Review article

Aids, drugs of abuse and the immune system: a complex immunotoxicological network

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Abstract. Two of the most interesting questions often asked about AIDS is why many people do not become immunodeficient or get complicating disease when first infected with Human Immunodeficiency Virus (HIV) and what are the “risk factors” making some individuals more susceptible to the disease. A large majority of people with AIDS have a well established history of drug and alcohol abuse. Both drugs of abuse and alcohol have immunotoxic properties as evidenced by a number of studies. These include marked changes in the cellular, humoral and other components of the immune defense mechanism. Such a compromise of the immune system can render it susceptible to the development of AIDS after HIV infection. This paper reviews the evidence suggesting possible links between substance abuse and its immunotoxicology, and their possible roles in the pathogenesis of AIDS.

Key words: AIDS – Drugs of abuse – Immune system

Introduction

The AIDS problem

Five cases of Pneumocystis carinii pneumonia and 26 cases of Kaposi’s sarcoma were reported in homosexual men in mid-1981 (Gottlieb et al. 1981 a, b; Friedman-Kien et al. 1981, 1982). This was the first indication of a new disease complex which was subsequently defined and given the name, Acquired Immune Deficiency Syndrome or AIDS. Other groups are also at risk of getting AIDS including intravenous drug abusers (IVDA) and hemophiliacs (Center for Disease Control 1982; Moll et al. 1982; Wormser et al. 1983). In Africa, the epidemiology is different from that in the Western countries, where the majority of cases occur in homosexuals and IVDAs. In the African setting the disease is mostly heterosexually acquired by those with multiple sex partners (Van de Pere et al. 1984; Piot et al. 1984).

Development of AIDS is initiated by the Human Immunodeficiency Virus (HIV) (Gallo et al. 1983; Fauci 1988). The spectrum of HIV infection is wide ranging, from an asymptomatic condition to AIDS. Acute infection with HIV can result in the minority of instances in an overt seroconversion illness; an acute infectious mononucleosis like illness; an acute infectious mononucleosis like illness or in some cases, an acute encephalopathy (Carne et al. 1985, Cooper et al. 1985). Acutely infected individuals may recover, but it is prudent to assume that they are infectious to others. A proportion of the acutely infected do not recover and go on to develop chronic infection with the virus. This can take many forms including a totally asymptomatic illness, cytopenia, constitutional symptoms and opportunistic infections. The best documented state is that of persistent generalized lymphadenopathy syndrome (PGL). It is estimated that up to 20% of the people with PGL progress to AIDS (Metroka et al. 1983; Miller et al. 1984). Thus, only a proportion of the people chronically infected with the virus progress to “end stage” AIDS or the AIDS related complex (ARC). This manifested in two major ways; either with tumors such as Kaposi’s sarcoma or with various opportunistic infections. The former can be localized or widely disseminated, while the latter can involve any body system (Rolston and Bodey 1986). The median survival time for end stage AIDS varies on the type of presentation. Median survival for individuals presenting with Kaposi’s sarcoma is about 31 months, for Pneumocystis carinii 9 months, and for most other opportunistic infections 4–5 months (Rivin et al. 1984).

Immune System

The immune system is comprised of many components intertwined in a complex network. It reacts in response to
materials recognized by the system as foreign or antigenic (Roitt et al. 1989). This system is responsible for the maintenance of host resistance to invasion and disease caused by a wide variety of pathogenic organisms. Of significant advantage to the host are the several alternative responses in the immunological arsenal that may be recruited to combat an infection. Reduced immunocompetence could lead to an increase in the frequency, duration, severity or outcome of an encounter with a foreign pathogen. Increased immune activity may be of benefit or harm to the host, since it may lead to enhanced response to disease or else culminate in the development of autoimmunity or hypersensitivity reactions (Sell 1987a). Since either an abbreviated or an enhanced immune response may be harmful to the host, the immune system is a “double-edged blade” and an ideal response would be one which is sufficient to tackle any pathogenic insult but does not overdo itself to the extent of autoimmunity or hypersensitivity.

The immune system is a delicately balanced network involving responses of two major classes of lymphocytes, T cells and B cells, with the former having at least four major subsets. Lymphocytes participate in the regulation of other cell types such as macrophages, mast cells and granulocytes. Involved in this interaction are numerous molecular regulators which include lymphokines, complement components, inflammatory mediators, prostaglandins and cytokines (Sell 1987b). The innate response of the immune system to pathogens or neoplastic change is believed to involve granulocytes, monocytes, macrophages, natural killer cells, lyzozymes and complement components. The adaptive immune system response is induced by a “non-self” or foreign antigen. Vital to an appropriate response is the processing of the antigen by antigen processing cells (APC) and its presentation to the respective group lymphocytes (Roitt et al. 1989). The resulting lymphocyte response may involve predominantly T cells, B cells or both. In addition to the above factors, the integrity of the immune system is coordinated by endocrine, neuroendocrine and nutritional factors. Most secondary immune deficiencies involve defects in cellular responses mediated by T lymphocytes, macrophages and NK cells (Sell 1987b) and in general no modification of the immune system is completely specific. No defect involving one cell population is without compensatory or related changes in other cell population (Sell 1987b). These factors assure that the study and analysis of immunotoxicity is extremely complex.

AIDS: relationship to drugs of abuse and alcohol

Two of the most interesting questions often asked about AIDS are (a) Why do many people not become immunodeficient or develop complicating diseases when first infected with HIV?, and (b) What is there about the “risk groups” that make them more susceptible? The fact that direct exposure alone does not usually cause AIDS is now known, based on several direct exposure to infected body fluids of all kinds by health workers with perhaps only two having developed seropositivity for HIV and none having developed AIDS (Center for Disease Control 1985). It is also known that at least over a 6-year period between 60% and 90% of HIV infected homosexuals did not develop AIDS (Jaffe et al. 1985). Also recently documented was the presence of anti-HIV antibody in 25–41% of “non-risk” group patients with acute malaria but without AIDS (Volsky et al. 1986), suggesting that exposure to HIV alone may not be sufficient for the development or at least rapid progression to AIDS.

The presence of other factors in addition to the known causative factor (HIV) has made the etiology and pathogenesis of AIDS much more intriguing. A variety of cofactors have been postulated to exist including constant and repeated exposure to HIV. Others include different viral infections (such as Hepatitis B Virus, Herpes Simplex Virus and Cytomegalovirus), nutrition and genetic susceptibility. Among the most obvious of cofactors would be drugs of abuse and alcohol, since they seem to be common factors in most high-risk groups with the probable exception of hemophiliacs (Watson 1989).

In discussing the potential effects of drugs and alcohol use on the development and progression of AIDS, it must be kept in mind that little direct evidence is available to indicate a close association between the two. The fact that AIDS is highly prevalent in drug addicts is probably due to the direct transmission of the virus through contaminated needles rather than to any effects of the drug on the body systems. However, the matter is more complex. A strong possibility exists that substance abuse could down regulate or modulate the body’s natural defense mechanisms in such a way so as to allow easy infection with the virus and its subsequent progression. Indeed, experimental studies have shown that substance abuse is associated with increased HIV replication in blood mononuclear cells (Bagasara et al. 1989).

Modification of the immune system by alcohol and various drugs of abuse could take place in two ways. Firstly, they could render the individual more susceptible to HIV infection and, secondly, they could further alter the immune system to allow the virus to proliferate and set the onset of disease. To better understand the possible mechanisms involved in the interactions mentioned above, it is necessary to review the various effects drugs and alcohol have on the immune system.

Effects of drugs of abuse on immune function

Heroin, morphine and opiates

From as early as 1907, evidence has been presented as to how drug use leads to immune dysfunction (Atchard et al. 1928; Terry and Pellers 1928). This was further highlighted by the fact that drug users often had serious opportunistic infections and were prone to malignancies (Loura 1974; Sadeghi et al. 1979; Harris and Gerret 1982). Many immunologic abnormalities have been found in drug abusers, including decreased cutaneous sensitivity and mitogen responsiveness as well as changes in T cell subsets and lymphocyte proliferation. Drug users can become malnourished with significant weight loss and chronic liver disease and may also have other reasons for immunoregu-