Pentamidine may have antidementia payoff

A drug now taken by most AIDS patients to prevent pneumonia may have the added benefit of protecting against the mind-warping symptoms of AIDS dementia, according to results from a preliminary study.

The test-tube study — performed by pharmacologists Ian J. Reynolds and Elias Aizenman of the University of Pittsburgh School of Medicine — suggests that the widely used drug pentamidine can help prevent brain cells from succumbing to the deadly effects of HIV, the virus that causes AIDS. Physicians currently administer pentamidine to nearly every AIDS patient, both as a treatment and as a preventive for *Pneumocystis carinii* pneumonia, a potentially fatal lung infection that commonly strikes people with AIDS. However, the study's authors and neurologists who treat AIDS patients caution that they must perform further tests to prove or disprove pentamidine's antidementia effects.

According to the American Academy of Neurology, roughly 60 percent of AIDS patients develop some symptoms of AIDS dementia, which range from forgetfulness and confusion to irrational or childlike behavior. Although the AIDS drug AZT (zidovudine) has shown some benefits against AIDS dementia, there is currently no effective treatment for the disorder.

Reynolds and Aizenman stumbled upon evidence that pentamidine might protect against AIDS dementia while searching for drugs that block the N-methyl-D-aspartate (NMDA) receptor on nerve cells. The recently isolated receptor, named for its ability to bind to the lab-made chemical NMDA, triggers nerve-cell death when overexcited by NMDA or by glutamate, a chemical released by brain cells after a stroke or other head injury (SN: 11/23/91, p.333). Many drug companies and academic laboratories are now developing "NMDA antagonists" to block this common mechanism of nerve-cell destruction.

Several groups of neuroscientists now believe the NMDA receptor plays a role in AIDS dementia. Although the exact cause of the disorder remains unknown, many studies have ruled out direct killing by HIV. Some neurologists surmise that HIV destroys nerve cells indirectly by prompting the overproduction of a brain chemical called quinolinic acid, which can cause toxic effects at high levels (SN: 3/7/92, p.151). Others support another indirect mechanism, in which gp120 — the outer protein of HIV — interferes with a brain protein called VIP. Some nerve cells need VIP to send electrical signals to one another (SN: 5/18/91, p.311).

In the March JOURNAL OF NEUROSCIENCE, Reynolds and Aizenman report that pentamidine outstripped another NMDA-blocking drug in binding to the NMDA receptors of fetal rat brain cells grown in the laboratory. Moreover, pentamidine protected the nerve cells from death in the presence of an otherwise lethal concentration of NMDA. The researchers cite a previous study in which investigators who performed autopsies on the brains of AIDS patients found pentamidine levels comparable to those used in the Pittsburgh experiment.

Reynolds says he and Aizenman intend to investigate pentamidine's antidementia effects by collaborating with neurologists who study AIDS dementia. "Presumably, what we would see is that patients who had taken pentamidine would have less dementia," he says.

One such neurologist, Bruce A. Cohen at Northwestern University in Evanston, Ill., terms Reynolds and Aizenman's study "potentially interesting, but at this point speculative." Cohen points out that most AIDS patients develop dementia despite pentamidine treatment, although he concedes that the inhaled form in which pentamidine is usually given might not reach the brain as readily as an injection of the drug. Richard Price, a neurologist at the University of Minnesota in Minneapolis, also cautions that injected pentamidine can cause seizures in some people. — *C. Ezzell*

Sneaking a peek at Earth's hardened heart

While Earth's iron core lies only 2,900 kilometers below our feet, it has proved less accessible than the outer reaches of the solar system. This week, two research groups report results that offer new insight into Earth's hidden heart.

Geophysicist Bruce A. Buffett and his colleagues at the University of Cambridge in England have for the first time succeeded in capturing some of the core's history within a mathematical formula. The researchers investigated the growth of Earth's inner core — a region squeezed by such intense pressures that it remains a solid despite the tremendous heat deep inside the planet.

Surrounding this hard center lies the outer core, a swirling pool of molten iron and other "lighter" elements. Geoscientists believe that liquid iron from the outer core gradually solidifies onto the inner core, steadily building up that solid center at a current rate of about 0.4 millimeters per year.

The Cambridge group's analysis addresses a central question about the Earth: What processes stir the liquid outer core? The movement of these fluids is important because they apparently generate Earth's magnetic field — one of the factors that makes this planet hospitable to life.

Researchers have long thought that heat differences drive the fluid motion within the outer core, much like the roiling convection of soup on a stove. In this theory, heat escaping up into the mantle would cool off the upper regions of the outer core, causing fluid to sink. At the base of the outer core, molecules of liquid iron would release energy as they solidified, heating the lowermost fluid until it rises.

Some geophysicists have advocated another theory. Instead of focusing on heat, they suggest that the freezing of iron on the inner core would leave behind lighter elements in the fluid, which would rise to the top of the outer core, causing convection.

The work by Buffett's group suggests that the separation of light elements and the cooling at the top of the core play roughly equal roles in stirring the outer core. Heat released by solidifying molecules represents a minor factor, they report in the March 26 NATURE.

Buffett and his colleagues estimate that the inner core began growing sometime between 3.6 and 1 billion years ago, depending on the rate at which heat escapes from the core into the mantle. Such calculations suggest that Earth's magnetic field may have developed before the birth of the inner core, because rocks dating back 3.5 billion years contain a record of the magnetic field.

David E. Loper at Florida State University in Tallahassee cautions that the analysis by Buffett's group does not resolve major uncertainties. "Their numbers aren't that reliable. We don't know enough about the thermal history of the mantle and core to tie these numbers down."

While the core's history remains fuzzy, its structure is gradually coming into focus through the use of seismology. Kenneth C. Creager at the University of Washington in Seattle compared seismic waves that passed through the edge of the solid inner core with almost identical ones that passed just outside the inner core. Rays passing through the inner core traveled 3.5 percent faster when they were moving parallel to Earth's spin axis, Creager reports in the same issue of NATURE.

Seismologists had detected this so-called anisotropy before, but previous work had not detected such a marked difference in speeds. To explain his findings, Creager suggests that iron crystals within the inner core have aligned themselves in an orderly fashion that affects the speed of seismic waves, depending on their direction. At present, though, geoscientists do not know why the crystals would position themselves in an orderly pattern rather than a random one. — *R. Monastersky*