

## Medicine John Grauerholz, M.D.

### New viruses resist antibiotics

*More and more strains we can't cope with are now arising in immunodepressed patients.*

As if the spread of HIV infection were not enough of a nightmare in itself, it appears to be contributing to another major problem. This is the emergence of antibiotic resistance on the part of other viruses which commonly infect immunocompromised individuals. These viruses, members of the herpesvirus family, were among the first viruses for which successful, and relatively non-toxic, antibiotics had been developed.

The Feb. 2, 1989 issue of the *New England Journal of Medicine* contains a series of articles reporting on the development of antibiotic-resistant strains of two common herpesviruses, cytomegalovirus (CMV) and herpes simplex virus type 2 (HSV-2). Of the 16 patients reported in the three articles, 15 had AIDS and one was an elderly female with lymphocytic leukemia.

Infection with cytomegalovirus is a major cause of disability and death among transplant recipients and AIDS patients. Over 90% of AIDS patients are infected with CMV and evidence of widespread infection is present in 93% of autopsies on AIDS patients. CMV can produce severe disease of the brain, eyes, lungs, liver, stomach, and other organs.

HSV-2 is the virus which causes genital herpes. It, too, is highly prevalent in AIDS patients, especially homosexuals, and causes recurrent infections, which may produce extensive and persistent ulcers of the genitals or the mouth.

The problem with developing antiviral drugs has always been finding a drug which specifically interferes

with virus reproduction while not affecting normal cells. This is much more of a problem with viruses, since they utilize the metabolic machinery of the cell itself to reproduce themselves, than with bacteria, which have their own independent metabolic machinery.

One of the first successful antiviral drugs which could be given by mouth or by injection is acyclovir, which is effective against herpes simplex viruses and Epstein-Barr virus. Systemic acyclovir is effective in treating disseminated HSV infections in immunosuppressed patients and has become the drug of choice for treating these infections.

It now appears that acyclovir-resistant strains of HSV are developing among AIDS patients. Researchers from Boston and San Francisco describe a 12 cases of severe ulcerations of the mouth, anus, and fingers in AIDS patients, which failed to respond to acyclovir and from which they were able to culture acyclovir-resistant HSV-2.

Acyclovir is structurally similar to another drug known as ganciclovir. Ganciclovir, which is presently not on the commercial market, is an experimental drug which is active against cytomegalovirus. It appears to be effective in treating CMV infections of the eye and stomach, which are a significant cause of disability in AIDS patients.

Ganciclovir is at the center of a controversy over a Food and Drug Administration decision to require further studies before approving the drug for general distribution. The drug

has been administered under a "compassionate plea" protocol which allows the use of unapproved drugs. Since it is apparently effective in preventing otherwise certain blindness caused by CMV infection of the eye, no controlled studies have been done.

When the FDA refused to approve commercial sales until a new clinical trial was completed, there was an outpouring of protest by doctors and advocates for AIDS patients. The FDA is now reconsidering its decision, but, ironically, it now appears that CMV is beating FDA to the punch and becoming resistant to the drug even before it is approved.

Researchers from Minneapolis, Minnesota, Portland, Oregon and the Burroughs Wellcome Co. in Research Triangle Park, North Carolina, reported three different patients in which CMV resistance to ganciclovir appears to have arisen by three different mechanisms. "One patient was infected with a resistant virus, another was infected with a susceptible virus that became resistant, and the third was infected first by a susceptible strain and later by a genetically distinct, resistant one."

Ironically, Foscarnet, a drug developed to treat HIV infection, seems to be effective in treating at least some cases of acyclovir resistant HSV.

As the HIV epidemic continues its spread, we can look forward to more and more antibiotic-resistant viruses arising in immunodepressed patients. Considering the mutability of HIV itself, it is only a matter of time before AZT-resistant forms of HIV emerge, if they haven't already. As long as we refuse to confront the reality of the biological holocaust which presently surrounds us, we are going to continue to find out that the microbes are one step, or more, ahead of our ability to cope with them.