Antiviral Drugs: Possibilities Against Herpes

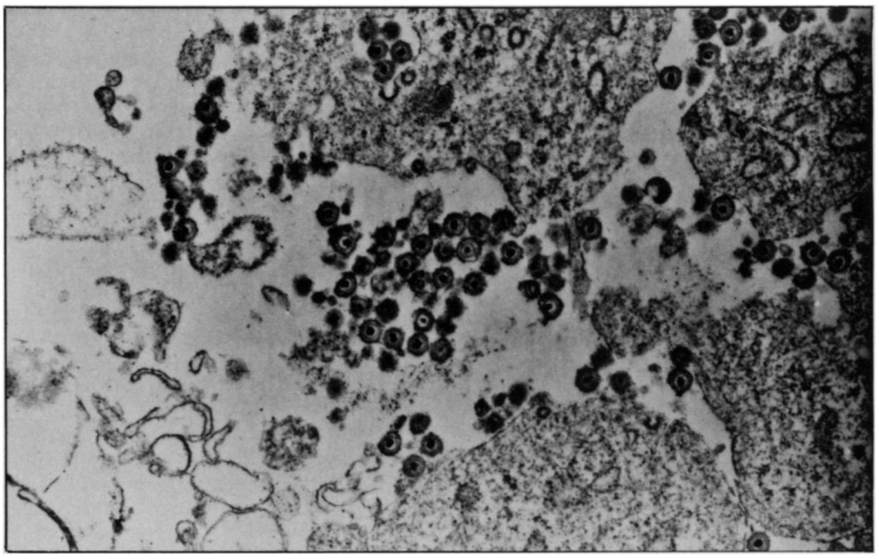
Unlike the development of antibiotics back during the 1940s and 1950s, the creation of antiviral drugs has been slow in coming. A primary reason is that antibiotics attack bacteria in the bloodstream without hurting cells. Hence, antibiotics are safe as well as effective. Antiviral substances, in contrast, have trouble killing viruses without also harming the cells they infect.

Nonetheless, medical scientists are finding or designing drugs that attack viruses selectively, that is, by largely or even totally sparing the cells that house them. Two of these drugs look especially promising in the treatment of more serious viral diseases, those that strike the body internally. One is Virazole. It has successfully countered flu in both animals and humans (SN: 3/20/76, p. 187). The other is adenine arabinoside or ara-A, which also goes by the trade name of Vira-A.

Last year, ara-A was found to lessen pain and to accelerate healing in immunosuppressed patients with herpes zoster infections. Herpes zoster can be extremely debilitating and sometimes fatal. Now ara-A has dramatically reduced both death and neurological damage among herpes encephalitis patients, thus constituting the first effective treatment of a life-threatening viral disease. Previously there was no way to counter this highly fatal brain infection that strikes several thousand Americans a year.

The study demonstrating ara-A's effectiveness against herpes encephalitis was conducted by Richard J. Whitley and Charles A. Alford of the University of Alabama at Birmingham and by researchers at both Alabama and 14 other medical centers. They describe their findings in the Aug. 11 NEW ENGLAND JOURNAL OF MEDICINE as a "breakthrough in systemic antiviral therapy." Richard Krause, director of the National Institute of Allergy and Infectious Diseases, hailed the results as a "major advance" at a NIAID press conference last week. NIAID financed much of the study.

Encephalitis due to herpes simplex virus is the most common cause of sporadic fatal encephalitis in the United States. If victims do manage to survive the disease, they are usually left with permanent neurological damage. So medical investigators attempted to treat it with two experimental antiviral compounds—idoxuridine and cytosine arabinoside. Idoxuridine looked promising until studies showed clear-cut toxicity without efficacy. That is when Whitley, Alford and their colleagues began conducting a clinical trial to see whether another experimental antiviral drug, ara-A, might be both effective and safe in the treatment of this disease.



Photos: National Institutes of Health

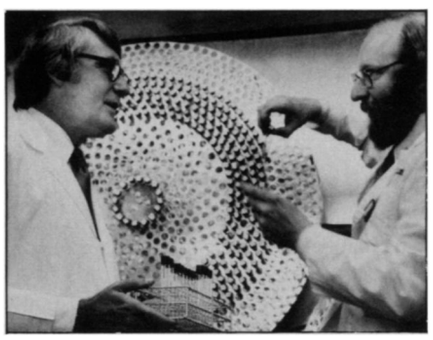
Encephalitis-causing herpes simplex virus (magnified 18,000 times). Ara-A fights back.

For patients to be enrolled in this trial, they had to first show symptoms indicative of herpes simplex encephalitis, such as altered consciousness, fever, personality change, memory loss, headache and vomiting. Herpes brain infection then had to be tentatively diagnosed with electroencephalograms, arteriograms and computerized axial tomography brain scans. Only if these procedures indicated that a herpes brain infection was present did patients then undergo brain biopsies. A biopsy consisted of drilling a tiny hole in that area of a patient's skull where herpes infection was suspected and withdrawing a bit of brain tissue for viral examination.

Twenty-eight patients proved to be brain-biopsy positive for herpes infections. Eighteen of these patients received ara-A, 10 a placebo, for a 10-day period. All of the patients were monitored daily for progression of disease, and clinical observations were recorded at five-day intervals for one month or until death. Follow-up exams, performed at 2, 3, 6, 12 and 24 months, focused on improvement or deterioration in neurological function.

Ara-A not only significantly reduced death among the patients, from 70 to 28 percent, but also the amount of permanent disability. Four of the surviving 13 drug-treated patients are now fully recovered, in contrast to only one of the three surviving untreated patients. What's more, these improvements were achieved without evidence of acute toxicity, such as damage to bone marrow, liver or kidney.

Ara-A had its origin 13 years ago when two French scientists screened a battery of plant and animal substances from land and sea for possible anticancer activity. Adenine arabinoside, from a Caribbean



Whitley and Alford diagnose brain tissues.

sponge, did little to retard the growth of cancer cells, the researchers found, but it did possess antiviral activity. So scientists at Parke, Davis and Co. in Detroit developed the chemical into an antiviral drug, and medical investigators began exploring its possible effectiveness against various herpes diseases.

Like some other promising antiviral drugs, ara-A appears to inhibit virus functions while partially sparing cellular ones. Whether it is free enough from toxic effects to be approved by the Food and Drug Administration for use against herpes encephalitis remains to be seen, though. The drug is known to harm bone marrow if used in large enough dosages. It has also triggered birth defects in the offspring of experimental animals and liver tumors in rats. However, the FDA did approve it earlier this year for external body use—specifically, to treat herpes infections of the eye.

Currently, only two other antiviral drugs are on the American market—idoxuridine, also for topical treatment of herpes eye infections, and amantadine, which has actually been approved by the FDA for preventing, rather than treating, a particular strain of flu. □