

# New Use for the French 'Abortion' Pill

The controversial drug RU 486 made headlines several years ago for its ability to induce abortion during the first trimester of pregnancy. Now, a Scottish study suggests that RU 486 has another use — as a “morning-after” pill. The new findings indicate the drug can safely and effectively prevent pregnancy when taken soon after a woman has had sexual intercourse.

“I think this article is going to irrevocably change the political landscape of RU 486 in the United States,” says David A. Grimes, an obstetrician at the University of Southern California School of Medicine in Los Angeles. “It has defined a potential new application for RU 486 that will shift the debate away from its use as an abortifacient.” Grimes believes that such a shift will help ease the tensions surrounding the use of RU 486 (SN: 2/17/90, p.100).

“This is a very, very important study,” agrees Irving M. Spitz of the Population Council in New York City. However, Spitz says it is hard to predict how the new findings will fare in the fray over abortion in the United States.

Nobody really knows how RU 486 prevents pregnancy, says lead researcher Anna Glasier of the University of Edinburgh in Scotland. In some cases, the drug may suppress ovulation. In other cases, RU 486 prevents the fertilized egg from implanting in the lining of the uterus, the first step of a pregnancy, Glasier says. When used as an abortifacient, RU 486 helps trigger the expulsion of an established embryo or fetus, she explains.

Glasier and her Scottish colleagues began their study by recruiting 800 women and teenagers who had come to an Edinburgh health clinic requesting emergency contraception after having had sex within the preceding 72 hours. The team randomly assigned 398 to receive the standard morning-after therapy, which consists of high doses of both the sex hormone estrogen and a synthetic version of the sex hormone progesterone. The remaining 402 recruits got RU 486, which is also known as mifepristone.

The researchers report that none of the women in the RU 486 group became pregnant, in contrast to four of those in the standard therapy group. Although the difference between the two groups was not statistically significant, Glasier believes that a study that includes more subjects will show RU 486 to be much more effective than the standard regimen. The number of pregnancies in each group was significantly lower than the number expected based on the day of the menstrual cycle during which sex had

taken place, Glasier says. Without treatment of any kind, about 23 women in each group would probably have become pregnant, she adds.

The team also found that women who received RU 486 suffered from fewer side effects such as nausea and vomiting than did recruits on the standard regimen. Young women may prefer the single-dose RU 486 over the standard regimen, which requires more than one dose of nausea-causing hormone pills, Glasier adds. The Scottish researchers report their data in the Oct. 8 *NEW ENGLAND JOURNAL OF MEDICINE*.

The researchers also discovered that women and teens who received RU 486 were more likely to report having a delayed menstrual period. Although not harmful, such a lag can alarm a woman, creating worry that her post-coital contraception has failed, Grimes notes in an editorial accompanying the research report. He suggests that women in such a predicament can turn to widely available pregnancy tests to allay their fears.

The editorial notes that RU 486 is

currently approved for use in France, the United Kingdom, Sweden, and China. So far, the drug has faced bitter opposition in the United States from antiabortion groups, who object to RU 486's use as an abortion pill, Grimes notes. As a result, the drug is likely to remain off-limits to women in the United States for any purpose — at least for now, says Gabriel Bialy, a contraceptive expert at the National Institute of Child Health and Human Development in Bethesda, Md.

A French pharmaceutical firm (Roussel Uclaf Company) developed RU 486 in the 1980s. However, Roussel Uclaf will not submit a new drug application to the U.S. Food and Drug Administration without government support of abortion, Grimes says. Thus U.S. women do not have access to RU 486 as an abortifacient or as a morning-after pill, he says. In fact, they have access to the standard regimen for post-coital contraception only because estrogen and other drugs used for that purpose are already approved by FDA for other indications, he adds.

— K.A. Fackelmann

## Devils Hole heats up debate over ice ages

For the last 15 years, most climate researchers have looked to space for an explanation of the ice ages that have repeatedly gripped our planet in recent geologic times. The established theory, called the Milankovitch hypothesis, holds that wiggles and wobbles in Earth's orbit serve as a pacemaker that determines when the planet plunges into a glacial period and when it thaws out of one. But new evidence from a deep crack in the Nevada desert threatens to overturn the Milankovitch theory and replace it with a more down-to-Earth solution.

Geoscientists report this week that the ice ages did not follow any pattern consistent with orbital variations. Rather, chaotic elements in Earth's own climate dictated when the planet slipped into and out of a deep freeze, the researchers suggest.

“We feel that the Milankovitch theory is incapable of explaining the climate shifts,” says Isaac J. Winograd of the U.S. Geological Survey in Reston, Va. He and his colleagues discuss their findings in two papers in the Oct. 9 *SCIENCE*.

The climate information collected by Winograd's group comes from Devils Hole, an open fault zone in southwestern Nevada. The fissure is filled with mineral-rich water that has coated the rock walls with layer upon layer of calcite over the last 500,000 years. Divers equipped with scuba gear entered the fault and used a

drill to cut a 36-centimeter-long cylinder out of the calcite coating.

By analyzing the ratio of two isotopes — oxygen-18 and oxygen-16 — at hundreds of spots along the calcite core, Winograd and his colleagues identified changes in the temperature of the atmosphere when rain fell in the Devils Hole region. They dated these climate shifts by using the radioactive decay of uranium within the calcite as a clock. Previously, they had drilled a core that recorded information going back 250,000 years (SN: 12/3/88, p.356). The new core doubles the length of that record.

Scientists who study the glacial cycle have traditionally relied on climate records constructed by measuring the oxygen isotopes in seafloor sediments. But the dates of the climate events in these marine records are less certain than those in the Devils Hole core.

The idea that ice ages result from alterations in Earth's orbit goes back to the 19th century. However, the theory did not enjoy widespread support until 1976, when oceanographers analyzed two marine records and found that the glacial cycle closely matched changes in the shape of Earth's circular orbit, the tilt of the planet, and the way its axis wobbles.

The marine records led researchers to suggest that these orbital variations paced the climate changes by altering the amount of sunlight reaching the sub-

Arctic region during summer. When the summer sunlight weakened, the snow from winter could survive the warm months, building up year after year to form a great glacial cap over Canada and northern Eurasia. When the summer sunlight intensified, it would melt the ice sheets.

But the Devils Hole record, with its superior chronology, shows that the timing of specific events in the last 500,000 years does not match the predictions of the Milankovitch theory, according to Winograd and his co-workers. Three of the last four ice ages ended when the summer sunlight in the sub-Arctic was relatively weak. What's more, the ice ages lasted different lengths of time, varying from 80,000 to 130,000 years in duration. This suggests that the climate changes follow no regular pacemaker, the researchers contend.

They propose instead that ocean circulation patterns, greenhouse gases in the atmosphere, and the behavior of ice sheets all interact chaotically to cause the irregular glacial cycles. Orbital variations may play a part in this story, but

they are by no means principal characters.

James D. Hays, a longtime champion of the Milankovitch theory, calls the Devils Hole data "a beautiful record" but argues that the new data do not sink the idea that orbital changes control the ice ages. Hays, a researcher at Columbia University's Lamont-Doherty Geological Observatory in Palisades, N.Y., points out that although the Devils Hole chronology has more accurate dates than other records, it still faces dating problems. Most important, he says, researchers don't know how many thousands of years rainwater takes to filter through the ground and reach Devils Hole — a factor that could alter the timing of climatic events recorded there.

The Devils Hole record, like the marine ones, includes variations whose frequencies match those of the orbital cycles. This suggests to Hays that these astronomical variables do play an important role. While summer sunlight in the sub-Arctic might not control the growth of ice sheets, a different pattern of sunlight changes may, he says. — R. Monastersky

## Life-or-death gene sheds light on lymphoma

A gene that normally controls the orderly death of unnecessary cells during the embryonic development of a humble roundworm may offer clues to a better understanding of some common cancers of the human lymph nodes, according to two new reports.

Michael O. Hengartner of the Massachusetts Institute of Technology in Cambridge told a conference of cancer researchers last week that the roundworm gene resembles a so-called proto-oncogene known to cause follicular lymphomas in humans. And in the Oct. 9 SCIENCE, a research team led by Jean-Claude Martinou of the Centre Medical Universitaire in Geneva, Switzerland, reports that injections of the human proto-oncogene, called bcl-2, can prevent the normal death of cultured nerve cells starved of growth factors.

Hengartner discussed his results regarding ced-9, the roundworm equivalent of bcl-2, at the 16th Bristol-Myers Squibb Symposium on Cancer Research, held at the Fox Chase Cancer Center in Philadelphia. He and his colleagues found the ced-9 gene by studying mutant roundworms that develop with extra growths. Hengartner's group determined that these growths consist of cells that would normally die during embryonic development because the worm no longer needs them.

This process of programmed cell death, or apoptosis, occurs in most organisms. Without it, humans would retain the webbed fingers and toes they had as embryos. The same mechanism ensures that old, worn-out cells within the

various organs of adults retire and die so that the body can replace them with fresh, lively cells that perform the same function.

"Programmed cell death is a way that multicellular animals have devised to properly get rid of cells that they do not want anymore," Hengartner says. The ced-9 gene regulates the process, he explains, by restraining two "suicide genes" that, when active, kill their own cell. A mutation that damages the ced-9 gene frees the suicide genes to spring into action, leading to cell death, he says.

The similarity between the roundworm gene ced-9 and the human gene bcl-2 may explain how a mutation involving bcl-2 causes human follicular lymphomas, Hengartner suggests. In many such lymphomas, complementary breaks in two different chromosomes allow bcl-2 to switch places with a member of the family of genes responsible for making antibodies. Because the antibody genes function continuously in most white blood cells, says Hengartner, the swap keeps ced-9 permanently turned on, letting some old white cells outlive their usefulness and proliferate as cancer.

"If you inhibit [the] process of cell death, you're going to get a tumor, because the cells are not going to stop dividing when they should," says Frank J. Rauscher III, a cancer researcher with the Wistar Institute in Philadelphia.

Research by Hengartner's team "really illustrates [that] what . . . some may feel are obscure [animal] systems may have absolutely critical relevance and application to what we see in human disease,"

## Record size for ozone hole



NASA

*This satellite image of ozone concentrations shows a record-breaking region of low levels, depicted in purple hues, sitting over Antarctica. By Sept. 23, this so-called ozone hole had an aerial extent of 8.9 million square miles, almost the size of the entire North American continent. The area of depleted ozone measured about 15 percent larger this year than last year, according to NASA researchers.*

*Created by chemical pollutants that destroy ozone in the stratosphere, the hole begins to form each year in August and reaches its greatest extent in early October. It then dissipates in November. This image was taken by the Total Ozone Mapping Spectrometer on board the NIMBUS-7 satellite.*

*The legacy of last year's eruption of Mt. Pinatubo in the Philippines may have worsened this year's ozone depletion. Tiny droplets of volcanic sulfuric acid high in the atmosphere can enhance the destructiveness of the chlorine chemicals that attack ozone. Atmospheric scientists believe such droplets from Pinatubo and a volcanic eruption in southern Chile also added to the severity of last year's ozone hole.*

says Robert L. Comis of the Fox Chase Cancer Center.

Martinou's group has added to Hengartner's cell-death findings by studying rat nerve cells grown in laboratory culture. They report that genetically engineered nerve cells containing extra copies of the bcl-2 gene live two to three times longer than normal nerve cells.

Martinou and his colleagues suggest that their finding might provide insights into degenerative diseases of the nervous system, such as Lou Gehrig's disease and Huntington's disease. Martinou has also found that nerves taken from aborted human fetuses contain active bcl-2 genes. This supports a widely held theory that embryos generate extra nerve fibers — some of which later undergo programmed cell death — to ensure that the nervous system develops the correct nerve connections. — C. Ezzell