

What's new about AIDS?

Aileen Gray

*Faculty of Medicine
Queen's University*

ABSTRACT: AIDS is often portrayed by the media as an unusual virus. This paper places the AIDS virus in a number of different contexts to demonstrate that the AIDS pandemic is not a unique or a non-repeatable occurrence. Viral characteristics in general, and those of HIV (Human Immunodeficiency Virus) in particular, are examined, as are the concepts of viral evolution, human-virus interactions and host-parasite relationships.

Popular literature has experienced its own AIDS epidemic. Generally, a review of current articles about AIDS in various magazines will reveal a poor understanding of viruses and their ecological relationships. To properly understand AIDS, and to critically evaluate our treatment of AIDS and AIDS patients, the Human Immunodeficiency Virus (HIV) must be placed in an appropriate framework. After briefly discussing some media-enforced misconceptions about HIV, it will then be examined within a larger context of characteristics of viruses, viral evolution and change, human-virus interaction and the host-parasite relationship. Hopefully it will then be apparent that the idea of AIDS as a unique or non-repeatable occurrence is nothing but a misconception.

In the popular literature (and indeed some of the more scientific literature), HIV is portrayed as an unusual virus, and an exception to the rule. According to one *Time* article (Gorman, Aug. 3, 1992) it is "fiendish", a "quick-change artist", and a "formidable opponent" because researchers do not yet understand the "method to its madness". It is a big surprise that researchers are talking about a new kind of AIDS, and because of HIV's attack on our immune systems, it is deemed a "much more difficult virus than anyone anticipated".

Examples of other viruses can easily be presented to counter these claims to originality. Influenza is a well documented "quick-change artist", for example, and if viruses can be called "fiendish" then surely the herpes simplex viruses qualify by hiding from our immune systems in our nerve ganglia. Many of the characteristics of HIV — including those that make the virus deadly and those that have contributed to the evolution of an AIDS pandemic — are not at all unique and will be outlined below.

CHARACTERISTICS OF VIRUSES

A virus is a structure composed of a protein coat surrounding a nucleic acid molecule, either RNA or DNA, which is capable of replication only within living cells. Viruses are not organisms; they have no metabolism and are wholly dependent for their reproduction on mechanisms provided by host cells (Burnet and White, 1972: 53). Viruses are ubiquitous and affect almost every species of organism, including bacteria. They reproduce by attaching to host cells, penetrating them, and turning them into "virus factories". Instead of manufacturing the necessary materials for its own upkeep, the cell produces the nucleic acid of the virus and the viral protein coat (Balfour and Heussner, 1984: 5). New viruses can be released by "budding" individually from the cell; alternatively, when a great number of them have been produced, the cell may burst.

HIV is a retrovirus, which means that it uses an enzyme called reverse transcriptase to make DNA from its RNA. This viral DNA then joins the host cell's DNA in the nucleus and becomes part of the host's chromosomal material. As part of the host DNA it is known as a provirus (Grmek, 1990: 78). It can remain latent for a number of years during which the cell seems to be normal, with no apparent viral infection. The viral DNA can be transmitted to each daughter cell with every cellular division, and in this state it is invulnerable to drugs. It can only be killed by killing the host cell. Activation of the AIDS virus, when it is in this state, depends on the activation of its host cell, the T-4 lymphocyte, which usually occurs during another type of infection (Grmek, 1990: 78). This lifecycle is especially typical of the lentivirus subfamily of retroviruses, of which HIV is a member. Retroviruses belonging to this group cause slowly developing diseases (Haynes and Palker, 1988: 243).

HIV does not solely attack the T4 lymphocytes as was once commonly thought. It infects all cells with a particular molecule known as "CD4" on their membranes (Grmek, 1990: 79). This phenomenon is known as CD4 tropism (Morse, 1991: 389). The CD4 molecule, while present on the T-4 lymphocyte is also present on the macrophages (cells derived from precursor white blood cells known as monocytes). In fact, the macrophages are probably the most important reservoir for HIV (Grmek, 1990: 79).

There are other immunodeficiency viruses besides HIV, notably bovine, feline and simian immunodeficiency viruses (Morse, 1991: 389). While, like HIV, these are all retroviruses, the ability to infect and kill T4 lymphocytes is not restricted to this group. A mouse herpesvirus (MTLV) has been shown to specifically kill T-4 cells, while not affecting those T cells lacking the CD4 molecule. In addition, two recently discovered human herpesviruses (HHV-6 and HHV-7) are also thought to be CD4-tropic (Morse, 1991: 290). Thus, several hallmarks of the HIV virus are characteristic of other viruses, both within the lentivirus subfamily, and in a completely unrelated family.

HIV is well known for its ability to avoid destruction by the immune system, but in this it is not unique. Antibodies are produced against the virus, but seem to have little neutralizing effect. This is due to a phenomenon called antigenic drift (Laurence, 1985: 88). Antigenic drift refers to the processes of point mutation and selection which

result in minor changes in the envelope proteins of a virus (Fenner and White, 1986: 130). This is well documented in other viruses, most notably influenza A (Mackenzie, 1980) and a sheep virus known as Visna. Mutations result in altered proteins "causing any antigenic-specific immune response to miss its mark" (Laurence, 1985: 88). HIV can avoid the immune system in this way, but it has another characteristic which makes this of secondary importance. T-4 cells have numerous important roles. They bolster the natural killer cells and they stimulate macrophages to engulf viruses and present antigen. They also signal the B cells to start the antibody-production sequence (Laurence, 1985: 88). HIV, by killing the T4 cells, interferes with a pivotal player in the immune system. But, since the main reservoir of HIV is the macrophage this does not explain how all the T4 cells are affected. The CD4-binding protein of HIV is a soluble envelope protein which can coat uninfected CD4 cells. This has two effects. It makes the coated cells more vulnerable to lysis by the host's immune system, and it is thought to function as an "off signal" to T-cell activation, even affecting those T cells which are not infected with HIV. This would effectively inhibit any anti-HIV cellular and humoral immune responses, most of which rely on the T-4 cell (Haynes and Palker, 1988: 243,244). Thus, the immune system is effectively depressed.

Depression of the immune system is also not unique to the AIDS virus. Measles has also been noted to weaken immunity, although the effect is temporary (Laurence, 1985: 88). Other viruses, however, particularly retroviruses, can have the effect of permanently depressing the immune response. The feline leukaemia virus (FeLV) is also known to produce an immunosuppressant envelope protein, and "evidence has accumulated from other laboratories suggesting that many other mammalian retroviruses have protein components that produce immune deficiencies" (Laurence, 1985: 91). These proteins, like the soluble envelope protein of HIV, affect T4 cell function which results in a breakdown of the immune responses that depend on these cells.

MECHANISMS OF GENETIC CHANGE AND ADAPTATION

Mutation is an important part of a virus' ability to reproduce. Viral nucleic acid interacts with the DNA of the host cell, and some types will recombine with it. Retroviruses can sometimes pick up human oncogenes this way. Oncogenes are the genes responsible for generating cancerous cells. With a few minor alterations, these become viral oncogenes and endow the retrovirus with the ability to produce tumours (Fenner and White, 1986: 98). Viruses can also interact with each other within the host cell, if two different virions (single virus structures) are simultaneously present. Different types of genetic interaction can occur such as recombination, reassortment and cross-reactivation, which occurs when one of the virions has been inactivated. Reactivation of specific genes can also occur between two or more virions of the same strain, if inactivated, for example by exposure to ultraviolet radiation. This type of reaction could lead to the rejuvenation of UV-killed viruses if they were used as a vaccine. As a result, this method of vaccine production is not used (Fenner and White,

1986: 101,102).

Already discussed was the process of antigenic drift and its importance to HIV's avoidance of the immune system, but there are other important functions of mutation. Genetic changes are integral to the evolution of viruses. Mutation, recombination and selection are the mechanisms of evolution of viruses as with other life forms. Because these are functions of generation time, viral evolution may be faster than that of multicellular life forms (Nahmias and Reaney, 1977: 31). Recombination within the genetic code of a virus, as well as between two different viruses, as mentioned previously, is also an important contributor to genetic diversity. Some retroviruses can be driven into DNA forms which could then, as described earlier, recombine with cell genes or viruses from different families (Nahmias and Reaney, 1977: 33). This can result in significantly different envelope proteins, a phenomenon known as antigenic shift (Mackenzie, 1980: 130). This is how new strains of influenza are created, and could explain the different strains of HIV.

These genetic changes are particularly relevant for the search for a vaccine against HIV. Those viruses against which successful vaccines have been developed are relatively stable, with only a limited number of antigenic forms. HIV, however, undergoes steady genetic change, "perhaps because of its very rapid and relatively inaccurate replication" (Laurence, 1985: 88). Vaccines against influenza A must be produced regularly, and outbreaks are still not under effective control. New pandemics may arise from the exchange of genetic information with avian strains, through the mixing vessel of pigs in Southeast Asia (Scholtissek, 1992). This is impossible to prevent as it would require altering the lifestyles of hundreds of millions of people. HIV changes even faster than influenza A. Samples of virus isolated from different people "can differ by more than 30% in the RNA sequences encoding proteins that are thought to be key to recognition by T cells and antibody" (Laurence, 1985: 93). If a vaccine were made, a subsequent exposure to HIV would probably not be able to stimulate the immunologic memory that the vaccination process created. The current search is for invariant regions of the envelope to which antibody is able to bind (Laurence, 1985: 93).

Viral evolution is an ongoing process, and new viruses have arisen repeatedly (Nahmias and Reaney, 1977: 38,39), taking the form of an adaptive radiation. A statement by Grmek is enlightening:

No pathogenic virus is entirely new. They do not spring up *ex nihilo*. They come from ancestors that must have had similar genetic characteristics and must replicate somewhere, be it an animal population or a human population, in which they have struck a sort of biological equilibrium (1990: 143).

The genealogy of the AIDS retroviruses has yet to be worked out, but some relationships based on genetic similarities have been determined. For instance HIV-2 is closer to the simian immunodeficiency viruses than it is to HIV-1. Studies indicate that HIV-1 and HIV-2 cannot be descended from each other, and HIV-1 cannot have

descended from most known strains of the simian virus, although the virus infecting green monkeys is situated between HIV-1 and HIV-2. HIV-1 is probably descended from a common ancestor of HIV-2 and most of the simian viruses, although it could still have an independent simian origin. It is also important to keep in mind that the ancestor of the immunodeficiency viruses was not necessarily harmful (Grmek, 1990), and that further adaptive radiations may still occur, perhaps resulting in an even deadlier form of the virus.

AIDS AS A PANDEMIC

"A pandemic always results from the convergence of biological and ecological factors" (Grmek, 1990: 156). The addition of social factors to this statement would be even more appropriate, especially when considering sexually transmitted diseases. As will be demonstrated, the biological, ecological and social factors conducive to the emergence and spread of the AIDS virus are conducive to the emergence and spread of many viruses.

New viruses are being discovered as a result of human invasion into previously unoccupied territories, and the concomitant interruption of already established infectious cycles. This is how HIV-2 is thought to have been passed to humans. Incursions into the rainforest through increased land development and farming brought humans into closer contact with the monkeys believed to have been carrying a related virus (Preston, 1992: 62). However, there are many more examples of viruses emerging from the rainforest. "The rainforest, being the earth's largest reservoir of both plant and animal species, is also its largest reservoir of viruses, since all living things carry viruses" (Preston, 1992: 62). Ebola and Marburg viruses are examples of rainforest viruses, and outbreaks of these infections have been devastating, with a mortality rate of 88% for Ebola (Preston, 1992: 59). These viruses are also much more contagious than HIV. Morse's concept of "viral traffic" is useful here: "the great majority of 'new' viruses are not really new at all but are by-products of ...viral traffic: the transfer to humans of diseases that exist within some animal populations" (Preston, 1990: 16).

Infectious cycles can be transformed with changes in ecological conditions as with the aforementioned destruction of the rainforests, and also with changing global temperatures, especially if arthropod vectors are involved. Yellow fever and dengue fever could become significant problems in North America with increased temperatures, since the mosquitoes which carry them have already been established in the United States (Shope, 1991).

The spread of diseases in populations is affected by two parameters: changes in the degree of closeness of humans with other animals, including arthropod vectors, and changes in the size of human aggregations and in interactions within and between them (Fenner, 1980: 9). Having already discussed the first parameter, the second will now be the focus. With increased interaction between groups, as seen in the twentieth

century with more efficient methods of travel, the globe can be treated as a single population, as far as some viruses are concerned. Air travel allows viruses to spread from one continent to another in a matter of hours, as has been well documented with influenza (Mackenzie, 1980). With increased urbanization, there has been a rise in the population of cities worldwide, and hence, increased opportunity for the spread of disease (Fenner, 1980: 17).

Other modes of transmission have resulted from particular technological or social practices. The use of needles by drug addicts has been effective in spreading hepatitis B as well as AIDS. Similarly, vaccination with a limited needle supply and inadequate sterilization procedures has contributed to the outbreak of disease. One of the outbreaks of Ebola was facilitated by the use of five needles to give injections of antibiotics and vitamins to hundreds of people attending a clinic in Zaire (Preston, 1992: 68). New patterns of sexual activity also affect the transmission of STDs. The development of the birth control pill resulted in a decreased use of condoms, which concomitantly increased the exchange of body fluids between sexual partners. Not only is this conducive to the spread of AIDS, but the Herpes Simplex Viruses and many bacterial, fungal and even arthropod infections.

Some diseases are becoming more common due to the increased number of immunosuppressed individuals resulting from organ transplantation or cancer treatment. As seen with AIDS patients, these people often die of opportunistic infections, many of which are quite rare in normal individuals (Mims, 1980: 244). These patients subsequently become a reservoir of infections which can then be passed on. Some diseases have been delayed because of stricter hygiene measures which create a new population of "hypersusceptible individuals" (Mims, 1980: 244). Good examples are the frequent outbreaks of mononucleosis among the young adult population. If the Epstein-Barr virus which causes this disease is acquired in childhood, the resulting illness is often very mild or non-existent. Other examples of infections which are more serious when they are delayed are poliomyelitis, chickenpox, mumps and hepatitis B (Mims, 1980: 244).

All of these factors shape the emergence of new infectious diseases, their spread, their target populations and the areas in which they are concentrated. We should expect that there will be many more emergences of new infectious diseases, since the factors contributing to the emergence of the AIDS pandemic are not limited to this one disease.

THE HOST-PARASITE RELATIONSHIP

AIDS should also be examined within the context of the general host-parasite relationship. Hosts and parasites are "in a continuous state of flux. They are evolving in relation to one another,...to other features of their environment, and to such agents as drugs and pesticides" (Levin et al, 1982: 213). This is important for research into anti-AIDS drugs. AZT, one of the most effective "slowers" of the virus' progress, only lasts an average of 18 months until the virus develops a resistant mutation (Gorman, 1992: 21). This is not surprising, given that drug resistance is a common problem in treating many diseases, tuberculosis for example, and is also seen at a different level

in pest control. The concept of pathocenosis (Grmek, 1990) is useful here. Parasites interact with other parasites such that "the frequency and overall distribution of each disease, above and beyond various endogenous and ecological factors, depends on the frequency and distribution of all the other diseases in the same population" (Grmek, 1990: 159). This brings into greater focus the ability of viruses to interact with each other, and the ability of bacteria to exchange genetic information through plasmids (Lederberg, 1988: 352). Grmek goes even further and suggests that we must consider the interaction of *all* microbes:

[a] sort of confluence unifies not only all the diseases in a given population, from now on in almost all the populations of the world, but also the totality of microbes. Between these tiny and seemingly so simple organisms there are subtle equilibria, exchanges of information, and adaptive potentials whose existence we have scarcely begun to suspect (1990: 159).

It has often been assumed that the host-parasite relationship evolves over time to one that ensures the survival of both host and parasite, hence increased resistance on the part of the host, and attenuation on the part of the parasite. The result of this would be a gradual change from virulence to commensalism (Levin et al, 1972: 213). While this is indeed the case for some relationships, it is by no means characteristic of all. Bull, Molineux and Rice (1991) propose that the "selection of benevolence" in a host-parasite system is determined largely by the mode of transmission of the parasite:

[c]ooperation is not expected to be maintained whenever the chief mode of transmission is horizontal: a parasite's progeny infect hosts unrelated to their parent's host. Cooperation is expected to be maintained if the chief mode of transmission is vertical: a parasite's progeny infect only the parent's host or descendants of that host (1991: 875).

This is directly related to selective pressures on the parasite involving the availability of hosts. AIDS is chiefly horizontally transmitted, although it can be transmitted vertically. So, by this consideration, it is not necessary that it evolve into a more benevolent form.

CONCLUSIONS

Having examined characteristics of viruses in general, and AIDS in particular, it is fairly obvious that viruses can be extremely adaptable and powerful structures, which reproduce as effectively and as quickly as possible. How little we appreciate this is neatly illustrated by the use of baculoviruses as pesticides (see Falcon, 1982; Altmann, 1992). AIDS is not an unusual virus; after all what is a usual virus? But it has arisen in the age of science and medicine when infectious disease was believed to be a thing of the past. The pre- and early AIDS attitudes with respect to infectious disease tend to emphasize and exhalt the wonders of science, the 'magic bullets' and the eradication of several specific diseases through vaccination. Nothing more was expected from infectious disease, at least nothing that modern medicine could not

control. With a more modern perspective it is obvious that this is completely false. The progress of medicine during the twentieth century has "obscured the human species' continued vulnerability to large-scale infection" (Lederberg, 1988: 343). The so-called 'miracle drugs' have left us with a legacy of complacency and unfounded optimism on the part of the general public (Lederberg, 1988: 346) and on the part of the scientific community as well. With the re-emergence of tuberculosis, and the development of drug-resistant strains, we find ourselves faced with mortality rates similar to the pre-antibiotic years. If the AIDS pandemic has done anything for us, it has awakened us from our torpor with respect to infectious disease, and has forced us to re-evaluate our prevention and treatment programs.

We are also able to examine HIV in great detail, and as a result are learning a lot more about viruses in general. The fact that after a decade of study there are still mysteries is both embarrassing and discomfoting, so descriptions of a difficult, unusual, out of the ordinary virus are not surprising, and they allow us both to excuse our lack of knowledge, and to hope for a time when science finds both the answers and a cure. No other virus has received as much attention, but researchers who work with and study other viruses are scared, and they, better than anyone, have an idea of what is, or might be out there. AIDS is not an anomaly, nor an aberrant occurrence. "In the end the novelty of AIDS may have reflected only our imperfect knowledge of the natural world, not a radical new trend in viral evolution" (Morse, 1990: 16,17).

Viruses are ubiquitous. Thankfully many are presently harmless. But they must be viewed within the characteristics of their family and subfamily and within evolution in general. Evolution is not a static process. Mutation, recombination and selection ensure that the permutations of virus interactions are unlimited. We may be devastated by the results, but we should not be surprised.

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