Mouse study suggests a cure for influenza

Scientists have developed a drug that cures mice of influenza and demonstrated for the first time that influenza's symptoms are not caused directly by the virus, but instead result from the action of oxidizing free radicals produced by the immune system. The finding not only suggests a cure for the disease in humans, but also holds "great potential" for treating a number of other inflammatory diseases — such as hepatitis, rheumatoid arthritis and Crohn's disease (a severe intestinal disorder) — says study leader Hiroshi Maeda, a biochemist at Kumamoto University Medical School in Japan.

Previous studies have suggested an overreaction of the immune system might contribute to flu symptoms. And other work has shown that immune cells produce free radicals — highly reactive compounds containing unpaired electrons that steal electrons from other molecules and cause tissue damage. But no one before now had demonstrated the importance of free radicals in influenza, Maeda says.

The scientists initially found that the levels of free radicals generated by immune cells taken from influenza virus-infected mouse lungs increased with time after infection. They also found T lymphocytes increased in number, suggesting that elevated free-radical production by immune cells, possibly primarily the T cells, contributes to influenza pathogenesis, Maeda says.

They then identified the enzyme, xanthine oxidase, responsible for the generation of the free radicals. Xanthine oxidase activity increased dramatically after infection in both influenza-infected mouse lung cells and infected mouse serum. Administering allopurinol, a xanthine oxidase inhibitor, "exerted a protective effect on the mice," the scientists write in the May 26 SCIENCE.

In a separate experiment, nine of 10 mice treated with a derivative of a naturally occurring free-radical scavenger survived, while all 10 controls died. The treated mice were injected daily for four days, beginning on the fifth day after infection, with a derivative of the enzyme superoxide dismutase. It was made to remain longer at the site of free-radical damage by linking it to a synthetic polymer. Treatment dramatically diminished the pathological changes within the lung, returning the mice to "almost like normal," Maeda says.

Maeda's work "opens up a whole new world of therapeutic chemistry in which one uses polymers as carriers [for drugs]," says oncologist William Regelson at Virginia Commonwealth University Medical College of Virginia in Richmond. — *I. Wickelgren*

Preschool self-control and pretzel logic

Do you want a couple of small cookies now, or can you wait 15 minutes for five pretzels? Children as young as 4 years of age who hold out for the bigger reward on tests of this kind cope better with frustration and stress as adolescents and may perform better academically, according to a report in the May 26 SCIENCE.

Young children develop specific psychological strategies to maintain self-control in the pursuit of future goals, say psychologist Walter Mischel of Columbia University in New York City and his colleagues. The ability to delay gratification, they add, constitutes an important aspect of intelligence that researchers have often overlooked.

In the early 1970s, the researchers tested 53 4-year-olds from middle-class families. An experimenter presented each child with a pair of treats before leaving the room. To attain the preferred treat—five pretzels as opposed to two cookies, for example — youngsters had to wait for the experimenter to return about 15 minutes later. They could press a buzzer at any time to end the waiting period and obtain the less preferred treat.

When rewards were hidden from view, children waited longer on average than when rewards were in plain sight. But the way children thought about the treats appears critical to their self-control, the researchers contend. Waiting time decreased for children asked to focus on "arousing" features of a reward, such as the taste of a pretzel. Delays increased if they were told to imagine "abstract" qualities of a reward, such as thinking about pretzel sticks as long, brown logs.

The spontaneous use of abstract thinking to foster self-control emerges between ages 9 and 12, Mischel and his coworkers say.

In a 10-year follow-up of the preschool sample, children who delayed longer when rewards were visible were rated in adolescence by their parents as significantly more attentive and able to concentrate, goal-oriented and intelligent. Their parents also viewed them as more able to resist temptation, tolerate frustration and cope with stress.

Scores on the Scholastic Aptitude Test, now available for 35 subjects, are also substantially higher for those who delayed gratification longer as preschoolers. A larger sample needs to be studied to confirm this finding, the researchers caution.

Nevertheless, they say, teaching children self-control strategies to attain desired goals may improve their academic and social skills later in life.

— *B. Bower*

New treatment may reduce breast surgeries

Researchers this week described an experimental therapy that may make radical breast surgery, or mastectomy, unnecessary in most women with tumors previously considered too large to treat more conservatively. The treatment shrinks tumors to a fraction of their original size, so surgeons can remove them using a less disfiguring operation popularly known as a "lumpectomy."

Apparent successes in nearly all of the first 90 patients studied suggest that total removal of cancerous breasts may fall almost entirely out of practice within the next five years, some experts say. But others express skepticism of such far-reaching conclusions, saying there remain compelling reasons for women to opt for mastectomy. Either way, the new findings provide fuel for a growing debate about how best to treat this potentially fatal cancer, which will strike 142,000 U.S. women this year.

Increasingly, physicians in the United States and abroad recommend lumpectomies for small breast tumors, especially when no evidence exists the cancer has spread. But tumors greater than 2 or 3 centimeters in diameter generally spur surgeons to perform a modified radical mastectomy, where they remove the entire breast and some surrounding tissues. Chemotherapy treatments often follow in an attempt to destroy any remaining tumor cells (SN: 3/4/89, p.135).

Gianni Bonadonna and his colleagues at the Instituto Nazionale Tumori in Milan, Italy, reversed this common therapeutic sequence for women with large tumors by treating them first with standard anticancer drugs for three months, then performing surgery. They found chemotherapy shrunk 95 percent of tumors with diameters of 3 to 5 cm and 73 percent of tumors measuring 5 to 8 cm to less than 3 cm, allowing surgeons to do lumpectomies. Even the largest tumor, 11 cm, withered to 3 cm.

"The findings imply that the classical indication for primary mastectomy can now be challenged," Bonadonna told the annual meeting of the American Society of Clinical Oncology in San Francisco. With the first group of patients now more than one year into the study, none has experienced a cancer recurrence. Although long-term survival data will take years to gather, Bonadonna says, "Let's begin to dismantle the mutilating surgery. Then we shall see whether these

data will make an impact on survival figures." He predicts that by 1994, the 100th anniversary of the first published description of radical mastectomy in a surgical journal, the procedure will be all but obsolete — an opinion echoed by oncologist Nikolay Dimitrov of Michigan State University in East Lansing.

Others, however, note that despite the encouraging results, women may be slow to trust the experimental regimen. Both Bonadonna and Hendre Falkson of the University of Pretoria in South Africa say all their women colleagues have told them they'd opt for mastectomy with reconstructive surgery rather than worry about the risk of recurrence that might come with lumpectomy. Moreover, Falkson notes that even under Bonadonna's regimen, lumpectomy patients receive six weeks of post-surgical radiation therapy. "Six weeks of radiotherapy is not innocuous treatment," she says.

Emphasizing that only large-scale, prospective trials of various treatments will settle the debate, she decries U.S. doctors' failure to enter their patients in controlled trials where treatment variables can be standardized and results interpreted in statistically meaningful ways. Of the tens of thousands of new breast cancer patients identified each year, she says, only a few hundred enroll in such research protocols. — *R. Weiss*

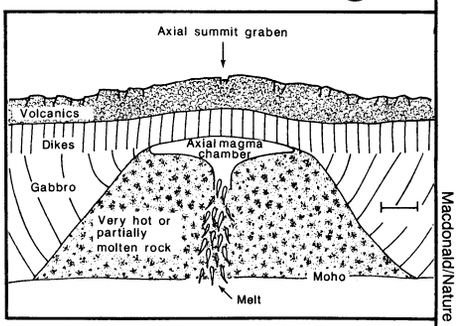
Magma reservoir seen under ocean ridge

In the geophysical equivalent of a CAT scan, scientists have identified key parts of the molten-rock plumbing system underneath a mid-ocean ridge — offering new insight into the process that forms two-thirds of the planet's surface.

Mark S. Burnett, David W. Caress and John A. Orcutt of the Scripps Institution of Oceanography in La Jolla, Calif., used computer tomographic techniques to analyze data from a 1982 experiment, called MAGMA, on the East Pacific Rise off the coast of Mexico. During MAGMA, researchers exploded thousands of charges near the ocean surface, generating seismic waves that traveled through the ocean crust. Instruments on the submerged ridge and the sea floor several kilometers to the east recorded waves that had refracted in rock layers underneath.

Researchers had previously only analyzed slices of the MAGMA data in a "trial and error fashion," says Orcutt. Tomography, used here for the first time to study a ridge, resembles the x-ray technique that produces three-dimensional medical images.

The new analysis helps resolve the structure of the magma — or molten rock — reservoir that feeds sea-floor spreading at the ridge, the researchers report in the May 18 NATURE. The seismic waves reveal that a long region of hot rock, only about 6 kilometers wide, sits underneath the ridge. Because of the way the seismic waves slow as they passed through the area, Orcutt says this hot zone is made of mostly solid rock, containing a small amount of melted material.



Macdonald/Nature

Simplified cross section shows thin magma pool on top of hot rock zone.

A more complete picture of the ridge emerged from combining these results with those from a different type of experiment, using reflected seismic waves. This project had shown that magma lies directly under the ridge at a depth of about 1.4 kilometers, but it could not resolve what sits beneath the magma. The composite results indicate that molten rock forms a thin "mushroom" capping the hot rock zone. The magma chamber itself may only be a few tens of meters thick, Orcutt says.

The new tomographic images in combination with other measurements "provide the best glimpse yet of the axial magma reservoir," says Ken C. Macdonald of the University of California, Santa Barbara. Researchers had overestimated the size of the melted pool in previous theories. Future studies will aim to determine the true size of the chamber. — *R. Monastersky*

Pluto's atmosphere: More than methane

Astronomers first detected methane on Pluto several years ago from spectral measurements, but could not tell whether it existed in the form of an atmosphere or solid frost on the surface. When Pluto passed in front of a star last June 9, the gradual refraction and dimming of the star's light as the planet got in the way showed a planetary atmosphere (SN: 6/18/88, p. 391), but researchers remained uncertain of its composition.

Now Roger V. Yelle and Jonathan I. Lunine of the University of Arizona in Tucson report in the May 25 NATURE that there is not only methane but also another constituent, a substance whose molecules are considerably heavier. Others have suggested the existence of such a constituent, based on assumed abundances of other gases in the cosmos, but Lunine describes the results of the new analysis as "the first real piece of evidence showing that there is heavier gas there."

The authors cite observations of the star's occultation made by other researchers from the University of Tasmania Observatory in Hobart, Australia, and from NASA's Kuiper Airborne Observatory. The atmosphere's average temperature, they calculate, is about 106 kelvins, rather than the 60 K surface temperature measured in 1983 by the Infrared Astronomy Satellite.

The researchers compared the amount of the sun's heat absorbed by the methane in the atmosphere with the amount reradiated upward to space and conducted down to the surface. They find that the resulting "energy balance" shows the thin mixture of gases around Pluto to have a mean molecular weight of about 25, meaning that "a molecule heavier than (and in addition to) methane must be present in the atmosphere."

Yelle and Lunine conclude that the likeliest candidate is carbon monoxide, with a molecular weight of 28 compared to methane's 16. Other possibilities include argon and molecular nitrogen. Carbon dioxide would probably freeze onto the surface instead of remaining as a gas, though Lunine notes cosmic rays might produce carbon monoxide from the CO_2.

The change in the starlight measured as Pluto blocked it off showed a "kink" that other observers have interpreted as evidence of a layer of haze in the atmosphere. In work reported at the recent American Geophysical Union meeting in Baltimore earlier this month and now submitted to the journal ICARUS, William B. Hubbard of the University of Arizona suggests together with Yelle and Lunine that the kink could result from the effect of Pluto's cold surface on its atmospheric density.

One implication of the cold plutonian surface could be that there are no cumulus clouds overhead, adds Lunine, because the atmosphere, unlike Earth's, gets warmer with altitude so that moisture does not condense into droplets, though there could be early morning ground fogs.

Hubbard and his colleagues suggest that Pluto's radius may be about 1,180 kilometers, though the presence of a dust layer could make the planet as small as 1,140 km. The Voyager 2 spacecraft's upcoming flight in August past Neptune's moon Triton, where methane has also been detected, could help understand Pluto, says Lunine, in the question of "how cold, thin atmospheres work."

— *J. Eberhart*