One-Two Punch for Hepatitis B

The most successful treatment yet for hepatitis B infection has been reported by a research team headed by Robert P. Perrillo at Washington University in St. Louis. The work could have a major impact, because about 200 million people worldwide chronically carry the virus; in the United States, about 1 million people carry the virus and more than 300,000 new cases of acute hepatitis B occur yearly. The virus can lead to cirrhosis of the liver and liver cancer, with 5,000 deaths yearly in the United States attributed to these complications. No consistently effective treatment for the infection now exists.

Although a vaccine for hepatitis B became available in 1982, the incidence of infection has increased nationwide in the past decade. Public health experts blame in part a general unawareness of who is at high risk of infection and thus should receive the vaccine. In addition, the effectiveness of the vaccine appears to be limited.

The new treatment combines two approaches tried previously. One is the use of immune-suppressing steroids. Administered long-term, these drugs ultimately result in increased viral replication, but when given over a relatively short time in high dosages they can lead to "immunologic rebound" — enhanced immune activity shortly after the drug is withdrawn — and remission of the disease. This method alone does not eliminate the virus and in some cases can cause life-threatening complications.

In the other approach, based on growing evidence that the development and persistence of chronic hepatitis B infection may be caused by insufficient production of alpha interferon by white blood cells called lymphocytes, researchers use the interferon itself — a small protein made by cells as a defense against viral infection and produced in quantity by laboratory recombinant techniques.

Perrillo and his colleagues gave patients a short (six-week) course of the steroid prednisone to "prime" the immune system, followed by alpha interferon. The investigators randomly assigned patients with proven chronic hepatitis B to two groups: 18 received the combination treatment and 21 were untreated. All patients were generally asymptomatic. Among those treated, replicating forms of the virus disappeared in nine. "Compared to the overall rate of response for treatment with interferon alone, which is about 30 percent," Perrillo told SCIENCE NEWS, "that is gratifyingly high."

But the "most exciting" aspect of the work was an even greater response to treatment by four in the group, according to an editorial by Richard D. Aach of Johns Hopkins University in Baltimore, which accompanies the report in the July 15 ANNALS OF INTERNAL MEDICINE. In these patients, who had been infected for a shorter time than the others in the treated group, the remaining evidence of infection — the hepatitis B antigen HBsAg — also disappeared. "If the nine are gold, this is the platinum standard," Perrillo says of the four from whom the antigen disappeared. These patients also developed hepatitis B antibodies, which the other patients in the study lacked.

The work, which Aach calls "the most promising approach to date," does not prove absolutely that the combination treatment can cure chronic hepatitis B, both Aach and the researchers point out, because of the short follow-up period. But it has spurred a large-scale investigation of 185 patients, now underway, comparing patients treated with alpha interferon alone to those receiving the combination and to untreated controls. Researchers express hope for the outcome of these trials next spring. "I'm excited," says Perrillo. "But I don't think this is the be-all and end-all. We are entering a whole new era for hepatitis, but no one treatment will succeed, because the patients and the stages of their disease are so different."

The latest findings of the Atlanta-based Centers for Disease Control, which charts U.S. hepatitis B occurrence, show that intravenous drug abuse has replaced homosexual activity as the major risk factor for the disease. Also, since 1985, the number of patients whose risk factor was heterosexual contact — with an ill person, with a carrier of the virus, or with multiple partners — has increased "modestly" to 24 percent, according to the July 22 MORBIDITY AND MORTALITY WEEKLY REPORT. — *C. Eron*

Charging ahead on antimatter microscopes

Materials scientists and biologists may get a new charge out of their microscopes with the development of two different positron reemission microscopes by separate research teams. These new antimatter microscopes should give scientists a much different view of subtle semiconductor flaws and delicate biological molecules, the developers say.

A high-resolution microscope that shoots not electrons but high-energy positrons — the electron's antimatter twin — through a sample has long been theorized but only recently developed. Since the January unveiling of such a transmission positron microscope, developed by two scientists at the University of Michigan in Ann Arbor, the Michigan team and a second group from Brandeis University in Waltham, Mass., and AT&T Bell Laboratories in Murray Hill, N.J., have sped along separate but parallel tracks to develop a far more useful microscope: the positron reemission microscope (SN: 2/20/88, p.124).

Positrons from a reemission microscope move fast when they leave their radioactive cobalt-68 source, but slow when they enter the sample, then bounce around at random until exiting the material. Besides causing much less damage to the sample than the speeding electrons in an electron microscope, the slow-moving positrons also reveal some of the subtle molecular and chemical structures around them. "Positrons are extremely sensitive to defects [in a crystal]," says James Van House of the University of Michigan. "They are far more sensitive than anything I know of."

Canter

White spots show the center of a beam of positrons that has passed through a thin wafer of nickel. The darker band through the center of the beam and the smaller band to the left are probably structural flaws in the crystal. The white square is a 1-micron scale marker.

Positron microscopes are so sensitive they can see where a single atom has been knocked out of position in a crystal, says Brandeis researcher Karl Canter. "A single missing atom will leave a hole in the material like a pothole, and it will trap the positron and annihilate it," resulting in fewer positrons reemitted from that position, Canter says. A head-on collision of a positron and electron converts both to pure energy.

The Brandeis and AT&T group has come up with a *transmitting* positron