Survival Bonus for People With AIDS

A viral infection that strikes many people with AIDS can spread like wildfire through the retina, leading to blindness if left unchecked. But a drug used to combat the eye infection may provide these patients with an unexpected, short-term survival bonus.

In a study of AIDS patients with cytomegalovirus (CMV) infection of the retina, people treated with the antiviral drug foscarnet lived an average of four months longer than those treated with a similar drug called ganciclovir, researchers announced this week at a press briefing held by the National Eye Institute in Bethesda, Md.

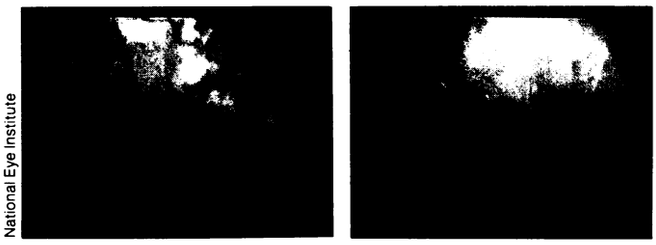
"The value of extra months of life with sight intact is immeasurable in alleviating the suffering of patients with AIDS," said Bernadine Healy, director of the National Institutes of Health, at the briefing.

In June 1989, the Food and Drug Administration approved ganciclovir to treat AIDS-related CMV retinitis; foscarnet received approval last month. While healthy people often carry CMV — a member of the herpesvirus family — without symptoms, the virus runs amok in people with damaged immune systems, especially those with AIDS. Approximately 20 percent of AIDS patients develop the progressive eye infection.

The recent trial, launched in March 1990 with funding from the National Eye Institute, was designed to compare the two drugs' safety and efficacy. On Oct. 7, an advisory panel of independent scientists cut the trial short after its review showed that AIDS patients taking foscarnet lived an average of 12 months after developing CMV retinitis, while those on ganciclovir survived for an average of eight months. Both drugs appeared equally effective in halting destruction of the retina, the panel found. On Oct. 17, the National Eye Institute sent a clinical alert to about 40,000 U.S. physicians, detailing the findings of the study.

Douglas A. Jabs of the Johns Hopkins University School of Medicine in Baltimore chaired the study, which involved investigators at 12 medical centers across the country. The researchers recruited a total of 240 AIDS patients right after their CMV retinitis diagnosis. Participants were hospitalized for two weeks of treatment with either foscarnet or ganciclovir, administered through a catheter inserted in a chest vein.

After controlling the CMV infection with this initial drug blast, the investigators discharged the volunteers from the hospital but kept them on lower intravenous doses to keep the infection in check. Throughout the study, the patients' personal physicians could prescribe other antiviral treatments, such as zidovudine (AZT), to combat the AIDS virus, HIV.



National Eye Institute

Left: AIDS-related CMV retinitis. Right: Retina looks healthy after foscarnet therapy, although infection may flare again.

In the statistical analysis, foscarnet's longevity bonus remained even when the researchers accounted for zidovudine therapy and other factors known to affect survival, notes epidemiologist Curtis Meinert of Johns Hopkins University. Although the underlying mechanism behind the survival bonus remains unknown, the researchers speculate that foscarnet may work synergistically with other antiviral drugs such as zidovudine. Another possibility: Foscarnet itself may combat HIV, Jabs says.

The new study is not the first to suggest an advantage to foscarnet. Because ganciclovir suppresses neutrophils, a type of white blood cell needed to fight infection, many AIDS patients who take it must reduce or stop zidovudine therapy, which can also deplete these cells. In contrast, foscarnet generally allows zidovudine therapy to continue at full strength.

However, not everyone with AIDS and CMV retinitis should take foscarnet, Jabs warns. Foscarnet can cause a decline in kidney function, he says, so patients who have already suffered kidney damage may do better on ganciclovir.

— K.A. Fackelmann

Galactic hot spots may signal supernovas

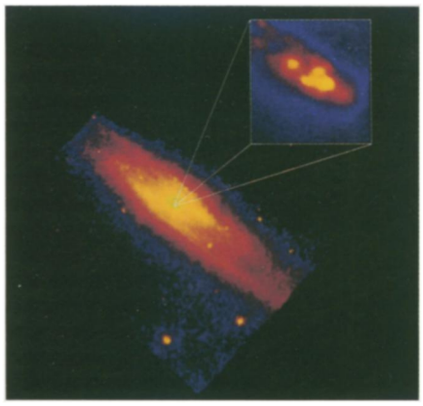
Tracking supernova remnants — the luminous matter ejected when massive stars explosively collapse — can help chart the evolution of galaxies. Astrophysicists now report a new technique for detecting these brilliant stellar objects. Using new, high-resolution infrared detectors that can home in on galactic hot spots, they scan for regions ablaze with infrared light.

Supernovas typically spew iron and other heavy elements into the surrounding space, irrevocably altering a galaxy's chemical composition. The associated shock wave can compress interstellar gas, an effect that might accelerate star formation. The shock also heats surrounding dust particles, causing them to glow brightly in the infrared.

Until recently, however, researchers lacked detectors sensitive enough to pinpoint the location of these telltale infrared emissions, notes Duncan A. Forbes of the University of Cambridge in England. Ground-based searches for supernovas in nearby, dust-shrouded galaxies, for instance, had to rely almost exclusively on radio surveys.

But with the development of more sensitive infrared detectors in the 1980s, that scenario began changing. The new detectors contain hundreds of individual light sensors, each of which possesses a resolution far exceeding previous infrared sensors.

Colin A. Norman of the Space Telescope Science Institute in Baltimore and Dave Van Buren, now at the California Institute of Technology in Pasadena, suggested in 1989 that astronomers could use the new devices to examine supernova activity in starburst galaxies. These dusty galaxies produce copious numbers of new stars — including many massive objects likely to end their life as supernovas. And although dust permits only a small amount of visible light to reach Earth, near-infrared light passes through dust unimpeded.



Forbes et al.

False-color infrared image depicts the starburst galaxy NGC 253. Inset shows the galaxy's nucleus, revealing four hot spots — one well-separated region and three that lie close together — that may indicate the location of supernovas.

Last year, Forbes and his co-workers imaged the nearby starburst galaxy NGC 253 using a large-format infrared detector at the Cerro Tololo Inter-American Observatory in La Serena, Chile. They were prompted in part by a 1988 report that the galaxy's nucleus contained several compact radio sources. The radio emissions hinted that NGC 253 might have a high rate of supernova explosions.

The team's investigation uncovered four previously unknown infrared hot spots near the center of the galaxy, Forbes says. Moreover, these active, infrared regions match the locations of the radio emissions, he and his group report in the Oct. 20 ASTROPHYSICAL JOURNAL LETTERS. These hot spots also coincide with radio sources detected in a follow-up, higher-resolution radio survey of NGC 253, reported by James S. Ulvestad of the Jet Propulsion Laboratory in Pasadena, Calif., and Robert R. J. Antonucci of the University of California, Santa Barbara, in the September ASTRONOMICAL JOURNAL, Forbes notes.

Forbes and his coauthors caution that the hot spots could result from activity not directly related to supernovas. For example, young supergiant stars and ionized hydrogen gas in the galaxy's interstellar medium also produce intense infrared emissions. However, unlike the spectra associated with supernova activity, these infrared signals would contain little radiation from ionized iron.

Since his initial study of NGC 253, Forbes told SCIENCE NEWS, he and a team that includes Reinhard Genzel of the Max Planck Institute for Physics and Astrophysics in Garching, Germany, have detected infrared iron emissions from regions of the starburst galaxy that appear to coincide with the hot spots. The new, unpublished finding all but clinches confirmation that the infrared emissions result from supernova activity, he says.

Van Buren disagrees, arguing that the brilliance of these hot spots suggests star clusters produced the radiation, not a supernova. But he concurs with Forbes that the infrared detectors "are more sensitive and can do a more thorough job" of searching for radiation characteristic of recent supernova explosions than radio telescopes. The new infrared detectors also probe more quickly and can image sources in more distant galaxies than radio telescopes, Van Buren says. Like Forbes, he plans to continue searching for infrared hot spots that may signify supernova activity. — *R. Cowen*

Drugs, depression and molecular ferries

Three teams of neurobiologists have characterized two types of nerve-cell proteins implicated in drug addiction and depression. Their findings, described in the Oct. 25 SCIENCE, may contribute to a better understanding of how stimulants, such as cocaine, and some antidepressant drugs affect the brain, according to the researchers.

The investigators focused on so-called transporter molecules, which serve a ferrying function in the brain. After neurotransmitters deliver a chemical message from one nerve cell to another, specific transporter proteins cart them back to their cells of origin. Drugs such as cocaine block the activity of some transporter molecules, creating a surplus of a particular neurotransmitter in the junctions between the nerve cells.

Two research groups — one led by Shoichi Shimada of the National Institute on Drug Abuse in Baltimore, the other by John E. Kilty at Yale University — isolated from rat brains the DNA sequences used by nerve cells to make transporter proteins that target the neurotransmitter dopamine. The researchers then inserted the DNA sequences into lab-grown cells, causing the cells to make dopamine transporters. When they exposed cells containing the dopamine transporters to cocaine and to dopamine-sensitive antidepressants, such as desipramine, the drugs significantly reduced the transporters' ability to take up dopamine.

Scientists believe dopamine influences pleasure-seeking behaviors.

The researchers also found that the dopamine transporters strongly resemble two other transporter molecules previously identified in rat brains by other investigators. One of these ferries the neurotransmitter gamma-aminobutyric acid (GABA) back to the cells that released it; the other handles norepinephrine.

In a separate study of rat brains, a team led by Beth J. Hoffman of the National Institute of Mental Health in Bethesda, Md., identified and characterized a serotonin transporter. Serotonin helps to regulate emotions.

In lab tests, cultured cells inserted with DNA sequences for making serotonin transporters displayed an ability to take up excess serotonin in the same way as brain cells, Hoffman and her coworkers report. But this activity dropped sharply when the experimenters exposed the same cells to antidepressants that block serotonin uptake, including the drug fluoxetine, better known as Prozac.

The researchers note that a comparable response occurred with exposure to amphetamines and related drugs that alter serotonin transmission, such as the appetite suppressant fenfluramine.

— *B. Bower*

Ultrafast first step for light into sight

Researchers have caught a glimpse of the first step in the chemical process leading to vision. Using extremely short pulses of laser light, two separate groups obtained evidence suggesting that the initial chemical change — the twisting of a chemical bond in the protein rhodopsin in response to the absorption of a photon — occurs in 200 femtoseconds. But the two groups offer conflicting interpretations of what happens during that brief interval.

"This is the first time that anybody has been able to resolve this transition," says physicist Robert H. Callender of City College of City University in New York, who heads one of the research teams. "It's really fast. There are a lot of things happening even at 200 femtoseconds."

"We are getting to the point where we can really understand molecularly why a photochemical process occurs," says chemist Richard A. Mathies of the University of California, Berkeley, a member of the other group. "Once we understand enough about what controls these things, we can essentially design molecules to do the kind of photochemistry we want. This is one of the first experiments getting us toward that."

A report detailing the City College group's findings will appear in the Nov. 1 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. Researchers from the University of California, Berkeley, and the Lawrence Berkeley Laboratory present their results in the Oct. 18 SCIENCE.

Both teams probed the pace of photon-induced changes in the structure of a light-sensitive portion of rhodopsin, the chief component of the rod and cone cells in the retina. And both identified two crucial stages in the process: one occurring about 200 femtoseconds after the initial absorption of a photon, and a longer stage lasting about 3 picoseconds.

According to the City College researchers, the first stage represents the formation of an intermediate chemical structure, in which a particular chemical bond in rhodopsin has only half twisted into its final position; the second stage completes the process. The Berkeley team, however, contends that the reaction is complete after 200 femtoseconds and the second stage reflects the time needed for the product to rid itself of excess energy.

"The experimental results do not contradict each other. It's the interpretation that is very different," Mathies says. Both teams acknowledge that the difference can be attributed in part to the fact that they studied the reaction using somewhat different wavelengths of light and laser pulses of different duration.

— *I. Peterson*