Whither Go the AIDS Treatments?

Will ribavirin and ampligen be used someday to routinely treat those with AIDS? Reports last week included the two drugs in a cornucopia of therapy possibilities, but it was evident that naming these, or any other drug, as acceptable treatments for AIDS will be a steady but slow process.

The drug ribavirin—subject of conflicting reports at last week's Third International Conference on AIDS in Washington, D.C. – is the most up-to-date case of a potential treatment awaiting final verdicts on its efficacy. In late 1984, researchers at the Centers for Disease Control in Atlanta reported that this known antiviral agent was effective *in vitro* against a virus possibly connected to AIDS (SN: 1/5/85, p.7). Ribavirin has not yet been approved for AIDS treatment in the United States, although recent changes in federal policy have shortened the experimental-drug approval process. Those changes were initiated by the approval of azidothymidine (AZT), currently the only AIDS drug clinically available in the United States (SN: 3/28/87, p.198).

After human clinical trials showed that ribavirin is relatively nontoxic, testing of the drug's effectiveness began last year, producing last week's contradictory results. "I don't know whether [ribavirin] works or not, but there are three or four pieces of preliminary evidence . . . that suggest it may have a benefit," Clyde S. Crumpacker said in an interview. He described a study, begun last July, by his group at Harvard Medical School and Beth Israel Hospital in Boston.

That preliminary study tested whether prolonged use of ribavirin would extend the lives of eight severely ill AIDS patients. In the six surviving patients, the drug thus far has prevented recurrences of pneumocystic pneumonia, a frequent cause of death in AIDS patients. (Although AIDS-related, the two deaths were not due to infection.) In seven of 10 untreated patients, the opportunistic lung infection reappeared within an average of 6.5 months, says Crumpacker.

Scientists elsewhere have concluded that prolonged ribavirin therapy can prevent the progression from lymphadenopathy (swollen lymph nodes) to AIDS in men immunosuppressed by the AIDS virus. Researchers at the University of Texas in Houston, the University of Southern California in Los Angeles, Cornell University in Ithaca, N.Y., and University of Miami (Fla.) performed the study, which included about 160 men who were infected with the AIDS virus but had not developed AIDS. According to P.W.A. Mansell of the University of Texas, during the six-month test period, none of the patients receiving 800 milligrams daily developed AIDS, whereas 11 percent of those taking 600 mg/da and 18 percent taking placebos did develop the disease.

However, Food and Drug Administration head Frank E. Young attacked these results during the meeting. "Regretfully," he said, "at this point we [the FDA] cannot find any evidence of effectiveness [of ribavirin]." (The drug's manufacturer, ICN Pharmaceuticals of Costa Mesa, Calif., was reprimanded late last month by the FDA for claims, based on this study, about the drug's efficacy. A similar ribavirin study at Johns Hopkins University in Baltimore and George Washington University in Washington, D.C., found "no statistically significant decline in progression to AIDS within 28 weeks" with ribavirin treatment, Andrew Vernon of Johns Hopkins said last week.

While ribavirin meets obstacles, another drug has entered the AIDS treatment race. Researchers at several centers in the United States, including Hahnemann University in Philadelphia, report in the June 6 LANCET that a drug called ampligen apparently plays a double role in restoring immune function and controlling AIDS virus (HIV) replication in patients. Made by mismatching periodic regions on a double-stranded RNA, the drug is thought to have broad cellular effects, including induction of antiviral enzyme production and release of factors like interferon.

In a pilot study of 10 patients with AIDS or AIDS-related syndromes, a multitude of changes were observed in both HIV numbers and immune response capability, say the authors. For example, in treated patients, levels of certain T lymphocytes and antibodies that fight HIV infection were either maintained or increased during the study – which lasted seven to 18 weeks, depending on the patient. Also, cellular immunity apparently improved, as did some symptoms like fatigue. However, given the preliminary nature of the study, the authors say it is too early to tell whether ampligen will "affect disease progression or survival" in AIDS patients. *– D.D. Edwards*

Whistling for lightning's rhythm

From our earth-bound perspective, lightning ranks high on nature's list of random and capricious acts. But a report in the June 5 NATURE suggests there is a subtle interplay between lightning and the magnetosphere, the region of the upper atmosphere dominated by the earth's magnetic field, and that this link can control the timing between lightning strikes.

William C. Armstrong at Stanford University found evidence for the lightning-magnetosphere link by studying radio signals that, when amplified, sound like the descending pitch of a whistle. Such "whistlers" are generated by lightning, but are heard in the opposite hemisphere. A lightning strike in Canada, for example, would create electromagnetic waves that travel along the earth's magnetic field lines to Antarctica, where the lines meet the earth. Along the way, the signal would be "spread out," causing the waves of higher frequency to arrive in Antarctica before the lower-frequency signals, giving whistlers their distinctive drop in pitch.

Scientists have known that following a lightning flash, whistlers can echo back and forth between hemispheres many times. What Armstrong has discovered, with data from Antarctica, is that on a few occasions new whistlers are heard at the same time as echoes. In one case, for example, a new whistler was recorded on the 12th echo of a previous whistler signal.

While this phenomenon is not very common, says Armstrong, it is intriguing because such periodic behavior probably cannot be caused by random processes. Armstrong speculates that new whistlers, and the lightning that generates them, are ultimately triggered by the first whistler in the following process: As the first whistler moves toward Antarctica, it gives northbound electrons (which are confined to move along the earth's magnetic field lines) in the magnetosphere enough energy to penetrate farther down into the atmosphere than usual. As they slow down, they produce X-rays that ionize the air, making it easier for an electric discharge to occur between thunderclouds and the upper atmosphere. As a result, lightning is released by the cloud, creating another whistler.

"Whether the details of Armstrong's ideas are borne out, only time will tell," notes Stanford's Donald Carpenter. "But [his work] is an exciting, provocative start," he says, and it supports a growing belief that the outer reaches of the earth are intimately connected to weather and other phenomena in the atmospheric layers closer to home.

– S. Weisburd