

Viruses in search of 'compatible' diseases

Despite massive efforts by medical science to match diseases with specific causes, new agents of disease can appear without warning and disrupt any scientific self-confidence. The viral cause of AIDS, for example, existed for many years, yet researchers only recently identified the human immunodeficiency virus (HIV) and its devastating results. Scientists meeting last week emphasized that there are other "new" viruses whose complete medical consequences are undiscovered. These viruses include those that may be responsible for fetal death, the controversial chronic fatigue syndrome and lymph node cancers, according to participants of the Interscience Conference on Antimicrobial Agents and Chemotherapy held in New York City.

One such agent, human parvovirus B19, was "a virus looking for a disease" until 1981 — when it was first associated with aplastic crisis, a shutdown of the bone marrow's production of blood cells, says Larry Anderson of the Centers for Disease Control (CDC) in Atlanta. Researchers later tied the virus to severe skin rashes and arthritis.

This year, says Anderson, reports to the CDC indicate that the virus also may be responsible for some fetal deaths, as well as for bone marrow failure among patients with defective immune systems. Scientists now think the threat of parvovirus B19 may be most severe for AIDS patients, who cannot defend themselves against additional infections. Studies are underway at CDC, says Anderson, to determine the prevalence of B19 infection in the general population and to confirm the link between the virus and specific diseases.

The human B-lymphotropic herpesvirus (HBLV), first described in 1986, is another example of a virus with an incomplete medical history. The virus is unusual in that it is released from infected cells in membrane-bound packets, rather than through disruption of the cell. But this lack of cell "lysis" during HBLV infection does not mean the virus is harmless. Preliminary studies by Zaki Salahuddin of the National Cancer Institute and others have found HBLV in patients with various lymph node cancers, although no direct association between the virus and malignancy has been established.

The new virus also may be a factor in the course of AIDS, suggests Salahuddin. A random screening of subjects without detectable disease found about 16 percent had low levels of antibodies against the virus, while a survey of AIDS patients found that up to 70 percent had high HBLV-antibody levels.

Salahuddin says the antibody profile produced in response to HBLV is "very confusing and interesting." Antibodies

from humans infected with the virus unexpectedly cross-react with the chicken herpesvirus, but not with herpesviruses from other animal sources. This cross-reactivity — which usually signals some similarity between two viruses — coupled with the fact that there is no satisfactory way to detect the virus, leaves many unanswered questions about HBLV.

"We're really nowhere near drawing a conclusion regarding [HBLV's] pathological role," says Salahuddin.

Scientists at CDC are developing an assay for a herpesvirus they recently isolated, which appears to be identical to the HBLV found by Salahuddin's group, says CDC's Carlos Lopez. "We do not know what disease it causes, but I think we can fairly assume that this virus can cause human disease," he says. Using the test, the scientists are tracking the virus, which they call human herpesvirus VI (HHV-VI).

On the basis of these studies, Lopez says that "first and foremost, this is a

disease of children." Antibody production against HHV-VI apparently peaks sometime early in life, then "dwindles" as a person ages, says Lopez. Despite its apparent affinity for children, the virus is being considered by CDC, along with Epstein-Barr virus, as a possible cause of the adult condition called chronic fatigue syndrome, which scientists say may or may not be a distinct medical disorder. Officials at CDC currently are writing a description of the disease to be used for diagnosis, says Lopez.

Other early data suggest that HHV-VI can be sexually transmitted, and that in the general population, women are more likely than men to be infected. Lopez suggests that this higher incidence among women may be due to mothers' handling of infected children, or to the fact that the virus can be passed sexually from men to women more easily than from women to men.

Another curious aspect of the new herpesvirus is that it apparently inhibits HIV replication in cell cultures by 50 percent. But Lopez says the significance of this observation is still unclear.

— D.D. Edwards

...and a disease seeking its *raison d'être*

Since it was first reported in a Japanese journal in 1967, a relatively rare childhood disorder called Kawasaki syndrome has stubbornly rebuffed scientists' efforts to understand it. Recently completed studies indicate that the disease's incidence may be increasing in the United States and that it may be caused by a virus from the same group as that causing AIDS. But the lack of consensus among scientists on these and other aspects of the disease shows that Kawasaki syndrome still retains its secrets.

Characterized by fever, rash and occasional damage to coronary arteries, Kawasaki syndrome is thought to be an infectious disease — given its cyclic epidemics that vary with the seasons (SN: 7/6/85, p.10). Researchers have studied a series of possible disease agents, including house dust mites scattered in the air during the shampooing of rugs. But no cause has been unequivocally identified.

At last week's Interscience Conference on Antimicrobial Agents and Chemotherapy in New York City, Jane Burns of Children's Hospital in Boston called Kawasaki syndrome "a disease in search of a virus."

Burns says her "very preliminary" studies suggest that a virus producing the enzyme reverse transcriptase may be responsible. About 70 percent of 33 Kawasaki patients tested showed an elevated level of enzyme activity typical of reverse transcriptase. Viruses

making this enzyme are broadly classified as retroviruses, a group that includes the AIDS virus.

But Marian Melish of the University of Hawaii in Honolulu says that the enzyme activity seen by Burns "probably came from the patients' cells" and that her own studies do not support a human retrovirus as the cause. Melish, who was one of the first to describe Kawasaki syndrome in the United States, also reports that the incidence of the disease in Hawaii has stabilized in the past few years, yet continues to affect primarily those of Asian ancestry.

Some scientists think Kawasaki syndrome is becoming more common in the rest of the United States, where clinicians are trying to measure its possible long-term effects. Although the fever and skin rash of Kawasaki syndrome disappear and most patients recover, there are structural changes in the blood vessels of the heart in about 20 percent of patients — most of whom are less than 5 years old.

"Kawasaki syndrome is now considered the leading cause of acquired heart disease in [U.S.] children," Stan Shulman of Children's Memorial Hospital in Chicago said at last week's meeting. "We believe the incidence has clearly increased since 1983." He estimates that 2,000 to 2,500 U.S. cases now occur during an average year. Underreporting of the disease by physicians, however, makes exact numbers impossible to determine, he says. — D.D. Edwards