The Forgotten Viruses

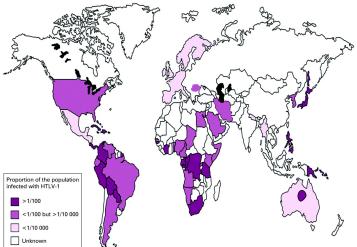


Before there was HIV there was HTLV, the Human T-Cell Leukemia Virus. In 1983, Robert Gallo and Luc Montagneir independently discovered the viral agent responsible for AIDS and called the newly discovered virus HTLV-3 and LAV, respectively. The name was eventually changed to HIV—Human Immunodeficiency Virus—but Gallo's initial use of the HTLV-3 tag is a reminder that two other HTLVs were known at the time.

Three years earlier, Gallo had isolated the first human retrovirus from patients with T-cell leukemia/lymphoma. This was <u>HTLV-1</u>. A year later, a second cancer-causing retrovirus (<u>HTLV-2</u>) was found.

The wealth of nations and a generation of scientists were directed at uncovering the mysteries of HIV's origins, genetics, epidemiology, and disease-causing properties. Thirty years later, many of those mysteries have been solved even as lingering questions have attracted the attention of a new generation of scientists and physicians. AIDS and HIV have cast a long, dark shadow over science and societies; still hidden in that 30-year-old shadow are the HTLVs.

They may have been forgotten by the public and many researchers, but these cancer-causing viruses did not disappear. It is likely they have infected <u>20 million</u> people worldwide and, in the absence of effective drugs and preventive vaccines, they continue to spread, causing significant sickness and death.



HTLV-1 causes two awful diseases: Adult T-cell Leukemia/Lymphoma (ATLL), and HTLV-1-Associated Myelopathy/Tropical Spastic Paraparesis (HAM/TSP). Though many HTLV-1 patients are carriers only and show no symptoms, they remain capable of transmitting the virus to others through blood donations, sex, and breastfeeding.

There is no effective treatment for HTLV-1 and -2 infections. The virus is

forever, but its clinical manifestations may be treated (albeit poorly) with a variety of drugs. Chemotherapy is the primary treatment for ATLL. Remissions occur, but relapse is common, and no available chemotherapy cocktail increases the median survival time of two years. HAM/TSP treatment options are even more limited. Therapies include drugs like corticosteroids, interferon, cyclophosphamide and therapies such as plasmapheresis (removal, treatment, and return of (components of) blood plasma from the circulation). There are no vaccines to protect against infection, and with limited therapies, prevention becomes key. Screening blood donors and pregnant women in places like Japan, Brazil, Europe and the U.S. is an effective way to prevent new infections from HTLV carriers. In other parts of the world, a lack of facilities and the odd clustering of viral locality make it difficult to estimate regional prevalence, effectively screen blood, or educate carriers.

More than 30 years have passed since the discovery of HTLV-1. During that time, the emergence of other dangerous viruses (HIV, West Nile, SARS, Monkeypox, Hendra, Nipah, MERS, Avian influenza, and Ebola, for example) has pushed HTLV-1 and -2 out of the medical limelight. Yet, these viruses never went away; they continue their silent migration among populations, slipping into the blood supply and passing undetected from mother to child. More recently, <u>two new HTLVs</u> (-3 and -4) were discovered in Africa. They have yet to be associated with any obvious disease, but more samples and further research may find new pathologies caused by these viruses.

So, the hunt goes on for new human retroviruses even as we continue to struggle with how to manage the older ones. Despite improvements in diagnostics there are still problems with test sensitivity and specificity, both of which complicate routine detection in donated blood. Moreover, the clustering together of positive cases in some regions and the total absence of virus in other regions make it difficult to estimate the number of carriers and the true burden of disease. As two French experts noted in 2012, "to give a precise estimation of HTLV-1 prevalence in a specific country or area is relatively difficult and, in some cases, nearly impossible."

Edward McSweegan, PhD 2015, GVN