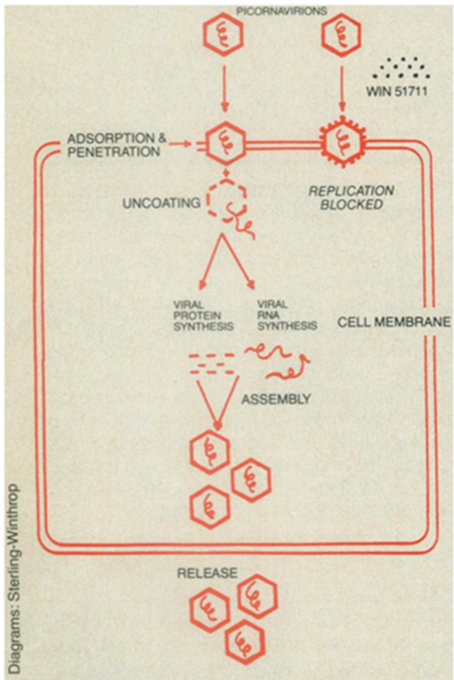
A Cure for the Common Cold?

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.



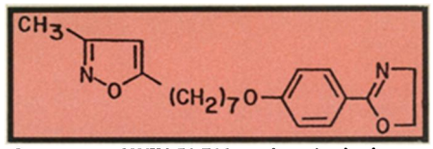
WIN 51,711 stops normal reproduction process, illustrated with virus at left.

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 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 antipicornavirus drug but instead a group of related compounds, each of whose activity has been optimized for a target class of the viruses.



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

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