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BEYOND BUZZWORDS IN AIDS PATHOGENESIS

The comedian David Brenner used to tell this story about anxiety:

One of the most maddening things in the world is to hear a mosquito buzzing in the darkness of your bedroom. Your whole consciousness becomes focused on the sound, on waiting for the insect to land and bite.

But the buzzing is the mating call of the male, and only females draw blood.

So, if you hear a buzzing in your room at night, don't worry.

But if you *don't* hear any buzzing....

That's an idea that can keep one awake at night. And here's another.

Last month, University of California, Berkeley, retrovirologist Peter Duesberg issued a "Challenge to the AIDS Establishment": How can a virus that infects less than 0.01 percent of susceptible cells cause a cataclysmically destructive disease like AIDS? How can a virus that kills most infected cultures within days have an incubation period in man of 3–5 years? And how can one claim the viral infection is cytopathic to T cells when the richest source of research virus is a productively infected T-cell line? (*Bio/Technology* 5:1244, Nov. '87.)

Duesberg's analysis leads to one of two conclusions: Either the human immunodeficiency virus is a passenger (the most common opportunistic infection in those at risk for AIDS), or the virus plays a catalytic role in pathogenesis. The burgeoning AIDS literature does, in fact, offer some support for the latter conjecture. It may be time to re-evaluate the conventional wisdom.

In 1986, J. L. Ziegler and D. P. Stites of the Veterans Administration published their "Hypothesis AIDS is an Autoimmune Disease Directed at the Immune System and Triggered by a Lymphotropic Retrovirus" (*Clinical Immunology and Immunopathology* 41(3):305–313). Their thesis is that, since the virus initiates infection by binding to the T-cell's CD4 receptor, it must mimic an invariant component of the class II major histocompatibility (MHC) antigen. This imperfect camouflage may or may not make the virus invisible to the immune system; if the immune system does see the virus, however, real trouble starts. The body may produce antibodies that bind not only to the MHC II mimic, but to the immune system's own self MHC II—effectively sealing off the T-cell mediated portion of the immune system, resulting, in the authors' words, "in progressive disruption of antigen recognition, immunodysregulation, and dysfunctional responses of catastrophic proportion."

Thus, it may not be the virus itself, but viral envelope that causes AIDS.

Earlier this year, G. E. Ozturk and co-workers at the University of Colorado School of Medicine reported that they had found antilymphocyte antibodies in 8 of 10 AIDS patients tested (and 6 of 10 of the patients' sexual partners). These antibodies reacted with T and B cells, but not with platelets or red cells. Thus, the antibodies are not specific for class I MHC, but the pattern is consistent with class II MHC specificity (G. E. Ozturk, et al., 1987. "The Significance of Antilymphocyte Antibodies in Patients with AIDS and their Sexual Partners," *Journal of Clinical Immunology* 7(2):130–139.)

Though there are other indications supporting Ziegler and Stites's hypothesis, the evidence is obviously far from complete. Robert Gallo's group at the National Cancer Institute has been over some of this same ground and has found alternative explanations (G. M. Shearer, et al., 1986. "A Model for the Selective Loss of Major Histocompatibility Complex Self-Restricted T-Cell Immune Responses During the Development of AIDS," *Journal of Immunology* 137(8):2514–2521).

Still, an important question remains. In studying AIDS, are we mistaking the buzz for the bite?

Applause for FDA on t-PA

Congratulations to the U.S. Food and Drug Administration for exercising both its prerogatives and its common sense, and approving tissue plasminogen activator.

—Douglas McCormick