

## 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 Istituto 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