SCIENCE NEWS of the week

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short time in high dosages they can lead to "immunologic rebound" — enhanced immune activity shortly after the drug is withdrawn — and remission of the disease.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."

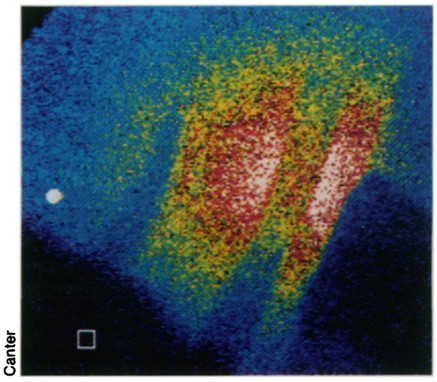
The latest findings of the Atlanta-based Centers for Disease Control, which charts U.S. hepatitis B occurrence, show that intravenous drug abuse has replaced homosexual activity as the major risk factor for the disease. Also, since 1985, the number of patients whose risk factor was heterosexual contact — 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

reemission microscope, in which positrons filter through the sample and come out the other side, while the Michigan team has developed a microscope that measures positrons that penetrate a sample's first 10 or 20 molecular layers and then are *reflected* back out the same side they entered. Both groups announce their findings in the Aug. 1 PHYSICAL REVIEW LETTERS.

The reflecting reemission microscope has the advantage of being able to scan thicker samples rather than the ultra-thin sample-wafers the transmitting microscope must use. But because of inherent design limitations, the reflecting microscope cannot get as high a resolution as the transmitting microscope, says Van House. The University of Michigan's reflecting microscope now has a resolution of less than 1 micron, while the Brandeis-AT&T microscope has a resolution about three times better. It eventually may be possible to push the transmitting reemission microscope's resolution into the atomic range by using a type of positron holography, Canter says.

Van House speculates that the positron's positive charge may allow chemists to spot the similarly charged hydrogen ions in chemical reactions. And because positrons interact with the electron "holes" that are central to the workings of semiconductors, positron reemission microscopes may also give computer engineers the opportunity to look into an operating integrated chip, he says. — *C. Vaughan*

Neural networks: The buck stops here

Neurocomputers are a breed of rapidly developing hardware on which artificial neural networks are trained to solve problems. Because these systems sort through immense amounts of information and pick out patterns from the onslaught of data, they may become useful tools in complex financial decision-making, according to computer scientists who presented reports in San Diego last week at the IEEE International Conference on Neural Networks.

One such neurocomputer-driven neural network, developed by Edward Collins and his colleagues at Nestor, Inc., in Providence, R.I., accurately makes decisions on mortgage risks commonly evaluated by mortgage underwriters.

Mortgages are usually underwritten by both a mortgage provider and a mortgage insurer, says Collins. A variety of information is considered before a mortgage is granted or denied, and disagreement is not uncommon between provider and insurer.

The researchers designed a neural network with three internal layers of processing elements. The strengths of connections that transmit messages between elements are altered as the system trains itself to achieve a desired output. In this case, the network was given information from 5,000 mortgage applicants; decisions on the applications made by a mortgage underwriter served as a training signal. Data fed into the computer covered each applicant's background and financial history, as well as the type of mortgage required and the property being sought.

Each layer of the network analyzed a piece of the complex financial input and determined the riskiness of granting a loan. A "controller" built into the neurocomputer then determined whether there was significant agreement between the three layers and, if agreement was reached, rendered a response.

When the statistical rules followed by the controller allowed for agreement in each case, the resulting decision agreed with that of the mortgage underwriter 82 percent of the time. When the statistical criteria for agreement between the three layers were tightened, says Collins, a response was obtained for one-third of the cases with 96 percent agreement.

Furthermore, notes Collins, the neural network was better than the mortgage writer at predicting who was a good loan risk and who would default. The system's three decision-making layers appear to enhance human judgments on loan applications, he maintains.

A similar neural network, designed by Shashi Shekhar of the University of California at Berkeley and a colleague, trains itself to rate the quality of bonds purchased by investors. Ratings reflect the probability of making a profit on a bond from a particular company. Financial information on a company is evaluated by ratings authorities who use standard mathematical equations to aid in their decisions.

When fed detailed, publicly available financial information on companies issuing bonds, the neural network predicted established bond ratings better than the typical mathematical procedures used by bond raters, says Shekhar.

"Neural networks provide a more general framework for connecting financial input about a company to an output, the bond rating," he asserts.

The stock market, however, is a tougher nut to crack. Economist Halbert White of the University of California at San Diego recently provided a neural network with daily rates of return on IBM stock over 500 days in the mid-1970s. The network did its best to extract predictable fluctuations in the stock's worth, White says, but so far only random jumps and dips are evident.

"It won't be easy to uncover predictable stock market fluctuations with neural networks," he remarks, "and if you succeed, you'll probably want to keep it secret." — *B. Bower*

Newton's gravity law may take a fall

Preliminary results from a gravity experiment conducted deep within the Greenland ice cap may lend support to the existence of a much-disputed fifth force of nature.

In the summer of 1987, investigators lowered a sensitive meter into a 2-kilometer-deep borehole in the ice and found gravity to be about 3 percent stronger than expected, says experiment coordinator Mark E. Ander of the Los Alamos (N.M.) National Laboratory (LANL), who collaborated with colleagues from several U.S. and British universities. Ander reported his findings to colleagues this week at Los Alamos and will discuss them next week at a conference in Australia.

In the experiment, the researchers compared their measurements with predictions based on the standard Newtonian law of gravity. The standard theory is called the inverse square law, because gravitational attraction is thought to depend on the square of the distance separating any objects. However, the results indicate "there is an *apparent* violation of the inverse square law," says Ander, who is still analyzing the measurements.

If the measurements are correct, says LANL theorist Richard Hughes, "it is telling us either gravity is more complicated than we ever thought before, or there is a new force of nature."

The Greenland experiment is the latest in a series of sensitive tests over the last two years that have reportedly found violations of Newton's law of gravity (SN: 12/19&26/87, p.388). Theorists have proposed that the minute departures from standard gravity may be manifestations of a fifth force — one that works over distances ranging from a few meters to several kilometers. Of the four traditional fundamental forces, gravity and electromagnetism act over infinite distances, while the strong and weak forces operate on the atomic and subatomic scales.

In design, Ander's project resembles a test conducted in Australian mine shafts two years ago. But the earlier experiment found gravity slightly weaker than predicted, an effect completely opposite that seen in the recent test. Ander says the Greenland borehole allows for greater accuracy because gravitational measurements depend on density and ice's density is more uniform than that of rock. He and others are planning further gravity tests in the Antarctic and in the ocean.

For now, physicists are not rushing to amend the inverse square law or declare the existence of a new force. Says geophysicist David Rubincam from NASA Goddard in Greenbelt, Md., "I think we're all waiting for more definite results since the Earth is a very dirty laboratory." — *R. Monastersky*