Does a Retrovirus Explain Fatigue Syndrome Puzzle?

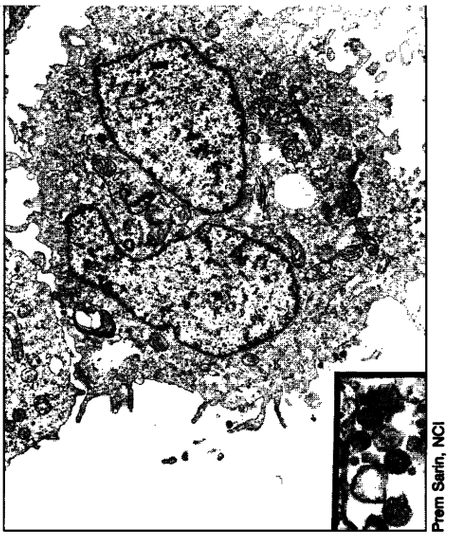
Provocative findings about a retroviral association with chronic fatigue syndrome made headlines, but scientists are skeptical

TEN DAYS AGO when Elaine DeFreitas of the Wistar Institute in Philadelphia presented some preliminary findings at a relatively obscure meeting in Kyoto, Japan, the news media pounced. Headlines appeared in almost every major newspaper in the United States. The reason? Her findings offered a possible cause for the still unexplained chronic fatigue syndrome (CFS). And the putative agent was HTLV-II, a human retrovirus—the same general category that includes the AIDS virus.

It now seems clear that the media's enthusiasm was, at the very least, premature. Even DeFreitas doesn't claim to have pinned down HTLV-II as the cause of the puzzling syndrome. And among other virologists, her team's findings are meeting a markedly cool reception, both because they are so sketchy and because several other viruses have been proposed as the cause of CFS only to fall by the wayside under closer scrutiny.

DeFreitas collaborated with two private clinicians who have dealt extensively with patients suffering from the syndrome: Paul Cheney of Charlotte, North Carolina, and David Bell of Lyndonville, New York. Cheney was one of the first to identify CFS in a 1984 outbreak around Lake Tahoe (see *Science*, 31 October 1986, p. 541). Bell recently identified a cluster of CFS in pediatric patients in a single town in New York.

According to a definition developed by the Centers for Disease Control (CDC), CFS is characterized by at least 6 months of debilitating fatigue that reduces normal activities more than 50%. In addition, a patient must be shown to be free of any preexisting organic or psychiatric disease and exhibit most of the following symptoms: headache, fever, sore throat, muscle aches, joint pain, generalized muscle weakness, lymph node pain, prolonged fatigue following exercise, and sleep alterations. All of the patients in the study (12 adults and 19 children) met the CDC criteria.



Prem Sarin, NCI

Viral Invader. *Electron micrograph of HTLV-II, a human retrovirus.*

Using the polymerase chain reaction (PCR), which amplifies rare stretches of DNA, DeFreitas examined blood from both adult and pediatric cases. In 10 of 12 adult and 14 of 19 pediatric patients she found DNA sequences extremely similar to some in HTLV-II, a human retrovirus discovered by Robert C. Gallo of the National Cancer Institute. DeFreitas also used in situ hybridization to find DNA sequences complementary to viral messenger RNA probes in lymphocytes, the white blood cells infected

Chronic Fatigue as Chameleon

London—As scientists from the Wistar Institute were announcing that HTLV-II might be linked to chronic fatigue syndrome (CFS), the Royal Society was holding a meeting to discuss the attitudes of British doctors toward that puzzling syndrome. The meeting made clear how little consensus there is about CFS: whether it is psychological or physical, indeed whether it exists.

Most of the scientists agreed that, in today's world, fatigue is a problem. Survey evidence suggests that one in five men and one in three women "always feel tired," said Anthony Mann, an epidemiologist at the Institute of Psychiatry in South London. And among the rest of us there's continuum of symptoms: On a 10-point fatigue scale, Mann said, most people score 1 or 2, while a few go all the way to 10. But Mann argues that "there is no evidence of a discrete syndrome. Like 'high blood pressure,' CFS is just one end of a continuous distribution of fatigue."

Furthermore, in the vast majority of CFS cases there is a psychological component. About 75% of CFS sufferers are clinically depressed, according to Peter White, senior lecturer in the department of psychiatric medicine at St. Bartholomew's Hospital in London. White said he believes depression is often a cause, rather than a consequence, of CFS and in preliminary studies he has seen marked improvement in CFS patients treated with an anti-depressant. Yet the presence of psychological factors does not rule out a role for infectious agents. Many viruses, including Epstein-Barr virus (EBV), have been associated with the syndrome. "But stopping EBV doesn't stop CFS," said Les Borysiewicz, a clinical virologist at Addenbrookes Hospital in Cambridge. "Whatever causes CFS, it isn't the virus itself."

The failure to find a conclusive link between CFS and a particular virus leads some researchers here to think there is no one cause. As Linda Parsons, senior research fellow in neurovirology at St. Thomas's Hospital Medical School in London, put it: "EBV and cytomegalovirus can do it. Coxsackie can do it. Maybe there is a single final common pathway in the brain for all these viruses. If so, we should be able to treat CFS whatever the cause."

Until there is a final understanding of what CFS is, there will be tension between doctors and the self-help groups for CFS patients. For example, Richard Edwards, a physiologist and clinician at the Royal Hospital in Liverpool, prescribes for CFS patients a graded exercise program—and says he gets good results. The toughest part, Edwards says, is persuading patients to start: self-help organizations say they should avoid exercise.

What angers the self-help groups most is the notion that CFS is not a specific disease with a specific cause. Anthony Clare, psychiatrist and medical director of St. Patrick's Hospital in Dublin, pointed out that in medical history there have been many fatigue "diseases" with shifting causes: "Neurasthenia, focal sepsis . . . food allergies, now viruses. Some people would always rather have a disease that might kill them than a syndrome they have to live with." ■ JEREMY CHERFAS