RISK OF HIV TRANSMISSION VIA BLOOD PRODUCTS

Ruth Camilleri B.Pharm.
Comprehensive Genetics Programme, Department of Health, Malta.
This article is based on the author's B.Pharm thesis entitled 'Safety of Blood Products'

Introduction

Blood services are inevitable and life-saving. However, the therapy with blood products includes the risk of virus transmission. This is reflected by the high infection rate observed in haemophiliacs by acquired immunodeficiency syndrome (AIDS) – inducing viruses which varies between 50 and 100 percent[1,2]. Unfortunately in Malta we have the figure of almost 100 percent. But not only AIDS can be transmitted by blood products: hepatitis B (HBV) is a long- and well-known risk of blood products, and since the early seventies an additional form of serum hepatitis has been diagnosed; the so-called Non-A, Non-B hepatitis (NANBH). Further viral diseases such as cytomegalovirus (CMV) and the Epstein-Barr virus (EBV) infections are of less importance and only life-threatening for immunosuppressed patients.

Donor Selection

The appropriate selection of blood donors is of prime importance towards the achievement of a safe blood supply. For this reason, the two blood banks in Malta are both non-profit organizations. In addition, the donors undergo a physical examination and are asked to answer a questionnaire. Nevertheless, since a full medical check up is not practicable, they rely heavily on the good faith of the donor. In a study carried out to analyse the motivations and social characteristics of the volunteer donor attending the National Blood Transfusion Centre, during a period of three weeks (Nov. 1989) it was found that the majority of donors are young men between the ages 18-35 years. Approximately 28% of donors are new donors, 9% make a donation every year, 21% twice a year, 25% three times a year while 17% donate blood four times a year. The majority, about 70% of both the new and regular donors stated that they give blood for altruistic reasons. The main motivations (Fig. 1) were a desire to help others and a sense of duty towards the community. Other reasons stated were to get a day off work, to get rid of headaches and for the benefit of a free medical check up which are rather egoistic reasons. An interesting fact which emerged was that although housewives, students and professional people (Fig. 2) form only a small percentage of donors they are the most altruistic.

It was concluded that out of 12,500 donations about 2,500 are made for non-altruistic reasons each year. This implies that the selection of donors by the establishment of a voluntary blood organization and on a medical examination and interview are not fully efficient.

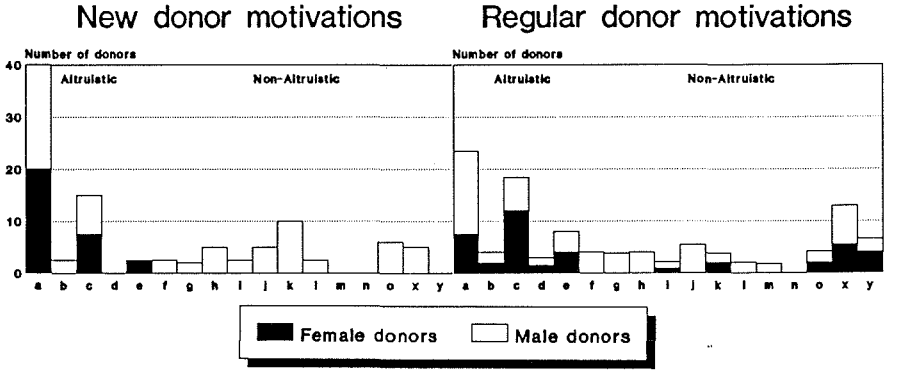

Fig. 1: New and Regular Donor Motivations

a. a desire to help others
b. gratitude for good health
c. awareness of need of blood
d. sense of duty to the community
e. the discovery of a rare blood group
f. to get a day off
g. for a free medical check up
h. to feel less tense
i. to get rid of 'excess' blood
j. to get rid of headaches
k. because a member of the family needed blood
l. persuaded by friends or relatives
m as a member of the armed forces
n. to feel heroic, superior, proud ...
o. others
x. a combination of altruistic reasons
y. a combination of non-altruistic reasons

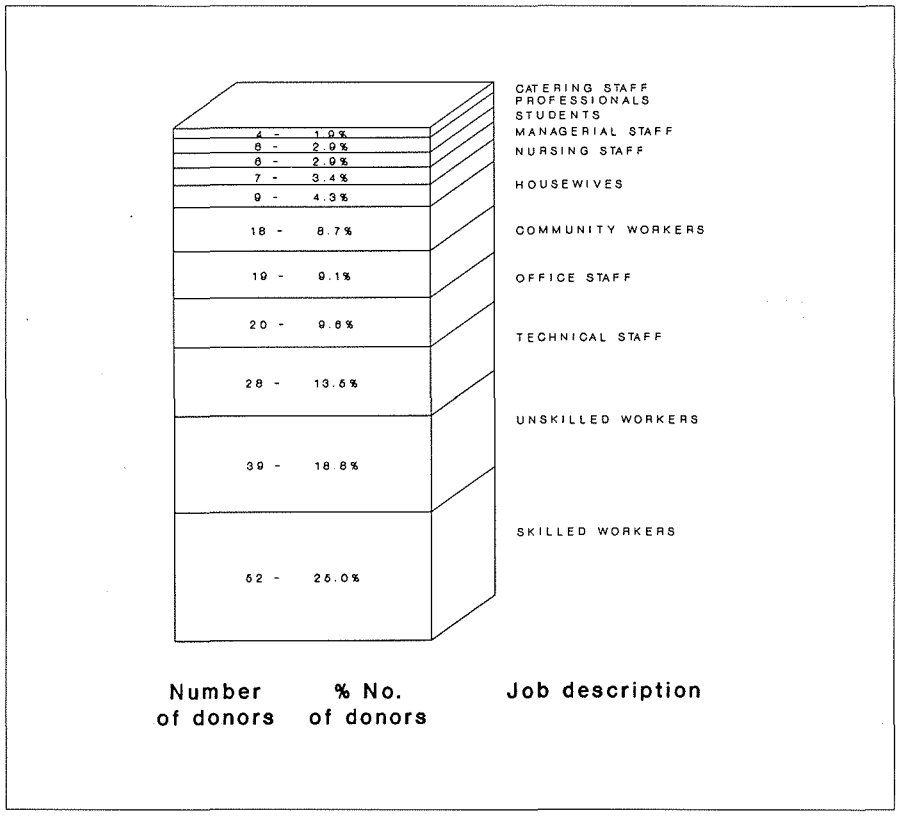

Fig. 2: Classification of Donors' occupations

Laboratory Screening

It is evident that laboratory HIV antibody screening has to be included together with other measures to prevent the transmission of HIV by blood and blood products especially those products which cannot be heat-treated eg. cryo-precipitate.

Anti-HIV screening became mandatory in most countries by the beginning of 1986. In Malta, routine screening for HIV antibodies started in mid-1985.[3]

During the period July 1985 up to the end of 1989, a total of 40,600 donations were anti-HIV tested (Table 1). The majority of tests were performed using the Wellcome assay. With this assay 2.3/1000 tests were initially positive or equivocal but only 0.33 in 10,000 were positive on repeat testing.

Of the 10,410 donations tested with Abbott assay, 8.0/1000 were initially positive and 3.8/10,000 were repeatedly positive. One confirmed positive result has been found with the Wellcome assay and one with the Abbott assay. The two donors found anti-HIV positive were male new donors. They were a homosexual and a bisexual i.e. both belonging to high risk categories. The former was found in 1985 when probably access to testing through the blood transfusion centre was the easiest, if not the only way of being tested. So, one may suppose that some first time donors - who suspect that they are at risk for HIV infection - attend the blood centre in order to ascertain their serological status. This emphasises the importance of access to alternative testing sites. Fortunately, free screening and testing facilities are now available in Malta.

The frequency of confirmed anti-HIV positive blood donations varies in different countries (Table 2)[4]. The incidence in Malta, which is 0.005% is comparable to most European countries but higher than in the U.K. and Scandinavia and lower than in Italy.

Table 1:
Results obtained using commercial ELISA assays for the detection of anti-HIV in Maltese blood donations, July 1985 to December 1989.

Test kit	Total number of donations tested	Number of tests repeated	Number of tests repeatedly positive	Number of tests confirmed positive
Wellcome	30,190	70 (0.232%)	1 (0.003%)	1 (0.003%)
Abbott	10,410	83 (0.797%)	4 (0.038%)	1 (0.010%)
Total	40,600			2 (0.005%)

Table 2:
The incidence of HIV positive donors in various European countries

Country	*Incidence %*
U.K.	0.002
Malta	0.005
Italy	0.019
F.R.G.	0.007
Scandinavia	0.002

The two ELISA assays studied are clearly associated with a significant percentage of false positive results. However the results seem to suggest that the Wellcome assay is of superior specificity.

Although both methods (the Abbott and the Wellcome assays) are reliable initial screening tests for the presence of HIV antibodies, it is important to adopt the most specific method in order to decrease the number of false positive subjects detected on screening and confirmatory stages.

In spite of donor and donor blood screening the transmission of viral infections may still be a serious complication of blood product therapy. This can be due to various

reasons, one reason being that anti-HIV screening tests do not detect infected donors who are in the window period which is said to be at least three months. Another reason is the poor specificity and sensitivity of commercially available methods to identify and quantitate NANBHV. In addition, by one wrong determination only the total plasma pool can be infected and all the fractions isolated therefrom.

So another approach towards the production of a safe blood supply would be the introduction of virus removal/inactivation techniques. These techniques include application of heat, irradiation or detergents. Many plasma fractionation centres seem to agree that the solvent/detergent technique is the most efficacious. Its increase in popularity is mainly due to two factors: (1) it does not affect plasma proteins and (2) it has been shown to have a high inactivation efficiency and product safety.

The method of detergent treatment is based on the principle that solvent/detergent mixtures cause extraction of essential lipid resulting in either total disruption of the viral structure or disruption of the receptor recognition site, thereby inactivating the virus. Products treated this way are approved for use in the USA and many other countries. Now since Malta is considering of becoming self-sufficient in the supply of Blood Products adoption of an efficacious virus inactivation technique will be essential in order to produce safe Blood Products.

Conclusion – The Blood Centre Pharmacist

The pharmacist involved in the preparation of Blood Products is in a good position to promote safety (Table 3). The pharmacist can play a role in assessing quality of techniques used to screen blood which must be subjected to continuous critical review for faults, omissions and improvements. For example as stated above, one of the problems associated with screening tests involving ELISA assays is the relatively high incidence of 'false' positive results. As a consequence there is a considerable loss of blood and hence additional need of blood collection. Choosing the appropriate screening method is hence of great importance to minimize or eliminate the problem.

Changes in procedure and policy may sometimes be required such as in the recent implementation of surrogate testing for NANBH. The pharmacist's role when introducing such changes is to evaluate the benefits versus costs. Although, reimbursement of costs are not in the pharmacist's purview, the final decision can be a direct result of the decision made by the pharmacist.

Another role of the pharmacist involves the quality control of the procedures employed and of the final product. The importance of undertaking every possible means to assure the safety of the finished product cannot be over-emphasized. This involves rigid control of reagents, testing kits and equipment plus vigilant control of all steps in the production procedure and finished product. Supervising this control programme is the direct responsibility of the Blood Centre pharmacist.

For the pharmacist to accomplish the above mentioned duties he/she must posses certain characteristics. Adequate training and knowledge is the main requirement for the pharmacist to function efficiently. Transfusion safety involves certain challenges which cannot be resolved unless the pharmacist is well prepared. Employment of specialized techniques to screen blood donations and methods used to eliminate viral infections require skill and sound judgement. A control programme must be established to assess the safety of blood and its derivatives. This involves the ability to evaluate all the steps in the production procedure and of the finished product. The blood centre's pharmacist must also possess and apply high moral professional ethics. The proper attitude of the pharmacist is of vital importance since transmission of viral infections through blood and blood products can result in serious, even fatal situations. An obvious example is the transmission of AIDS through transfusion which before screening tests were developed, have resulted in grave consequences. Scruplous procedures have now nearly eliminated this problem.

The Blood Centre pharmacist can also be greatly involved in clinical or bench research. The blood centre offers an excellent setting for doing research and hopefully this will enhance the safety of the blood and blood product supply.

Table 3:
The Pharmacist's Role at the Blood Centre

Educating and providing information.
Assessing quality of techniques.
Quality Control of the preparation procedure and finished product.
Decision making.
Maintaining interaction among the blood centre, manufacturers of reagents and equipment, clinicians and tech-nologists.
Participating in research.

References

1. Allain, J.P. (1986). Prevalence of HTLV/LAV antibodies in patients with haemophilia and intersexual partners in France. New Engl. J. Med. 315, 517-518.
2. Johnson, A.J., Semar, M., Newman, J., Brandt Harris, R.B., Brand, D., Middleton, S., Smith, J. (1975). Removal of Hepatitis B surface antigen (HBsAg) from plasma fractions, J.Lab.Clin. Med 98.
3. Camilleri Ruth, (1990) Safety of Blood Products, B.Pharm Thesis, Department of Pharmacy, University of Malta.
4. International Society of Blood Transfusion (I.S.B.T.) (Dec 1988). The International experience in anti-HIV screening, third update (Meeting).