Viral risks of blood transfusion

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Summary. Viral complications of modern blood transfusion are negligible, but transfusion can never be called totally safe. The most important risks are transmission of hepatitis and human immunodeficiency (HIV) viruses. Systematic screening of blood donors for HBsAg greatly reduced the incidence of post-transfusion hepatitis B, but virus transmission is still possible in the convalescence period when HBsAg test has become negative. To avoid this possibility, some countries have started additional screening for anti-HBc. The decision depends on the prevalence of hepatitis B, and no universal recommendation can be given. The great majority of non-A, non-B post-transfusion hepatitis cases seem to be caused by hepatitis C virus (HCV). The second generation tests for anti-HCV are very useful for screening blood donors, and surrogate testing (e.g. ALT and anti-HBc) is not needed anymore. Careful donor selection and other preventive strategies including systematic laboratory testing for anti-HIV have greatly reduced the risk of HIV transmission, but in the seronegative phase of the disease transmission of infection is still possible in donated blood. Antigen screening in donors does not solve this problem. Cellular products may transmit HTLV and CMV. In the latter case, depletion of blood products of leukocytes is as good as using seronegative donors. The prevention of transmission of all viruses includes, in addition to donor selection and laboratory screening, viral inactivation of products. This has been achieved with most plasma derivatives, and research is active with cellular products. Different preventive strategies should be used simultaneously to minimize the risk as much as possible.

Introduction

Modern blood transfusion is a very safe procedure, but nevertheless there remains some risk of transmission of infectious disease. Syphilis was once a feared complication, and hepatitis viruses caused high morbidity in recipients of pooled plasma during and after the second World War. The emergence of the acquired immune deficiency syndrome (AIDS) epidemic gave a new degree of priority to efforts to avoid blood-borne viral infections. At present, developed blood transfusion services screen every donated unit at least for hepatitis B surface antigen (HBsAg), for antibodies against human immunodeficiency virus (HIV) and against hepatitis C virus (HCV). Other viral tests may have been already included in the test array or are likely to be started in the near future. The general public is now much more aware of possibilities for infectious complications of blood transfusion, and the 'acceptable' rate of infections due to transfusion is constantly decreasing resulting in increased complexity and cost of testing donations.

Hepatitis

Viral hepatitis is usually caused by hepatitis viruses A, B, C, D and E, but may also be associated with other infections such as cytomegalovirus (CMV) disease, infectious mononucleosis, etc. Hepatitis A (HA) is very seldom transmitted by blood transfusion because of the short viraemic phase of the infection. In addition, antibodies to HAV seem to neutralize the virus in pooled products. Very little is known about blood-borne transmission of hepatitis E, a disease prevalent in some parts of the developing world, but the enteric route seems to be overwhelmingly dominant. Delta agent, causing hepatitis D requires the presence of hepatitis B virus and therefore screening for the latter excludes also the former.
It is possible that the list of hepatitis viruses should be extended to include F and G. Time will show whether these are distinct entities and whether they play any role in the safety of transfusion.

Hepatitis B

Hepatitis B (HB) used to be called 'serum hepatitis' because of the strong association between injection or infusion of human serum or plasma and jaundice. The causative virus was identified in the late 1960s, and in 1970 the World Health Organization recommended detection and exclusion of blood donors carrying HBsAg. The wide application of sensitive screening methods to detect HBsAg has proved effective in reducing post-transfusion hepatitis B (PTHB), but this disease has not been completely eliminated.

Before new donor selection criteria were applied in the early 1980s to exclude blood donors with risk factors of AIDS, it was estimated that about 10% of PTH cases were HB. In the Transfusion Transmitted Viruses Study from the USA, 15 out of 1523 recipients of blood developed HB. However, transfusion plays a very minor role as the source of clinical HB. In a population-based study, transfusion was the likely cause of infection in only 1.4% of all cases.

In the last 10 years, the incidence of PTHB has been reduced further. This is related to several factors. Homosexual men and users of intravenous drugs, both groups which are known to have, in addition to anti-HIV, high prevalence of serological markers to HBV, are asked to self exclude from giving blood. At least two countries (the USA and France) have used antibodies to hepatitis B core antigen (anti-HBc) as surrogate test for non-A, non-B hepatitis (NANBH), and this practice seems to have contributed to the reduction in the incidence of PTHB as well.

The first viral marker of acute HB to appear in serum is HBsAg. During the convalescence period the antigen disappears, often before formation of antibodies to the surface antigen (anti-HBs). These antibodies clear the remaining virus particles from blood. There is a time, a window period, when the antigen disappears, often before formation of antibodies to the surface antigen (anti-HBs). These antibodies to the surface antigen (anti-HBs) clear the remaining virus particles from blood. There is a time, a window period, when the antigen disappears, often before formation of antibodies to the surface antigen (anti-HBs).

Anti-HBc remains elevated throughout the convalescence period. Excluding units with anti-HBc from the blood supply would therefore all but eliminate the possible transmission of the virus during the window period. This prompted the Food and Drug Administration (FDA) of the US Government to recommend in September 1991 that all blood establishments screen blood units for anti-HBc. It is worth noting that the recommendation aims at reducing PTHB, and it does not take any stand as to its value as a surrogate test for NANBH. Japan started screening for anti-HBc in 1989 with apparently significant decrease in PTHB.

Most anti-HBc positive people are not infective, i.e. the antibodies simply indicate a past infection. In Finland, the prevalence of anti-HBc in blood donors is about 2% whereas the HBsAg carrier rate is 0.05% and PTHB is very uncommon. In such conditions, the benefits of anti-HBc screening to reduce further the very low risk of PTHB must be carefully weighed against the consequences of reducing the blood supply, instituting donor counselling etc. and against the appreciable costs involved.

Furthermore, in countries where HB infection is much more common, the prevalence of anti-HBc may reach 40 or 50%. The exclusion of all these donors would result in serious shortages in blood supply. The decision of health authorities whether or not to require anti-HBc screening of blood donors depends thus on the prevalence of this marker and on the seroconversion rate in the population in question. No universal recommendation can be given.

Hepatitis C

After institution of routine HBsAg testing, NANBH remained the predominant type of PTH. For a long time, the causative virus eluded researchers despite numerous attempts and several 'definitive' reports of its discovery. The final breakthrough was achieved by the application of recombinant gene technology.

This method led to identification and isolation of one clone which was used to produce a protein called C100-3. It turned out later to be part of a non-structural protein of the hepatitis C virus (HCV).

HCV belongs to the family to flaviviridae which includes the flav- and pestiviruses. The complete sequence of its RNA genome is now known. The virus shows some variations in different parts of the world, and it has been suggested that at least three different strains may be present in the same geographical area.

The production and use for diagnostic purposes of the viral protein was patented, and an enzyme-linked immunosorbent assay ELISA to measure anti-HCV antibodies was developed. The same antigen is being used by several manufacturers. The first generation assay showed very promising for diagnosis and prevention of NANBH. In patients with NANBH the test gave positive results in a high percentage. In a US study of 16 well-defined PTH cases who had converted anti-HCV positive, the antibody was found in 14 (88%) of respective donors.

In subsequent studies from Europe, the percentage was, however, lower. The test was sufficiently specific to study high prevalence populations such as hepatitis patients but it gave many false positive results when applied in blood donor screening. There was no true confirmatory test since everything was dependent on only one recombinant antigen. Partially to circumvent this drawback, a recombinant immunoblot assay (RIBA) was developed using two different sources of the
protein (yeast and *Escherichia coli*). One of the antigens was a part of the other one.

A Finnish prospective study on 685 patients with open heart surgery revealed 11 (1.6%) cases of PTH. Of these, 6 were anti-HCV positive. For each patient, an anti-HCV donor was found. Furthermore, every one of these donors had two bands in the RIBA. This was in contrast to 29 other donors who were also found positive in the screening test but who did not transmit hepatitis to the recipients of their blood. Samples from these donors produced either only one band or were completely negative in the RIBA. The results were thought to indicate that the presence of two bands in the RIBA was indicative of infectivity of a blood unit whereas RIBA negative or indeterminate blood was not likely to transmit hepatitis notwithstanding the primary screening result. However, even though this seems to be the rule, there are exceptions, i.e. blood positive with only C100 band in RIBA may cause hepatitis in the recipient.

The sensitivity and specificity of the test have been improved by adding two more antigens to the assay, the non-structural protein C33c and the structural core protein C22. The second generation RIBA consists thus of 4 antigens (the two variations of C100, C33c and C22). In the corresponding second generation ELISA screening assay the non-structural proteins have been combined into a larger C200 protein, and the core fragment C22 has been added. This improvement is reflected in an increased percentage of seropositive PTH cases. In the Finnish material, the number of seropositive patients increased from 6 to 9 when assayed with 4-RIBA indicating that at least 82% of all PTH were of type C.

In a similar Dutch study, the number of seropositive increased from 6 to 9 out of the total of 9 PTH patients when the C200/C22 ELISA was applied. In this material, two of the patients showed indeterminate results in 4-RIBA (one with isolated anti-C22, and one with isolated anti-C33) and one was negative. The authors conclude that 4-RIBA may not be quite as sensitive as C200/C22 ELISA, and that indeterminate results may represent individuals in the early phase of the infection. This is supported by the observation that some samples with indeterminate 4-RIBA results may carry the virus as indicated by a polymerase chain reaction (PCR). Other manufacturers have used other approaches to establish confirmatory tests. In principle, they are not very different from 4-RIBA. Antibodies can also be neutralized by soluble antigen fragments to produce a blocking test, and the test conditions can be varied to produce other supplementary testing procedures.

Anti-HCV is a relatively late indicator of the infection. Antibodies appear on average 10-12 weeks after inoculation with infected blood, but it may take 6-12 months before the tests become positive. Direct tests measuring the virus would obviously be preferable but the presumably low titres of the virus make immunological detection difficult or impossible. PCR has been much used for this purpose, but there are some limitations in its widespread use. On the one hand, the samples are sensitive to prolonged storage in routine conditions, repeated freezing and thawing etc., on the other the extraordinary sensitivity of PCR may detect cross contamination and lead to false positive results in inexperienced hands. In any case, PCR is too complicated and expensive for routine screening, but it may be useful when evaluating infectivity of different samples. It does not, however, replace the value of prospective transfusion studies.

The prevalence of positive results with the primary screening method varies between 0.3% and 2.0%. If a second generation test with four antigens is used as confirmatory assay, only about 10% of these samples turn out to be true positives in low prevalence populations. However, the sensitivity of the confirmatory tests is not yet optimal, and it can be estimated that the true prevalence of anti-HCV antibodies in Northern European populations is approximately 0.05-0.1%, and it increases up to 1% or more in geographical areas where hepatitis viruses are more common.

The clinical significance of HC infection is not fully established. Longitudinal studies have shown that about half or more of NANB PTH cases become chronic, and that 10-20% of these eventually develop cirrhosis of the liver. There is also an association between NANB PTH and hepatic carcinoma which is especially marked in Japan.

NANB PTH incidence, before the screening for anti-HCV, was estimated at 15-20% in Southern Europe, 10-12% in the USA and 2-4% in Northern Europe. This relatively high incidence is in contrast to the rarity of hepatic carcinoma in Europe and the USA. When clinical cases of chronic hepatitis and cirrhosis are evaluated, transfusion seems to play a very minor role as the source of the disease. Only in Japan do the clinical cases seem often to have a history of transfusion. Despite the well-established chronic nature of HCV infection, the possibility remains that an appreciable proportion might ultimately resolve or remain benign in nature without developing into disease.

In the absence of a specific test, non-specific markers such as alanine aminotransferase (ALT) and anti-HBe have been used to identify donors with risk factors for NANB hepatitis. After general institution of anti-HCV screening, the use of such surrogate markers for this purpose seems not to be warranted.

**AIDS**

**HIV-1**

The discovery of the causative virus of AIDS in 1983-1984 and the subsequent development of antibody assays took place at an unprecedented rapid
pace. In March 1985, FDA licensed their use in the USA, and most industrialized countries started general screening of blood donors in the same year.

The grave consequences of transmission of AIDS through blood and blood products, especially coagulation factor concentrates, and the extent of contamination in one patient group, haemophiliacs, have created a fruitful ground for legal disputes. In court, days and hours have been counted in retrospect in order to prove that the transfusion services did not start the screening and exclusive distribution of tested units at the moment when it was physically possible.

Progression of HIV infection into AIDS often takes a long time. The progression rate seems to be approximately the same in homosexual men and recipients of blood or contaminated coagulation factor concentrates. It has been calculated in cohorts of haemophiliacs that 10 years after seroconversion half of virus carriers have developed AIDS. Treatment may prolong this period (see Addendum on page 39).

The presence of HIV antibodies seems always to indicate the presence of virus as well, i.e. they do not exist as innocent markers of past infection. At least 90% of antibody-positive blood units are infective. Additionally, it has been confirmed that haemophiliacs who do not have antibodies to HIV, despite their high risk for HIV infection through untreated coagulation factor concentrates, do not carry the virus either.

The remaining slight risk for transfusion transmitted AIDS lies in the early seronegative phase of the infection. Presently the risk in the USA of acquiring HIV infection through transfusion has been calculated to be of the order of magnitude of 1 per 50000–150000 units administered. This is very low when compared with 1 per 100 in 1982–1983 when no measures had been taken to prevent transmission of AIDS. The different preventive strategies -- including careful donor selection and self deferral of people with risk factors have clearly been successful. The risk is still lower in Northern Europe or Japan where the prevalence of HIV infection in populations is much less than in the USA.

The probability of transfusing blood from a person in the seronegative but contagious phase of the infection depends on the sensitivity of the screening test, the seroconversion rate in the adult population and the success of self exclusion strategies. If the window period is assumed to be 8 weeks, then the annual probability for HIV transmission can be calculated by multiplying the conversion rate in first time donors by a factor of 8/52. The risk is calculated similarly in repeat donors but taking into account the frequency of donation.

The AIDS epidemic shows signs of levelling off in some industrialized countries, but it is increasing in many developing countries. If the seroconversion rate is high, and if transfusion services are suspected of being used as testing sites in the absence of properly organized alternate testing possibilities, the question of transmission in the window period deserves special attention. Authors from Thailand recommend additional screening for HIV P24 antigen, but they add, realistically, 'if affordable'.

In Zimbabwe, the donor recruitment is targeted in populations where the rate of seroconversion is lowest (G Myllälä, personal communication).

The global process of demanding, and receiving, monetary compensation through legal action and political pressure has involved, besides solicitors and transfusion service directors, health ministers, governments and even heads of state. Since AIDS, blood transfusion is not what it used to be; the general public increasingly requires transfusion without any risks. However, it is clear that a zero risk can never be achieved.

**HIV-2**

HIV type 2 (HIV-2), which is related to the simian immunodeficiency virus prevalent in some monkeys, is at present largely confined to West Africa. Cases of HIV-2 have, however, been reported also in Europe and North America. In most instances the persons have been immigrants from West Africa, and in Europe the highest incidence has been in Portugal, France and Germany. Compared to HIV-1, HIV-2 plays a minor role in the AIDS pandemic. The virus seems to cause a more benign version of AIDS than HIV-1. The incubation time is probably longer and the pathogenicity may be milder.

Because of cross reaction with HIV-1, most of the current anti-HIV screening assays are able to find a large proportion of HIV-2 infections as well. However, the competitive assays, which are practical in the blood transfusion services because of their low rate of false positives and the short time needed for completion of the test, have been poorest in detecting HIV-2 antibodies. Therefore, many manufacturers have developed combined HIV-1/HIV-2 tests.

The restricted epidemiology of HIV-2 would not warrant systematic screening for this agent in blood donors from many countries. However the sensitivity of combined screening tests now equals the sensitivity of tests for HIV-1 alone, so it is reasonable to use these combination tests even in areas where there has not yet been a single case of HIV-2 recorded. The infection is known to be transmitted through infected needles, and persons with known risk factors to HIV-1 could spread HIV-2 to areas of low current prevalence.

**Cell-associated viruses**

Some blood-borne infections are transmitted only by blood products which contain whole cells. Viruses such as CMV, human T-cell lymphotrophic viruses (HTLV) I and II and Epstein-Barr virus (EBV) have not been observed to be transmitted by pure plasma
derivatives such as coagulation factor VIII concentrate, but fresh frozen plasma may occasionally contain enough cellular elements to be the source of infection. Preventive strategies can therefore be focussed on either providing products from serologically-negative donors or by removing infectious cells from the product.

CMV

CMV infection is common in many populations. Antibody prevalence in industrialized countries varies from 30-80%. In normal immunocompetent people the disease varies from subclinical to lymphadenopathy and mild hepatitis. However, the immunocompromised, such as patients undergoing aggressive cytotoxic treatment or bone marrow transplantation, or grossly premature infants, may acquire a very serious, often fatal disease. Prevention of CMV transmission is therefore not applied to all transfusions but is targeted to defined patient groups.

After primary infection the virus becomes latent. PCR techniques have shown viral DNA in cells of all or most antibody-positive people, but attempts to culture the virus from cells of such persons have generally failed. Symptoms of CMV disease are not necessarily due to a primary infection from exogenous sources but may be a reactivation of the latent virus. It is not fully understood why only a small proportion of seropositive blood units may cause the disease, but at least one factor seems to be that the more viable neutrophils and monocytes there are in the blood product, the higher are the chances for transmitting the infection into a seronegative recipient. Consequently, fresh blood is riskier than stored blood in this respect.

Since the methods to detect the virus or viral DNA directly are cumbersome and require specialized laboratories, antibody assays are used to indicate viral presence. Many transfusion services have established panels of anti-CMV negative donors, and seronegative patients who are undergoing bone marrow or solid organ transplantations, who are under cytotoxic treatment for malignant diseases, who have acquired or congenital immune deficiency, and premature babies, are given cellular blood products only from such donors. Seropositive recipients gain no advantage from receiving CMV negative units.

The policy of transfusing only seronegative units to seronegative patients at risk has been quite successful in preventing serious CMV disease, but there are also several problems. The donors, once determined seronegative, may meanwhile acquire the infection, and thus all units designed for transfusion have to be retested for anti-CMV before administering them to the patient. Creation and maintenance of a sufficient donor panel with all ABO and Rh groups may require extensive efforts in a population where the infection is common (up to 80% or more). Finally, blood with no measurable CMV antibodies may still be totally safe. Sensitive PCR techniques have found viral DNA in some seronegative individuals, and there are also some, very exceptional, clinical cases of transmission of the infection from seronegative donors.

A certain viral load is needed before CMV infection is transmitted. Sufficient depletion of virus-carrying white cells is therefore another preventive strategy. Modern blood filters have made this approach highly successful. When the results of six different studies were combined, none of the 207 patients receiving exclusively filtered red cell and platelet concentrates were infected whereas out of 171 patients who were given standard preparations, 25 had serological evidence of CMV infection.

Our own experience has confirmed this. Depletion of leukocytes provides some additional advantages such as prevention of HLA immunization and possibly also graft versus host reaction due to transfusion. It is essential that the filtered red cell concentrates contain less than $5 \times 10^7$ and platelet preparations five times less leukocytes, but even lower concentrations can be relatively easily achieved. A strict quality control is needed to ensure that in no instance is the white cell concentration unacceptably high.

HTLV

HTLV-I is a RNA retrovirus that may cause two types of disease: HTLV-associated myelopathy (HAM), also called tropical spastic paraparesis, and adult T-cell leukaemia. The virus is prevalent in some areas of the world, notably in the Caribbean, parts of Africa and Southern Japan. Most infected individuals are symptomless carriers, and the infection results only occasionally in either leukaemia or myelopathy. Although the average incubation time and the natural course of the infection remain largely unknown, it has been estimated that the lifetime risk of an infected individual developing adult T-cell leukaemia is a few per cent.

It was first shown in Japan that HTLV-I is also transmitted through blood transfusion. There are reports of cases of myelopathy acquired through blood transfusion, but so far there is no direct evidence that transfusion might have caused leukaemia. However, it may be only a question of time before such link is established, even if the great majority of people transfused with contaminated blood remain symptomless for all their life.

In Europe and North America this virus has been encountered almost exclusively in individuals who have been infected abroad. According to the results of the American Red Cross, among 4.5 million donations screened for HTLV-I/II, the confirmed positivity rate was 0.017%. The prevalence in Northern Europe is still much lower, and in many countries the virus has not been observed at all. This, combined with the low pathogenicity of the virus, makes the probability of transfusion-transmitted disease very low.

EBV

EBV, i.e. EBV, is transmitted via saliva and by direct contact. The virus is common (up to 80% or more) in the world's population, and the occurrence of some diseases is strongly associated with EBV infection. EBV causes a variety of infections, including infectious mononucleosis (IM), Burkitt's lymphoma, nasopharyngeal carcinoma, and post-transplant lymphoproliferative disease (PTLD).

HTLV-I is a retrovirus that causes adult T-cell leukaemia and myelopathy. It is transmitted through blood transfusion, and the prevalence of HTLV-I infection is highest in the Caribbean, parts of Africa, and Southern Japan. The virus is also transmitted through sexual contact and by vertical transmission from mother to child.

HTLV-II is another retrovirus that causes adult T-cell leukaemia and myelopathy. The prevalence of HTLV-II infection is highest in the Caribbean, parts of Africa, and Southern Japan. The virus is also transmitted through sexual contact and by vertical transmission from mother to child.

HTLV-III is the retrovirus that causes AIDS. The prevalence of HTLV-III infection is highest in the Caribbean, parts of Africa, and Southern Japan. The virus is also transmitted through sexual contact and by vertical transmission from mother to child.

HTLV-IV is the retrovirus that causes adult T-cell leukaemia and myelopathy. The prevalence of HTLV-IV infection is highest in the Caribbean, parts of Africa, and Southern Japan. The virus is also transmitted through sexual contact and by vertical transmission from mother to child.
disease extremely low even without any preventive measures. Antibodies to HTLV-1 can be easily tested for by techniques based on enzyme immunoassay. There is no good confirmatory test but both Western blot and radioimmunoprecipitation (RIPA) tests have been employed for that purpose. Antibodies against HTLV-I cross react with HTLV-II, which is presently believed to be a rather innocent virus not responsible for clinically serious disease. In the American experience, HTLV-II seems to be more common in the blood donors than HTLV-I. From the counselling point of view, distinction between these two viruses is important.

General screening of blood donors for antibodies to HTLV-II has been started in Japan, the USA and France. In the last country, only blood intended for preparation of cellular products is required to be tested. This limitation makes little difference in practice. The cost effectiveness of the screening in very low prevalence areas is questionable.

Other viruses
Parvoviruses cause a number of diseases in animals, but only type B19 is an important cause of human disease. The infection is symptomless or causes a benign erythema and arthropathy. It is common since more than 50% of adult population has antibodies against this virus. In selected people, such as blood donors, blood transfusion services have not so far added Parvovirus B19 into the increasing array of virological screening tests. However, one centre in Japan has very recently judged the risk high enough to warrant general testing of blood donors for B19 (T. Hosoi, personal communication).

Prevention
Prevention of infectious complications of blood transfusion is based on five strategies:

1. Selection of donors
2. Laboratory screening
3. Microbiological inactivation of products
4. Confining blood transfusion to cases with strict clinical indications
5. Use of autologous blood.

In most cases, all these strategies should be used in parallel, one not excluding another.

Selection of donors
Voluntary and nonremunerated donors are more prone to give a candid health history than donors receiving cash payment. Markers of viral infection are also more common in paid than unpaid donor populations. For these, and other reasons, it is a worldwide policy that all donors of whole blood should be voluntary and unpaid. The commercial plasma industry, mainly in the USA, uses paid plasma donors, and its main approach to increase the safety of plasma products has been to develop viral inactivation methods. Admittedly, it has been quite successful in this policy, but recent accidents in the manufacturing process have shown that a single means to prevent infection is not sufficient. The European Community, Japan and many other countries have elected to use exclusively voluntary and unpaid donors for providing both whole blood and source plasma.

Laboratory screening
By definition, blood donors are healthy. For viral markers they represent a very low prevalence population which sets special requirements for the specificity of a screening test. A specificity of 98% is unacceptably low, since the great majority of the remaining 2% will be false positives and represent a large number of donations which would be incorrectly discarded. A rate of false positives approaching 1 in...
Inactivation of viruses

Plasma products are usually made from pools consisting of thousands of individual plasma units. Contamination of such a pool may have catastrophic consequences as shown by the haemophilia tragedy. Effective viral inactivation without affecting the biologically-active, often labile, blood proteins has remained many technical problems, but this may be in addition to consideration.

A new screening test should not be introduced if the risk of transmitting a disease is very remote. Cost considerations aside, each new test complicates the logistics of releasing safe and screened blood units. The risks of mislabelling, mixing two samples or blood units, errors during maintenance of a large quarantine stock and handling a very large data base may be greater than the risk of infection per se if the screening procedures are not well planned. In addition, factors such as exclusion of a number of blood units and donors, and the necessary counselling of donors thought to be healthy must be taken into consideration.

References


Addendum

Cases with unexplained severe immunosuppression but without evidence of HIV infection have been described. A recent expert meeting of the World Health Organization concluded, however, that they are not epidemic in nature, they may represent different entities with various causes and that at present there is no evidence that such a condition would be transmitted by blood. 48