Transmissability of HIV,¹
The Causative Agent of AIDS,
By Blood and Blood Products

The human immunodeficiency virus (HIV-1), previously named lymphadenopathy-associated virus (LAV) or human T-lymphotropic virus type 3 (HTLV-III), is a retrovirus which has been spreading around the world from 1978 to 1980. A large body of epidemiological and virological evidence implicates this virus as the causative agent of the acquired immunodeficiency syndrome (AIDS). It is unknown where this virus originated from; but we have to be aware of the fact that it might be present everywhere¹. In the last 3 years, a new variant of HIV-1 was found² which is now named HIV-2. This virus includes the isolates HTLV-IV and LAV-II present in several countries of West Africa. HIV-2 seems to be indistinguishable from the simian T-lymphotropic virus type 3 (STLV-III), recently renamed SIV-2, found in African green monkeys.³ The clinical course of the HIV-2 infection seems to be more benign, but cases of full blown AIDS due to this virus have also occurred² and people have died.

After entering the body, a virus has to infect a cell to survive. HIV-1 enters CD4-lymphocytes (i.e., helper T-lymphocytes) or macrophages or oligodendrocytes of the brain by binding to the CD4 receptor molecule via its envelope glycoprotein,⁴ gp 120. After penetrating the membrane, the envelope of the virus is unrolled, the core opened and the ribonucleic acid transcribed to DNA by the key viral enzyme reverse transcriptase. These DNA sequences are integrated into the genome of the host cell. As long as a cell is alive, virus may be produced by such a cell. While most viruses need activation of the cell for their production, the HIV-1 has its own activation mechanism consisting of proteins produced by the transcriptional transactivator (TAT) and/or the alternative reading transactivator (ART) gene(s).⁵

A CD4-lymphocyte may produce millions of HIV particles before actually being killed by the virus. The action of HIV on macrophages is, on the other hand, not cytopathic. Some of the lesions of the AIDS victims with neurologic disorders are caused by activated macrophages destroying the Schwann cells. Severe encephalopathy is due to multifocal destruction of cells within the brain.⁶

¹ The article is a review of the literature until April, 1987.
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The CD4–lymphocyte is essential to the composition of the cellular immune system. By its action, B–lymphocytes are triggered for an anti-HIV specific response i.e., the production of antibodies directed against the different viral components. It is the CD4–carrying cells which induce the formation of antigen specific killer cells necessary for the destruction of virus presenting cells within the body. The severe liver injury in hepatitis B virus infection is caused by the destruction of liver cells by the body’s own immune system. Part of the T–cell depletion, which occurs in the final stage of the AIDS disease cannot be explained by the viral action alone; the cellular immune system must also be involved.\

Having at least 3 different cell types in the body where HIV replicates, it is not surprising that the virus has been isolated from blood, plasma, semen, saliva, urine and tears, as well as from cervical fluid. Thus every body fluid may be potentially infectious despite the fact that the amount of virus found in semen is in no way comparable to that in tears. Consequently there are two main routes of transmission of HIV: by sexual contact and by blood or blood products.

One remark is noteworthy about the sexual mode of transmission. Generally one out of 200 contacts leads to a new infection of an individual but, similar to impregnation, one sexual contact may be enough. In this sense, it does not matter if the sexual contact happens between man and man, man and woman or woman and man. If the exchange of body fluid is prevented, the chance of viral transmission is reduced drastically (hence recommendation of the use of condoms).

The handling of an infectious disease is normally approached in two ways. One is cure of the disease by specific therapeutical agents. For viral diseases, a limited success has been achieved in the last decade using acyclovir for Herpes simplex infections and dipropanylhydroxyguanosine for the treatment of cytomegalovirus infections. Some of the patients treated with azidothymidine to reduce the symptoms of the HIV infection have benefitted, while others, especially with signs of encephalopathy, remained in the severe stage. Some patients, in whom the azidothymidine doses had to be reduced because of the toxic side effects (anaemia, drastic fall in the white blood cell count), worsened and died very quickly. Other drugs for treatment have been presently either withdrawn or are not available.

The other approach to a disease is prophylaxis, such as by vaccination. For instance, the use of vaccines has lead to a drastic drop in the infection of hepatitis B virus, especially in medical staff. The experience with this vaccine has shown an efficient way for the prevention of a viral disease, which like the HIV infection is blood borne and sexually transmitted. However, despite multiple
efforts worldwide to produce a HIV vaccine, a safe and efficient material is not available at the moment but probably within sight in the next two years.

To date, the only way to reduce HIV transmission in the population at large is by educating people about the route of virus infection and the methods of prevention.

Apart from sexual contact, the other mode of transmission stated was by blood and blood products. By this route, more than 500 recipients of blood transfusions and organ transplants have been infected worldwide. Many of these patients have died of AIDS. The statistical mean after receiving an infected single donation and developing AIDS is 5 years. Cytoprecipitation of fibrinogen and factor VIII out of large plasma pools and subsequent lyophilization of the isolated end-products is such a gentle treatment that most viruses survive this process, including HIV. By administration of such factors, 50 to 90% of the patients with severe haemophilia have been infected. Without exception, these patients also suffered from other viral diseases like hepatitis B and hepatitis non-A, non-B until special treatment of these preparations had been introduced.

Since the spring of 1985, a screening test for the presence of HIV-1 antibodies has been available, and HIV-1-infected blood donations could be detected and withdrawn. The number of newly infected individuals due to blood transfusion has fallen drastically since that time, showing the efficiency of this measure.

As was known from hepatitis B infection, screening of blood donations and collecting the plasma into a large pool is an insufficient method to prevent infection, since one unrecognized plasma donation is sufficient to infect the entire plasma pool. The reason may be lack or failure in the sensitivity of the laboratory methods employed, insufficient synthesis of protective (virus neutralizing) antibodies or the diagnostic window in freshly infected individuals where the virus is already present but the antibody production has not begun.

Screening for the presence of antibodies and of antigen will allow the elimination of viruses for which assays are available. However, this procedure will not eliminate common agents which cannot be assayed, such as hepatitis non-A, non-B virus or agents whose virus nature is still unclear, such as the agent causing Creutzfeldt Jakob disease. These reasons have compelled finding inactivation procedures for blood products, which would be able to eliminate most of the known and supposed viral infective agents. Blood itself cannot be sterilized since all available methods lead immediately to cell destruction.
Two approaches for the inactivation of blood products are currently available: treatment with physical methods like heat and UV light or with chemical methods like β-propiolactone or tri (n-butyl) phosphate and sodium deoxycholate. Inactivation of blood components is complicated by two facts: on the one hand the virus has to be brought to a state of unreplicability, on the other hand the enzymes (especially the clotting factors) have to be preserved in their native (active) state.

Physical methods: Frequently employed is inactivation by heat, in the dry or liquid state of the blood product preparation. Inactivation in the dry state (i.e., lyophilisate) is performed at 60 to 68°C for at least 30 hours; shorter periods have not led to a total inactivation of all viruses (HIV, HBV, HNANBV). More efficient than heating in the dry state is treatment of the lyophilized material by steam at high pressure in a lamellar layer. According to the results of clinical trials with such material, HIV and HBV are destroyed but the efficacy of inactivation for HNANBV remains to be determined. A further and quite efficient method is treatment of the blood products in the liquid state at high temperature for various times in the presence of stabilizers and it appears that all known viruses can be destroyed by this procedure, depending on the conditions employed.

Chemical methods: The only procedure presently available uses tri (n-butyl) phosphate and sodium deoxycholate. This procedure is most efficient for viruses enveloped by a lipid membrane, including HIV and HBV. According to the results of inactivation experiments with the Hutchinson strain of HNANB virus, this is also destroyed; but a final answer can be given only by clinical trials of the product, which are in progress. According to the above consideration, parvovirus, the causative agent of German measles and some kinds of fetopathy in pregnant women, should resist this treatment because it lacks a lipid envelope. Laboratory trials to answer this question are presently under way.

Combined chemical/physical methods: The procedure used for many years is the treatment of blood products with β-propiolactone and UV irradiation. Both procedures work by inducing ruptures in the nucleic acid strands and by protein modification. The combination of both methods leads to a total inactivation of all known viruses and various other pathogens (bacteria, fungi, phages), which is of great potential interest. However, the denaturation of clotting factor VIII is so harsh under these conditions that most of its activity is lost. Less sensitive proteins survive this process and are used for clinical treatment. Clinical trials with products inactivated by this method have shown that all known viruses including those relevant to blood products are inactivated (HIV, HAV, HBV and HNANBV).
The treatment of patients with products of human origin (insulin substitution, blood transfusion, cornea or cartilage transplants) is one of the fundamental concepts in modern medicine. If materials are used which originate from multiple donors, the risk of the presence of an infectious agent which then is distributed to whole batches of product rises enormously. Because of demands on the safety of these products, inactivation procedures, which lead to an efficient destruction of viruses, are indispensable.

References


