These "enhancing" antibodies, as they are called, do not neutralize the virus when they bind to it. Instead, Levy says, they may serve to promote the entry of the virus into cells, including macrophages, that the virus might not otherwise penetrate. There have been no problems with enhancing antibodies in the limited vaccine experiments so far.

No one is currently willing to predict how long it will be before an AIDS vaccine will be ready for human use. However, Bolognesi in his talk pointed out that when researchers were developing a hepatitis B virus vaccine, it took 10 years just to identify the viral antigen to use to stimulate a protective immune response. That is the stage that AIDS vaccine work is at now.

With the exception of the vaccine developments, scientific news from the AIDS conference was sparse. Still, there were a few surprises. Even the well-studied AIDS virus, known as HIV-1, has not yielded up all its secrets. William Haseltine's group at Harvard's Dana-Farber Cancer Center in Boston has found that the genome of HIV-1 has at least one, and perhaps two, previously unrecognized genes.

One of the new genes codes for a protein that stimulates the synthesis of HIV-1 proteins. "We believe it promotes the growth of the virus," Haseltine says. The Dana-Farber workers consequently call the new gene "*rap*" for "rapid growth gene."

The *rap* gene may have been missed in previous studies, Haseltine suggests, because the viral isolates used carried subtle mutations that inactivated it. The AIDS virus is notorious for its high mutability. A single infected individual can carry many different genetic variants of the virus.

The Dana-Farber workers have also discovered a second possible new gene in the HIV-1 genome, but have not yet found a function for it.

Simon Wain-Hobson of the Pasteur Institute in Paris also raised a warning flag about the extreme variability of the AIDS virus and what it might mean for attempts to correlate the molecular properties of the virus with its pathogenic effects in patients. Researchers have to grow the virus in cultured cells to get enough to study its molecular and genetic properties.

But Wain-Hobson and his colleagues have now compared gene sequences from cultured isolates with those of viral genes obtained from AIDS patients. "What we see in vivo is not the same as what we see in culture. To culture is to disturb," Wain-Hobson says. This means that studies of cultured virus isolates may not be relevant to what is happening in the patient. That, in contrast to the vaccine developments, is not good news. ■ JEAN L. MARX

Illuminating Jet Lag

Experiments show that bright light can reset the human internal clock by any desired amount, offering treatment for sleep disorders

WANT TO BEAT JET LAG? Spend a day at the beach once you get where you're going. That's the advice of sleep researchers Charles Czeisler and Richard Kronauer.

Czeisler and Kronauer headed a team of researchers from Brigham and Women's Hospital, Harvard Medical School, and Harvard University who studied how the human circadian clock responds to bright light. Their results, reported on page 1328 of this issue, indicate that our internal clocks respond to light in a fundamentally different way than previously thought. In particular, these clocks can be set forward or back as much as desired, with only two or three doses of light exposure. The discovery may open the door to treatment of sleep problems in not only international travelers but also shift workers and other people whose inner clocks malfunction for various reasons.

The claim of strong light resetting will be "very controversial among some people in our field," Czeisler predicts. Since the mid-seventies, many sleep researchers have held that humans are not sensitive to light resetting, and that people's internal clocks are synchronized by social contact. The new results contradict that view.

The first evidence that humans' internal clocks are indeed sensitive to light came in 1978, when Czeisler showed that ordinary room light of about 200-lux intensity is enough to synchronize the human circadian system to a 24-hour day. (Without some clues as to what time it is, a human's sleep/wake pattern, body temperature, hormone secretion, and various other physiological functions all follow a rhythm of approximately 25 hours.)

Then, in 1986, Czeisler began to wonder if he could take people whose circadian clocks were set to the wrong time of day and reset them. He exposed a 66-year-old woman with a chronic circadian disorder to 4 hours of bright light (7,000 to 12,000 lux, comparable to outdoor brightness at twilight) every day for a week, and even he was surprised at the result. Previous studies had shown that exposure to light would reset primate clocks by no more than 1 or 2 hours a day, Czeisler recalls, and "we thought her system would respond no more briskly than other mammals." Instead, within 2 days, the woman's clock was reset by 6 hours, enough to get her back in sync with the world.

Working from data obtained in resetting the older woman's clock, Kronauer, a mathematician, produced a theoretical model of how light affects the human circadian clock. Using the model as a guide, Czeisler began a new series of trials. He put subjects through 3 days of treatments, with 5 hours of bright light (about 10,000 lux) each day, timing the light at various points during the subjects' internal cycles.

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Airline terminal: *Circadian clocks awry.*

The results were dramatic. In subjects who were exposed to light during subjective nighttime, the treatment reset internal clocks by as much as 12 hours, unprecedented in human research.

The treatments involve more than simply exposing someone to bright light, Czeisler and Kronauer note. Getting the desired response demands timing the exposures properly. To this end, they have generated a phase response curve—a drawing that indicates how much a person's clock will be reset, depending on when the light exposures are given. ("Phase" refers to the time on a person's internal clock.)

Arthur Winfree, a specialist in circadian rhythms at the University of Arizona, says that as far as he knows this is the first published phase response curve for humans. He adds, however, that for years he himself has been using a "best guess" phase response curve gleaned from the little data available. To overcome jet lag when traveling, he spends a couple of hours in bright sunlight at the time indicated by the response curve—in the late afternoon after flying

from New York to Los Angeles, for instance. "Ten years ago I had a lot of problems with jet lag," he says, but with his bright light treatments, he adjusts easily to new time zones.

Czeisler notes his data also imply that the result of 3 days of exposure to light was not simply three times the result of 1 day's exposure. The first pulse of light, Czeisler says, made the circadian cycles irregular and suppressed their magnitude—that is, the changes in the body temperature throughout the day were smaller than normal. "Two cycles of exposure crushed the amplitude," he says, and the third exposure reset the pacemakers to new phases.

For theoreticians such as Winfree, the Czeisler data have important implications for the correct mathematical description of how the human circadian clock responds to light. Weak resetting is analogous to moving the hands on a clock ahead or behind by a hour or two. But in the strong response elicited by Czeisler, the clock is shifted by 10 or 12 hours without moving the hands through the intermediate positions—there is, in some sense, a discontinuous jump. Mathematically, these are two fundamentally different types of responses, called Type 1 and Type 0. (The 1 and 0 refer to a concept from algebraic topology—the winding number of the response curve.)

The fact that humans exhibit Type 0 resetting has an intriguing consequence, proved by Winfree: The right amount of light applied at the right time can bring the inner clock to a stop, so that there is no longer a strong circadian rhythm. Czeisler's claim that he crushed the amplitude of the circadian rhythm in some subjects seems to verify Winfree's theoretical prediction.

Kronauer brings all this down to earth with a simple example based on the predictions of his model, which he says agree with the data from Czeisler's trials. Suppose you fly to Sydney, Australia, 14 hours ahead of Eastern Standard Time. If you immediately go to work, so that you are exposed only to interior lighting, your clock will be reset only by about 1 hour each day. It will take 10 days to fully adapt.

But if you spend the first day outside, 6 to 8 hours of bright sunshine (about 100,000 lux) should do the work of the first two exposures in Czeisler's experiment: It will crush the amplitude of your internal circadian pacemaker and prepare it to be reset to the proper time with light exposure on the following day. Another day outside should lock your clock into Australian time.

So if you're flying to Australia, be sure to get there a couple of days early—go to the beach, catch some rays. Tell your boss it's doctor's orders. ■ ROBERT POOL

New Machine Sparks Rivalries at CERN

An intense 10-year effort by physicists and engineers at CERN is soon to bear fruit, when LEP, the world's largest particle accelerator, comes on-line next month

Geneva

LIKE SPRINTERS PREPARING for the big race, international teams of physicists at the European Laboratory for Particle Physics (CERN), Geneva, are operating in an atmosphere of rising tension and excitement as they make their final preparations for the "big event."

If all goes according to plan, the first week in August will see the maiden run of colliding beams of electrons and positrons in what will, for several years to come, be the world's largest particle accelerator, the 200-GeV Large Electron-Proton Collider (LEP).

The sense of anticipation in Geneva is intense. Four separate detectors, each a complete piece of experimental apparatus manned by its own team of several hundred physicists from around the world, are located at four different points around the LEP ring. And each has a chance to come up with the first anticipated result of major importance to physicists: a description of the chargeless Z particle that is sufficiently detailed to answer key questions about the fundamental building blocks of matter.

Later on, when the accelerator has been brought up to its full operating energy, the same groups will have an even bigger prize in their sights, namely proof of the existence of the two particles next on the "to be discovered" list. These are the top quark and the elusive Higgs boson, widely postulated as the source of the mass of the W and Z particles (both of which were first seen at CERN in the early 1980s).

With such attractive quarries looming, it is perhaps not suprising that scientists at CERN are working overtime to improve the chances of their team being the one that grabs the headlines. The one big surprise is that the CERN physicists are moving toward their prized goal virtually without competition from a key research facility in the United States, once seen as a big threat.

Carlo Rubbia: *His drive has brought LEP on-line at a rapid clip. He'll be looking for dramatic results.*

Late last year CERN physicists had watched anxiously as the European laboratory's main rival, the newly commissioned Stanford Linear Collider, seemed all set to crank out Z particles, precisely what LEP is designed to do. It looked as if CERN would not only be the loser in the race, but also would have lost to a more modest machine. The brainchild of Burton Richter, director of the Stanford Linear Accelerator Center (SLAC), the linear collider was seen in Europe as something of a spoiler—a deliberate attempt, fueled by appeals to U.S. chauvinism and the vaunted merits of "Yankee ingenuity," to cream off the most exciting discoveries in a cut-