The problem of human immunodeficiency virus (HIV) infection and transplantation

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Abstract. The problem of human immunodeficiency virus (HIV) infection and that of the acquired immunodeficiency syndrome (AIDS) are becoming increasingly important in clinical transplantation. The epidemiologic characteristics of this infection are important factors in determining the impact of this infection on transplant patients: in particular, the presence of a transmissible virus in the blood, tissues, and body fluids of even asymptomatic individuals for prolonged periods; the role of lymphocyte activation in accelerating the pace and effects of HIV infection, with the transplant patient having more reasons for lymphocyte activation than other patient categories; and the possible contributions of immunosuppressive therapy to the course of HIV infection. Already, at least 20 cases of primary HIV infection conveyed by infected blood or allografts at the time of transplant have been noted; a similar number of transplants have been carried out in asymptomatic carriers of the virus. The initial impression is that the course of HIV infection in these patients is accelerated, but information is incomplete and an international registry for the study of this problem has been established.

Key words: Transplantation - AIDS - HIV infection.

The most dramatic medical event of the 1980s has been the advent of the hitherto unprecedented epidemic of opportunistic infection and malignancy now known as the acquired immunodeficiency syndrome (AIDS). As in most areas of medicine, AIDS is having and will continue to have an important impact on clinical transplantation. The epidemiologic exposures of the transplant patient, the use of immunosuppressive therapy for the life of the patient, the virtually universal presence of a variety of infectious agents in these patients, and the occurrence of allograft rejection all interact to produce a clinical condition in which AIDS is likely to be manifest. That this prediction has been fulfilled has already been documented in a series of reports in the literature [3, 8, 14, 15, 17, 21, 23, 24, 26, 29].

The purpose of this review is threefold: (1) to delineate the epidemiologic and pathogenetic reasons for the especially high risk of the transplant patient for this condition, (2) to outline what has thus far been clinically observed in this patient population, and (3) to suggest steps that might be taken to limit the influence of this epidemic on the practice of transplantation.

Epidemiologic considerations

Since AIDS was first described in 1981, nearly 75,000 cases have been documented throughout the world, with a mortality rate in these individuals approaching 100% within three years of diagnosis. The etiologic agent of AIDS, the human immunodeficiency virus (HIV), previously known variously as the lymphadenopathy-associated virus, the T-cell leukemia virus type III, and the AIDS-associated retrovirus), is thought to infect an additional 1-2 million Americans, thousands of Europeans and, perhaps, millions of Africans. This asymptomatic but infected population is thought to serve both as the reservoir from which future cases of
AIDS will emerge and as the major source of future spread of the virus [9].

The epidemiologic aspects of HIV infection are determined by the following general characteristics: (1) HIV has a prolonged viremic phase in both symptomatic and asymptomatic individuals; (2) HIV is present in transmissible form in virtually all bodily fluids of infected individuals; (3) there is a high rate of asymptomatic but transmissible infection among individuals of high risk population groups; and (4) this asymptomatic, albeit infectious, state can persist for periods of years [1]. Not surprisingly, then, three modes of transmission of HIV have been defined:

1. **Inoculation with blood.** This method of inoculation includes transmission of HIV with blood and blood products, needle sharing among intravenous drug users, injection with a contaminated needle, and needle stick, open wound, and mucous membrane inoculation with contaminated blood.

2. **Sexual transmission.** Although the greatest impact of the AIDS epidemic has been observed among homosexual men, it is now clear that HIV can be transmitted heterosexually as well, from women to men as well as from men to women.

3. **Perinatal transmission.** HIV infection may be acquired by the neonate from an HIV-infected mother in three possible ways: (a) by infection in utero, (b) by the inoculation or ingestion of blood and other infected fluids during labor and delivery, and (c) by the ingestion of infected breast milk.

It should be emphasized that neither personal contacts that do not fit into one of these categories nor insect bites can transmit HIV from infected individuals to others [9, 26].

These observations are of the greatest importance for the practice of transplantation. Blood transfusion is clearly an effective means of transmitting HIV; the minimum risk of HIV infection occurring in the recipient of a unit of blood from an infected donor is at least 66% [30]. It should be emphasized that HIV transmission has been noted with the administration of whole blood, blood cellular components, plasma, and clotting factors. In contrast, immunoglobulin preparations, albumin, plasma protein fraction, and hepatitis B vaccine - all prepared from human blood - are without risk of transmitting HIV. In particular, immunoglobulin preparations that have contained antibodies to HIV do not contain infectious virus, unlike the previously listed blood components in which the presence of antibodies connotes infectivity. The difference here is that HIV is inactivated by the process of preparing immunoglobulin. Immunoglobulin preparations that are presently being marketed have an extra safeguard: they are prepared from units of blood that are antibody- and virus-negative [2, 26].

Although it has been suggested that the transmission of HIV with allografts is uncommon [8], more recent data suggest that transplanting an organ from an HIV-infected individual is as efficient a means of transmitting the virus as is transfusion [3, 14, 15, 24, 26, 29]. A recent experience in North Carolina [3] underlines this point.

A victim of a motor vehicle accident received 56 units of blood and blood products in a heroic attempt to save his life. Following the declaration of brain death, multi-organ donation was carried out. A blood specimen tested after the transfusions (and just prior to organ donation) was negative for HIV, although a specimen that was drawn prior to transfusion and that was later tested was floridly positive. The two organ recipients who survived for longer than three months (one kidney and one liver allograft recipient) developed evidence of primary HIV infection. Thus, although the amount of HIV in the circulation of the donor had been thoroughly diluted by the massive blood transfusions, the organs themselves all harbored sufficient amounts of virus to serve as efficient vectors of infection. Whether the virus conveyed with the allografts was present in residual traces of donor blood or in passenger leukocytes within the allografts themselves is currently unknown. Suffice it to say that organs and tissues of HIV-infected individuals are an extremely efficient means of transmitting HIV infection, and that transplant patients may be infected at the time of transplant with either blood transfusions or an allograft from an HIV-infected donor.

**Pathogenetic considerations**

The causative agent of AIDS, the human immunodeficiency virus, belongs to a group of non-transforming, cytopathic retroviruses called the lentiviruses. Other viruses of this group include visna virus (a sheep virus), caprine arthritis encephalitis virus (a goat virus), the simian T cell lymphotropic virus type III (STLV-III, which affects non-human primates), and another group of human T cell lymphotropic retroviruses more closely related to STLV-III than HIV, termed HIV-2 (which has been isolated from humans in West Africa). The first two of these produce chronic neurodegenerative diseases, whereas the latter two produce an immunodeficiency syn-