Biomedicine

Melissa Hendricks reports from Bethesda, Md., at the annual meeting of the National Cancer Institute's Laboratory of Tumor Cell Biology

Two AIDS drugs may be better than one

The drug zidovudine, also known as AZT, prolongs the lives of some AIDS victims and is the only drug federally approved for treating the disease. But it has its drawbacks. It does not cure AIDS, and often creates anemia, nausea and fatigue while decreasing levels of certain bone marrow cells. Rather than abandon zidovudine, researchers have begun investigating its use in combination with other drugs. They now report evidence that such combinations may work better to hinder the AIDS-causing virus, HIV. Says Samuel Broder of the National Cancer Institute (NCI), one of the first scientists to test zidovudine, "We can make a great deal of progress in treating AIDS with already existing drugs."

Updating an ongoing clinical trial (SN: 2/6/88, p.84), the NCI's Robert Yarchoan reports that three patients receiving alternating one-week doses of zidovudine and a distantly related drug, 2′3′-dideoxycytidine (ddC), have passed the one-year mark with striking improvements in brain and peripheral nerve function and free of zidovudine's customary ill effects. Also promising is the finding, reported by the NCI's Carlo-Federico Perno, that drugs like zidovudine and ddC appear to halt HIV replication in macrophages, immune cells now recognized as one of the main targets of HIV infection. Previous research on AIDS drugs had focused mainly on immune cells called T-cell lymphocytes. Perno has discovered *in vitro* that zidovudine, ddC and other related drugs stop the spread of HIV in infected macrophages without harming the macrophages themselves. He noted this effect occurs with drug doses one-tenth to one-fifth the concentration used to obtain the same result in T-lymphocytes. Since macrophages carry HIV into the brain, the effect of zidovudine and ddC in cell culture may explain why they improve brain function in AIDS victims, says Perno, whose results will appear this month in the JOURNAL OF EXPERIMENTAL MEDICINE.

Together with zidovudine, another drug — amphotericin methyl ester (AME) — also works better than either drug alone in combating HIV in cell culture, reports Prem Sarin of the NCI. The two drugs may hit HIV with a double punch, says Sarin. While zidovudine inhibits the enzyme helping HIV reproduce, AME pokes holes in the protein coating surrounding HIV's genetic material. At yet another stage in the HIV cycle, Sarin has examined the drug abaerol, thought to block the packaging of HIV components into whole virus. Findings that will appear in an upcoming issue of BIOCHEMICAL PHARMACOLOGY show that abaerol also improves zidovudine's potency, he says. Therapies combining two drugs, such as AME or abaerol with zidovudine, are attractive because they allow doctors to lower dosages of each drug and thereby reduce the risk of side effects.

But other scientists advise caution in giving combinations of drugs. Mariano Busso of the Mount Sinai Medical Center in Miami reports certain drugs may diminish zidovudine's effectiveness. Busso and Lionel Resnick tested zidovudine given with each of three different molecular forms of the experimental AIDS drug dextran sulfate on two different laboratory isolates of HIV. One form of dextran sulfate increased zidovudine's potency in both isolates. But each of the two other varieties of dextran sulfate improved zidovudine's effectiveness in only one of the strains. In the other strain, each of the dextran sulfates counteracted zidovudine's anti-HIV action. These results suggest some patients may respond better than others to dextran sulfate, whose molecular formula and concentration are critical, Resnick says.

While experimental drug treatment in AIDS patients remains risky, scientists in the field agree it must continue. "Though there is toxicity with many drugs," Broder says, "scientists would be mistaken to wait for perfect solutions before conducting clinical trials on drugs against this lethal disease."

Science & Society

Healing the acid wound

Acidic pollution has seared its mark on lakes and forests across Europe and eastern North America. For those combating the problem, it is important to know whether pollution control can reverse the effects of the acidic rain, snow and particles that settle out of the atmosphere. Now the results of a unique project in Norway provide the first experimental evidence that acidified areas can begin to recover.

The four-year-old RAIN project (Reversing Acidification in Norway) has focused on a small drainage basin — called a catchment — in the southernmost region of Norway, a sensitive area that receives a significant amount of acidic precipitation. Norwegian and Swedish researchers covered the 800-square-meter catchment with a large transparent roof that protects the area from natural precipitation. Rain collected from the roof is cleansed with an ion exchanger and then sprinkled over the covered land. Commercial snow-making equipment supplies artificial "clean" snow to the catchment during the winters. By analyzing runoff within the catchment, project members have tracking the protected plot and compared its evolution with that of control catchments. One control is covered and receives "normal" acidic precipitation, while another control remains uncovered.

Results indicate the protected catchment has started on its way to recovery, report Richard Wright from the Norwegian Institute for Water Research in Oslo and his colleagues in the Aug. 25 NATURE. The acidity of runoff has dropped and so have the concentration of sulfate and nitrate ions, which are principal components of the sulfuric acid and nitric acid in acidic precipitation.

While the project provides some answers about an area's ability to recover from acidification, other questions remain. The protected catchment was less than half the size of a football field — too small to hold any lakes or real streams — so researchers may have difficulty relating these results to larger areas. It also remains unclear whether the catchment will recover completely. Yet James Galloway of the University of Virginia in Charlottesville, who studies acid rain in the United States, says the results of the RAIN project have confirmed predictions from computer simulations — a finding that tells modelers they are on the right track.

With an ear to the Soviet soil

Several dozen technical experts from the United States will get their first closeup chance to monitor a Soviet nuclear blast later this month. Officials from the Energy, State and Defense Departments will be on hand at the Kazakh testing site to demonstrate the CORRTEX system, a hydrodynamic technique that measures the strength of an explosion by means of an electric cable buried near the blast. These tests are part of a series of Joint Verification Experiments aimed at removing obstacles to unratified treaties from the 1970s that limit the size of nuclear tests to the equivalent of 150 kilotons of TNT. In August, Soviet officials visited the U.S. test site in Nevada to measure a nuclear explosion using their own hydrodynamic system as well as seismic monitoring equipment (SN: 1/30/88, p.71).

Also observing the Sept. 14 Soviet blast will be several private U.S. scientists at three seismic stations, each located 100 miles away from the Kazakh test site. These scientists are working in conjunction with the Washington, D.C.-based Natural Resources Defense Council — a private environmental group that has negotiated its own monitoring agreement with the Soviet Academy of Sciences. Through this project, the council hopes to demonstrate that seismic equipment can reliably verify a total or near-complete ban on testing (SN: 4/16/88, p.245).