

## She who laughs gas conceives last

Infertility among women who work in dental offices might result from exposure to nitrous oxide used to anesthetize and sedate patients, if new findings in laboratory animals hold true for humans. In a study presented last week at the American Association of Dental Research meeting, nitrous oxide or "laughing gas" disrupted hormonal cycles and prevented conception in female rats.

For more than 20 years, anecdotal reports and epidemiologic studies have hinted at a link between nitrous oxide and miscarriage or infertility. One study, for example, showed higher-than-usual rates of fetal deformity, miscarriage and infertility among female anesthesiologists — but it didn't prove nitrous oxide responsible. Animal studies have implicated laughing gas in both male and female infertility, deformed offspring and miscarriage, but only at very high doses.

The new study is the first to implicate nitrous oxide in amounts commonly received by dental workers and to suggest how the gas sabotages the hormonal cycle. Gerard Kugel, a dentist and neurobiologist at Tufts University in Boston, along with colleague Carlos Letelier, described the results at the San Francisco meeting.

Eight hours a day for 35 days, Kugel and Letelier exposed 12 female rats to 500 parts per million nitrous oxide — a dose comparable, they say, to what a dentist might breathe over the same time period. In examining the exposed rats, they found the normal four-day ovulation cycle stuck in the proestrus phase, which occurs right before ovulation. Only six of the 12 conceived when mated, whereas all 12 control rats conceived.

To determine the cause, Kugel dissected the brains from some of the rats. In exposed rats, he discovered that an excess of a crucial reproductive hormone, called luteinizing-hormone-releasing hormone (LHRH), was apparently trapped in the hypothalamus. Normally, in rats and humans, the hypothalamus produces LHRH, which is then channeled to the pituitary gland to trigger the next step leading to ovulation. Kugel suggests the LHRH in the exposed rats became backed up like water in a clogged sink.

He says his results are not terribly surprising in light of the profound effect nitrous oxide has on the brain's pain response. It increases the production of brain chemicals called opioids, known to suppress pain and to interfere with the release of reproductive hormones, he notes.

Kugel stresses his study examined only the effects of chronic exposure — not the one-time dose a patient receives. An earlier study, he notes, revealed that

dentists get a higher dose than other medical workers because they often work in closed offices, hovering close to the mouth of a patient who is exhaling the gas. To reduce exposure, Kugel says, some dentists use a "scavenger" machine that sucks excess laughing gas out of the office. In studying the effectiveness of these machines, he found many left potentially harmful levels behind.

Kugel also points out that some people increase their exposure by nipping at nitrous oxide after work. Some medical and dental workers, he says, use laughing gas as a recreational drug. One dental assistant who suffered eight years of

infertility told Kugel she had been slipping into the dentist's chair and administering the gas to herself every day after work during that period. Research has shown abusers can become addicted to nitrous oxide, he adds.

Kugel says he doesn't want to scare doctors and dentists out of administering laughing gas to their patients. He still uses it occasionally to calm very anxious patients. His aim, he says, is to make medical professionals aware of any possible risks. "If you are careful with it, use it only when needed and get a scavenger," he says, "you cut down on these risks."

— F. Flam

## What tells anemones to kill their enemies?

Beneath the ocean surface, a tiny marine vessel receives orders to fire. A hatch blows open and a lethal payload blasts free. Within three-thousandths of a second, the missile reaches a velocity of 2 meters per second — more than 10,000 times the acceleration experienced by shuttle astronauts at liftoff — before crashing through the armor of its target: a tiny brine shrimp barely visible to the naked eye.

Welcome to the world of cnidarians — a family of sea anemones, jellyfish and other marine invertebrates that kill their enemies and prey by firing poisonous, microscopic projectiles called nematocysts. Scientists know little about cnidarian launch mechanisms. But new research tells a lot about the chemical and mechanical receptors that trigger an anemone's decision to fire.

The work provides the first evidence that some cnidarians, which are virtually blind, can "hear." They have a good ear, too, apparently differentiating among various planktonic pedestrians by the audio frequency of their "footsteps." Moreover, cnidarians appear unique among animals for their use of a primitive sense of smell to fine-tune their hearing organs to a few key frequencies.

Scientists have known for decades that cnidarians fire nematocysts in response to a combination of chemical and tactile stimuli. Glen M. Watson and David A. Hessinger, both of Loma Linda (Calif.) University School of Medicine, looked at the relationship between the chemical and mechanical receptors on the small sea anemone *Haliplanella luciae*. First they whetted the anemones' appetites by adding doses of N-acetylated sugars to their seawater. The sugars are the building blocks of chitin — the tough outer shell of shrimp and other anemone foods. Like odor molecules binding to smell receptors in the nose, these sugars bind to chemical receptors on cells adjacent to nematocyst-firing cells.

Then the researchers touched the anemones with a tiny, vibrating, gelatin-coated probe and counted the number of

nematocysts shot into the probe under varying conditions.

They found that in the absence of the sugars, a 55-hertz vibration triggered the biggest volley. But with the sugars, firing was best triggered by a 5-hertz vibration — the same frequency generated by the swimming movements of the anemone's favorite shrimp. "Nobody knew that these things were sensitive to vibration," Hessinger says. "We knew they were sensitive to contact, but this is the first time that, in a sense, we can say they hear."

More intriguing, he says, is the link between the anemone's chemical and mechanical receptors. The creature senses vibrations through tiny, hair-like cilia. When the anemone's chemoreceptors "smell" chitin-like sugars, these cilia instantly lengthen by as much as 70 percent, making them sensitive to 5-hertz frequencies instead of 50-hertz.

"I don't know of any case where any receptor can modulate the response frequency of a mechanoreceptor," Hessinger says, noting that similar sensory hairs, such as those in the human ear, have fixed lengths and respond to fixed frequencies. Apparently, he says, the anemone is "tuned to an unrealistically high frequency unless it smells the prey first. Once it gets a whiff, the tuning occurs rapidly, and it's ready to respond to the proper vibration should the prey be close enough to bring about a triggering."

Hessinger speculates that the receptor interactions evolved as a sort of "on-off" switch that helps prevent unnecessary firing of "expensive" nematocysts. "Nematocysts are very complicated structures, and it costs the anemone something to make them," he says.

The findings, described in the March 24 *SCIENCE*, are "pretty exciting," says Richard Mariscal, a marine researcher at Florida State University in Tallahassee. "This could be a real breakthrough to understanding the combined mechanical-chemical stimulus for a very important prey-capture structure in these animals."

— R. Weiss