

HIV Is Not the Cause of AIDS

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Human immunodeficiency virus (HIV) is not the cause of AIDS because it fails to meet the postulates of Koch and Henle, as well as six cardinal rules of virology.

1) HIV is in violation of Koch's first postulate because it is not possible to detect free virus (1, 2), provirus (3–5), or viral RNA (4, 6, 7) in all cases of AIDS. Indeed, the Centers for Disease Control (CDC) has established guidelines to diagnose AIDS when all laboratory evidence for HIV is negative (8).

2) In violation of Koch's second postulate, HIV cannot be isolated from 20 to 50% of AIDS cases (1, 9–11). Moreover, "isolation" is very indirect. It depends on activating dormant provirus in millions of susceptible cells propagated in vitro away from the suppressive immune system of the host.

3) In violation of Koch's third postulate, pure HIV does not reproduce AIDS when inoculated into chimpanzees or accidentally into healthy humans (9, 12, 13).

4) In contrast to all pathogenic viruses that cause degenerative diseases, HIV is not biochemically active in the disease syndrome it is named for (14). It actively infects only 1 in 10^4 to $>10^5$ T cells (4, 6, 7, 15). Under these conditions, HIV cannot account for the loss of T cells, the hallmark of AIDS, even if all infected cells died. This is because during the 2 days it takes HIV to replicate, the body regenerates about 5% of its T cells (16), more than enough to compensate for losses due to HIV.

5) It is paradoxical that HIV is said to cause AIDS only after the onset of antiviral immunity, detected by a positive "AIDS test," because all other viruses are most pathogenic before immunity. The immunity against HIV is so effective that free virus is undetectable (see point 1), which is why HIV is so hard to transmit (9, 12, 13). The virus would be a plausible cause of AIDS if it were reactivated after an asymptomatic latency, like herpes viruses. However, HIV remains inactive during AIDS. Thus the "AIDS test" identifies effective natural vaccination, the ultimate protection against viral disease.

6) The long and highly variable intervals between the onset of antiviral immunity and AIDS, averaging 8 years, are bizarre for a virus that replicates within 1 to 2 days in tissue culture and induces antiviral immunity within 1 to 2 months after an acute infection (9, 17). Since all genes of HIV are active during replication, AIDS should occur early when HIV is active, not later when it is dormant. Indeed, HIV can cause a mononucleosis-like disease during the acute infection, perhaps its only pathogenic potential (9, 17).

7) Retroviruses are typically not cytotoxic. On the contrary, they often promote cell growth. Therefore, they were long considered the most plausible viral carcinogens (9). Yet HIV, a retrovirus, is said to behave like a cytotoxic virus, causing degenerative disease by killing billions of T cells (15, 18). This is said even though T cells grown in culture, which produce much more virus than has ever been observed in AIDS patients, continue to divide (9, 10, 18).

8) It is paradoxical for a virus to have a country-specific host range and a risk group-specific pathology. In the United States, 92% of AIDS patients are male (19), but in Africa AIDS is equally distributed between the sexes, although the virus is thought to have existed in Africa not much longer than in the United States (20). In the United States, the virus is said to cause Kaposi's sarcoma only in homosexuals, mostly *Pneumocystis pneumonia* in hemophiliacs, and frequently cytomegalovirus disease in children (21). In Africa the same virus is thought to cause slim disease, fever, and diarrhea almost exclusively (22, 23).

9) It is now claimed that at least two viruses, HIV-1 and HIV-2, are capable of causing AIDS, which allegedly first appeared on this planet only a few years ago (20). HIV-1 and HIV-2 differ about 60% in their nucleic acid sequences (24). Since viruses are products of gradual evolution, the proposition that within a few years two viruses capable of causing AIDS could have evolved is highly improbable (25).

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Blattner and Colleagues Respond to Duesberg

Biology is an experimental science, and new biological phenomena are continually being discovered. For example, recently some RNA molecules were shown to act as enzymes, ribozymes, even though biochemistry text books state that all enzymes are proteins. Thus, one cannot conclude that HIV-1 does or does not cause AIDS from Duesberg's "cardinal rules" of virology. In fact, the Henle-Koch postulates of 1840 and 1890 were formulated before the discovery of viruses. They are a useful historical reference point, but were not regarded as rigid criteria by Koch himself and should not be so regarded today (1).

Duesberg's description of the properties of viruses is in error and

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provides no distinction between knowing the cause of a disease, that is, its etiology, and understanding the pathogenesis of this disease. Duesberg is noted for his discoveries about the viral oncogene *src*. There is no question that the expression of this gene in chicken fibroblasts results in sarcomas. However, no one can yet explain how the expression by the *src* oncogene of an altered tyrosine protein kinase results in a cell becoming neoplastic. Similarly, there are many unanswered questions about the pathogenesis of AIDS, but they are not relevant to the conclusion that HIV causes AIDS.

Duesberg presents six (or nine) cardinal rules for viruses. Most are not relevant to the question of etiology and are misleading or wrong about viruses in general and HIV in particular.

1–2) It was formerly true that evidence for the presence of HIV-1 could not be found in all AIDS patients. But the overwhelming seroepidemiologic evidence pointing toward HIV as the cause of AIDS spurred research to improve the sensitivity of the detection methods. Better methods of virus isolation now show that HIV infection is present in essentially all AIDS patients (2).

The CDC definition of AIDS has been revised several times as new knowledge has become available and will undoubtedly be revised again. The 1981 CDC definition of AIDS did not mention HIV, since no strain of HIV was known until 1983. Many cases of AIDS are diagnosed on clinical grounds alone because of the lack of availability or expense of HIV-1 antibody testing or because HIV testing is discouraged in some communities. Thus, rates of confirmation of AIDS cases by HIV testing in the United States vary geographically as reflected in CDC surveillance statistics.

3) It is true that HIV does not cause AIDS in chimpanzees. Most viruses are species-specific in host range and in capacity to produce disease. For example, herpes B virus, yellow fever virus, and dengue virus cause serious diseases in humans, but produce no disease symptoms during infection in many species of monkeys (3). Moreover, a virus closely related to HIV, simian immunodeficiency disease virus or SIV, causes an AIDS-like disease in rhesus macaques, but seldom, if ever, causes immunodeficiency in African Green monkeys (4, 5).

HIV-1 does indeed cause AIDS when inoculated into humans with no underlying medical condition. Accidental needlestick injuries with HIV-contaminated needles have resulted in HIV seroconversion and then clinical AIDS (6).

4) It is true that HIV infects only a small fraction of T cells. However, about 15% of the macrophage and monocyte cells from AIDS patients are positive for a viral protein, p24 (7), and the high concentration of this protein in the blood of AIDS patients indicates virus activity (8). The exact mechanism of CD4 cell depletion in AIDS patients is not known, but several indirect mechanisms are known by which HIV can cause CD4 cell depletion in laboratory studies and could operate in vivo.

5–6) Many viruses are highly pathogenic after evidence of immunity appears. For example, reactivated herpes zoster virus causes shingles, and reactivated herpes simplex virus causes local lesions as well as lethal necrotizing encephalitis; moreover, hepatitis B virus causes chronic active hepatitis, equine infectious anemia virus causes anemia, and visna virus causes central nervous system degeneration after the appearance of specific neutralizing antibodies (3, 9). (The last two viruses are lentiretroviruses as is HIV.) These diseases also can have long and variable latent periods.

7) It is true that some retroviruses, in particular, the highly oncogenic retroviruses of the kind that Duesberg has worked with, are not cytotoxic and promote cell growth. Most retroviruses have no effect on cell growth (9, 10). However, Rous-associated virus-2, spleen necrosis virus, visna virus, and HIV kill infected cells in

culture and can establish a chronic stage of infection in which surviving infected cells continue to divide (11).

8) It was apparently “paradoxical for a virus to have a country-specific host range and a risk group-specific pathology.” The properties of HIV resolved this paradox because the distribution of AIDS was found to mirror the distribution of HIV. The nature of the spread of the virus and the type of the AIDS-related clinical syndrome depend on social and environmental factors. Sexually active gay men and parenteral drug abusers were the first conduit for spread of HIV in the United States, whereas in some developing countries of Africa, young heterosexually active men and women were the major focus of spread. It is common for life-style to be a major determinant for the spread of an infectious agent. For example, until a vaccine became available, hepatitis B virus was clustered among the same U.S. populations that are now infected by HIV.

The underlying pathology in AIDS is immune deficiency. The nature of the opportunistic agents that invade the susceptible host is a function of which agents are most prominent in a particular population. For example, in the United States *Pneumocystis* is most prominent in affluent gay men, while human mycobacterial infections and toxoplasmosis are more frequent in socially disadvantaged Caribbean immigrants. Other agents, such as *Cryptococcus*, are more prominent in developing countries.

9) It is true that there are two viruses that cause human AIDS, HIV-1 and HIV-2. The origin of these HIVs is an interesting scientific question that is not relevant to whether or not HIV causes AIDS. Since a primate lentiretrovirus also causes an AIDS-like disease in rhesus monkeys, just as a cat lentiretrovirus, feline immunodeficiency virus, causes an AIDS-like disease in cats (12), one can suggest either that there is strong selection among retroviruses for this kind of pathology (13) or that the virus ancestor to HIV already had this property. In favor of the first hypothesis is the existence of feline, murine, and primate AIDS caused by retroviruses in a different subfamily from the lentiretroviruses (14).

In summary, although many questions remain about HIV and AIDS, a huge and continuously growing body of scientific evidence shows that HIV causes AIDS.

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