in 1986. Healthy HTLV-I carriers are found in 1–2% of Japanese blood donors.[2] A higher prevalences (8%) is seen in Kyushu, southwestern Japan. A high HTLV-I seroconversion rate (>50%) was observed among the

TABLE I Blood donation in Japan

Year	*Number of donors*	*200 ml*	*400 ml*	*Haemapheresis*
1985	8,696,105	100%	—	—
1986	8,597,507	92.6%	7.2	0.2
1987	8,211,340	86.5%	12.8	0.7
1988	7,974,147	83.0%	15.7	1.3

TABLE II Donor blood screening 48,512 samples (1989 12.1-19990 2.28)

	Positive (%) after: 1st screening	*2nd screening**
HB (sAG & cAb)	8.84 PK	1.65
HCV	1.98	1.21
HTLV-1	3.88 PK	2.08
HIV-1	0.21 PK	0.06†
Syphilis	0.53	0.46
GPT	2.69	2.49
Irregular Ab	3.23 PK	0.28
Total	21.36%	8.23%

*Positive samples after 2nd screening are disqualified.
†None of the HIV-1 seropositive samples after second screening were positive by confirmatory test.

patients who were transfused with cell components from seropositive donors.[3] No case of adult T-cell leukaemia (ATL) has been reported among the patients who demonstrated seroconversion after transfusion. However, there is a strong association between transfusion-associated HTLV-I infection and endemic spastic myelopathy (or HTLV-I associated myelopathy, HAM).[4]

In one study, 80% of transfusion-associated non A non B hepatitis (NANBH) cases were anti-HCV positive (K. Nishioka, personal communication). Although the virus has not been fully characterized and no confirmatory test is available, the Japanese Red Cross started HCV seroscreening in December, 1989. The HCV seroprevalence in Japanese blood donors is 1–2%.

Only 34 donors from a total of 21 million donations were found to be HIV seropositive in the period from 1986 to 1989. Screening blood donors for HIV has to be continued in Japan because international communication may result in HIV-1 infection becoming endemic in the Japanese population.

Automated screening

Screening for infection should become automated as more pretransfusion tests are being conducted at blood centres to supply safer blood products. Three kinds of autoanalyzers are used for biochemical tests, cell counts, and for serological screening. Data from the autoanalyzers are stored on floppy diskettes and then transferred to the host computer.

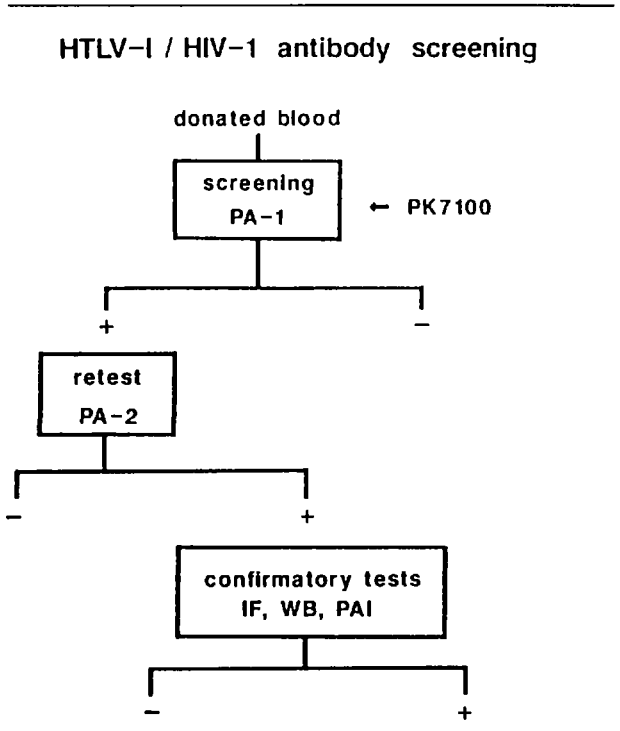

FIGURE HTLV-I/HIV-I antibody screening. Donated blood which is positive at PA-2 is not used for transfusion (abbreviations: PA-1 and PA-2: gelatin particle agglutination; IF: immunofluorescence; WB: western blot; PA-I gelatin: particle inhibition).

An autoanalyzer has been developed for agglutination tests,[5] because most of the serological screening tests in Japanese Red Cross have been carried out by agglutination methods. For example, the HTLV-I and HIV-I screening tests are by gelatin-particle agglutination (PA) (Figure). The twice positive sample is finally subjected to confirmatory tests. Automated screening can be applied at the first screening step (PA-1) and we have confirmed that the automated screening does not yield false-negative results.

Prospect of transfusion safety

Viral infection and allosensitization are the two major side-effects of blood transfusion. Since blood bankers are responsible for transfusion safety, donor blood screening to eliminate virus-infected or mismatched blood has been the blood bankers' primary concern. However, dependence on screening may not be sufficient to provide safe blood. New viruses occur and screening tests are not 100% sensitive. Multiple transfusions of random donor blood units may eventually produce allosensitization by HLA or other alloantigens. Leukocytes are the major

factor for allosensitization, and may make recipients refractory to platelet transfusion. Moreover, lymphocytes may cause graft-versus-host disease (GVHD) in immunosuppressed patients[6] and transmit infectious diseases.

Some blood bankers are trying to remove or inactivate viruses or to deplete leukocytes from blood units. Infectious viruses can be removed or inactivated in the preparation of plasma products.[7] However, there is no effective method to remove or inactivate viruses in fresh-frozen plasma or fresh plasma. Recently, it was reported that HIV[8] and HBV[9] could be removed through the hollow fibre type of microporous membrane. Leukocyte filters may remove more than 95% of leukocytes from packed red cells[10] or platelet preparations,[11] which may protect transfused patients from allosensitization, GVHD, or leukocyte-associated virus infection.

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