

# A Cure for the Common Cold?

An experimental drug has shown broad antiviral effects on a large number of the picornaviruses against which it has been tested. The tests, say scientists, while still preliminary, could yield the first drug capable of treating this family of disease agents, whose members can cause a wide variety of illnesses ranging in seriousness from polio, hepatitis A, viral meningitis and neonatal sepsis (a generally fatal disease affecting newborns) to those mild rhinovirus infections responsible for half of all common colds.

Based on the efficacy demonstrated thus far in animals and cell-culture experiments, the drug—known as WIN 51,711—“holds the potential for curing the common cold” and a broad spectrum of other previously untreatable infections, says Guy Diana, group leader for medicinal chemistry at the Sterling-Winthrop Research Institute in Rensselaer, N.Y. Diana reported on relationships between the drug’s chemical structure and its antiviral activity in a presentation last week at the American Chemical Society’s 189th national meeting in Miami.

To reproduce, an infectious virus first adheres to a cell’s membrane. Then it penetrates the cell, shedding its own outer protein covering and releasing its store of genetic material. If allowed to replicate and reencapsulate, this genetic material would form new viruses that could infect other cells. The new drug halts the reproduction and spread of a virus by preventing the initial uncoating of the protein

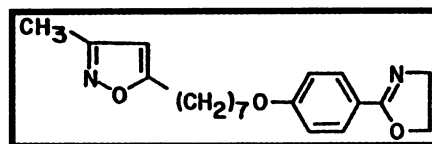
shell that encapsulates its genetic material.

By halting viral reproduction so early in the viral-uncoating phase, the drug’s mechanism of action may be unique, says Mark A. McKinlay, a virologist on the project. Exactly why it selectively binds with viruses and prevents their uncoating, however, is not fully understood.

Used therapeutically, the drug halted development of paralysis in mice that had recently been infected with polio-2 or a paralytic ECHO-9 picornavirus. Used prophylactically, the drug prevented viral infection altogether when given to mice immediately before and again immediately after their exposure to various picornaviruses.

Since there are no animal models other than chimpanzees for studying rhinovirus infections, McKinlay says tests of the drug’s efficacy against these cold viruses were performed using several types of cultured human cells. To date, WIN 51,711 appears effective against 34 of the 40 rhinoviruses tested. Testing isn’t over, however; there are more than 120 rhinoviruses capable of causing colds.

So far, McKinlay says, WIN 51,711 is



Structure of WIN 51,711: a chemical whose formal name is 5-[7-[4-(4,5-dihydro-2-oxazolyl) phenoxy] heptyl]-3-methyl isoxazole.

somewhat more effective against enteroviruses — the picornavirus family’s major class of nonrhinoviruses causing human disease — than against cold viruses. Last week Diana reported data on a close analog of the drug that showed the opposite effect — slightly better action against rhinoviruses. This leads to speculation that the end product of the research may not be a single anticornavirus drug but instead a group of related compounds, each of whose activity has been optimized for a target class of the viruses.

Initial toxicity tests suggest the new drug is safe. The next step is clinical trials. A critical question to be answered there will be whether, by the time symptoms appear, these viral diseases are already too advanced to treat.

— J. Raloff

## Spacelab: Success amid frustration

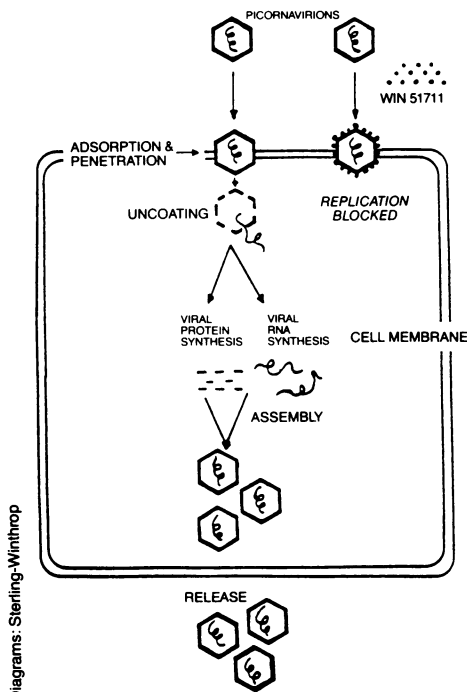
As the first operational flight of the Spacelab research module, the 17th space shuttle mission was heavily laden with life forms (7 humans, 2 monkeys, 24 rats) and scientific experiments (15), as well as carrying two satellites to be launched in orbit. There were problems in each area during the voyage’s seven days (one of the satellites never emerged from its Getaway Special canister), but by the time the shuttlecraft Challenger landed on the desert sands of California’s Edwards Air Force Base, mission officials were enthusiastic about their week’s results.

Only one of the 15 experiments never worked at all — a stuck hatch cover blocked a French ultraviolet camera from conducting a sky survey of celestial objects. Two other experiments would have been largely or totally ruined by technical problems, but on-board repairs by the astronauts (following lengthy analyses by colleagues on the ground) saved them both.

Fluid physicist Taylor Wang, from Jet Propulsion Laboratory in Pasadena, Calif., was in Challenger’s crew as a “payload specialist.” He was to conduct tests of “containerless processing,” in which sound waves would be used to suspend and manipulate fluid droplets that might otherwise be contaminated by contact with the walls of an enclosure. When Wang

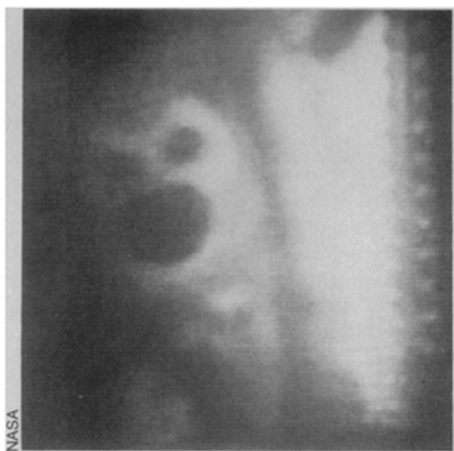
first activated his apparatus, however, it kept tripping its circuit breakers. Several hours of orbit-to-ground conversation and study indicated that the problem was a short-circuited power supply, and Wang (who is also the experiment’s principal investigator) was advised to rewire the device to an alternate supply. It was a simple “fix” — though the consultations to be sure it would work and get all the necessary approvals consumed two more days — but it made the difference between success and failure. As for the results, radioed Wang from space, “It’s amazing. It’s totally different from what we thought.” Another experiment, to study the ionization of solar and galactic cosmic ray nuclei, was similarly brought back from the brink.

Both the astronauts and NASA officials said little about how the crew was faring in the weightless environment with the “space sickness” that has affected about half of U.S. astronauts so far. The squirrel monkeys, however, were sent along to aid studies of just that problem, with astronaut/physician William E. Thornton serving as their handler. One of the monkeys seemed to take readily to life in zero-g, but the other spent the first few days looking listless and moving around very little. Both seemed to acclimatize, however, and the day before the mission ended, Thornton noted that “we’ll be



WIN 51,711 stops normal reproduction process, illustrated with virus at left.

Diagrams: Sterling-Winthrop



Squirrel monkey aboard Challenger.

bringing two monkeys back to earth that are even friendlier than they were to begin with. Those primates are part of the crew right now." As for the rats, said Thornton, gesturing during a TV transmission at a rat cavorting in its cage, "They've loved every minute of this flight."

That is not to say that the presence of the rats and monkeys during the flight was an unmixed blessing, however. During the flight's first few days, large numbers of particles from the rats' food trays escaped from their cages and floated around the cabin; specialists on the ground finally worked out a technique whereby the astronauts would store each old food tray in the plastic storage bag that had just been removed from its replacement. In addition, waste pellets from the rats and fecal matter from the monkeys would float across the Spacelab enclosure, and were even found in the shuttle cockpit, about 25 feet away through a tunnel with two elbow-bends in it.

"This is really discouraging," said astronaut Robert F. Overmyer, the mission's commander. "We told those guys all these years that the monkey cages wouldn't work." If he said more on the subject, it was cut off from the publicly audible communications circuits by mission control on the ground. Next year, however, NASA plans to fly another mission with twice as many monkeys and twice as many rats. The cages, said one NASA official after the five Spacelab mission specialists had had to put on surgical masks, smocks and gloves, "are likely to see some changes" before the next trip.

The mission ended not at Kennedy Space Center in Florida, as had been originally planned, but in the Mojave Desert. The previous mission, using the shuttlecraft Discovery, had rolled to a stop from its landing on a hard runway with one tire blown and three others badly frayed, possibly due to crosswinds during the touchdown. Challenger's desert landing did not represent a permanent change, but provided a safer chance to evaluate the effects of cross-loads on the tires, which survived the touchdown with only normal wear.

— J. Eberhart

## Ion therapy charges forward

Medical therapy using ions has progressed so far in a few years that a major national laboratory and a large university are planning to build an ion accelerator on the grounds of a large hospital. In Berkeley, Calif., at last week's Symposium on Heavy Charged Particles in Research and Medicine, Edward L. Alpen of the Lawrence Berkeley Laboratory made public the plans of LBL and the University of Arizona to build a synchrotron with a maximum energy of 1 billion electron-volts (1 GeV) at the Merritt Peralta Medical Center in Oakland, just south of Berkeley.

Medical therapy using electrically charged subatomic particles began about 30 years ago, but only in the last few years has it included the use of ions (atomic nuclei). Up to now the most used ions have been hydrogen (protons) and helium, which have been used mostly on cancers of the eye (SN: 9/24/83, p. 204). At the same Berkeley meeting, early reports were given on two promising extensions of the technique: the use of heavier ions than helium on tumors and the use of helium ions on certain abnormalities of blood vessels in the brain.

The new synchrotron would be called ABRA (Advanced Biophysical Research Accelerator) — please note, they say, *not* abracadabra — and would be able to accelerate ions of all elements between helium and silicon in the periodic table, as well as argon and iron. The purpose of building it at a medical center is to shift the responsibility for patient treatment to hospital personnel, leaving the research physicians, biologists and physicists to concentrate on studying the effects of different kinds of ions on cells and tissues. The total cost of the installation will be between \$74 million and \$77 million. They hope for an appropriation to begin in fiscal year 1987, and if that comes through, the installation could begin supplying ions for treatment and research in fiscal year 1990.

The planners opted for a synchrotron that can deliver a variety of ions at variable energies because they see possibilities for the heavier ions. Joseph R. Castro of LBL reported that of 800 patients treated at LBL with heavy charged particles, 87 have been treated with ions heavier than carbon, most (77) with neon. Their conditions included inoperable tumors in the abdomen (carcinoma of the pancreas), thorax and brain (malignant gliomas). The procedure, says Castro, is to "approach slowly from the known to the unknown," studying the radiation's effect on the tumors and on nearby normal tissue. Later, randomized studies of its effectiveness are planned. Not much is known about delayed effects of the heavy ion treatment, Castro reports, as this group of patients, confined for ethical reasons to those for whom all other treatments had failed,

yielded only two who survived as long as 36 months.

At the same time, the much-used protons and helium ions have begun to treat a condition called arteriovenous malformation (AVMs). AVMs are not tumors but distortions of the capillaries connecting an arteriole and a small vein in the brain. The capillaries develop "balloons" and serpentine twists. AVMs can bleed, causing severe headaches, seizures, even death. There are 500,000 cases in the United States and Canada, says Jacob I. Fabrikant of LBL—250 new ones a year in California alone. Twenty-five percent of AVMs are inoperable, he says.

Three institutions are experimenting with ionic treatment of AVMs, Fabrikant reports: the University of Uppsala in Sweden, Harvard University and LBL. So far 110 patients have been treated with helium at LBL. The treatment eradicates the AVM, restoring a normal appearance to the blood vessels, and does it better than X-rays, gamma rays or protons, Fabrikant says. There is also a cost advantage: Radiation treatment for this condition costs \$8,000; a comparable neurosurgical procedure, \$30,000.

— D.E. Thomsen

### Weighing the neutrino

Does the neutrino have a rest mass? When physicists first postulated its existence, the neutrino had to be a neutral particle of 0 rest mass, which was needed to properly balance energy in certain radioactive decays. When it was discovered experimentally, the mass was found to be 0, within the accuracy limits of the experiment. Recent theories give the neutrino an important place in the overall scheme of physics, and part of that importance depends on whether or not it has a tiny rest mass.

A few years ago some experimenters in the Soviet Union reported a small rest mass for the neutrino. Since then one experiment done in the United States has claimed a positive result; several have come up 0. Now J.J. Simpson of the University of Guelph in Ontario claims a positive result of 17,100 electron-volts — about 4 percent of the electron's mass, the smallest now known for certain. Simpson's experiment observes radioactive decay of tritium (an isotope of hydrogen) embedded in a silicon-lithium detector. Although the neutrino is not directly seen, the energy balance of particles emitted with it can be used to figure its mass. In the April 29 PHYSICAL REVIEW LETTERS Simpson invites others to copy his method with the remark, "The effects of such neutrinos should be seen in all [beta decay] spectra for which their emission is energetically allowed." □