Estrogen's Emerging Manly Alter Ego

Estrogen is usually described as the animal kingdom's primary female sex hormone. That's a gross oversimplification, however. Even that quintessentially male preserve—the sperm—depends on estrogen, scientists report this week. Without estrogen, males are infertile.

The new study, by Rex A. Hess at the University of Illinois at Urbana-Champaign and his colleagues, focuses on estrogen's role in male reproductive function. Nevertheless, the researchers observe that their findings also suggest a mechanism by which DDT and other estrogen-mimicking pollutants (SN: 7/3/93, p. 10) could wreak havoc on fertility. If these weak estrogens displace the body's more potent natural ones, they might diminish estrogen exposure—and sperm activity (SN: 1/22/94, p. 56).

Hess and his colleagues study mutant mice. These animals were bred to produce estrogen normally, but they lack the gene for an estrogen receptor—a protein that allows cells to take up the hormone. As a result, the mice cannot respond to the estrogen in their bodies.

Since this hormone plays a pivotal feminizing role in development, the scientists expected that mutant females would develop abnormally. "The big surprise," notes Patricia M. Saling, a reproductive cell biologist at Duke University Medical Center in Durham, N.C., was the finding 4 years ago that the males were infertile. Since then, Hess and others have been probing why.

Last year, Mitch Eddy of the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, N.C., and his colleagues showed that although the mutant males initially make sperm, their testes quickly degenerate. They traced the problem to a backup of excess seminal fluid.

In the Dec. 4 NATURE, Hess and his colleagues uncover the cause of the backup. It's not overproduction of the secreted fluid, as many had suspected. Instead, it's a drainage problem: The tubes running from the testes to the epididymis, where sperm mature and acquire the ability to fertilize eggs, are unable to drain off the excess liquid.

Besides damaging the testes, this excess fluid "also results in a very dilute ejaculate," notes Hess' colleague Kenneth S. Korach of NIEHS, a developer of the mutant strain of mice. If sperm are not packed densely in seminal fluid, fertility is impaired.

The tubes—known as efferent ducts—and the epididymis have never been considered "dominant in terms of making or breaking fertility," Saling says. The new study suggests otherwise. In fact, she says, "if manipulating the epididymal environment can lead to whopping amounts of infertility, this would suggest a new organ to target in the development of [male] contraceptives."

Ineffective fluid removal may not explain all of the mutant males' fertility problems, however. Eddy's team found that any sperm produced fail to mature and become capable of fertilization. Yet excess fluid might play a role here, too, speculates Richard M. Sharpe of the Medical Research Council in Edinburgh. In a commentary accompanying the NATURE report, he says that ". . . the abnormal amounts of fluid will effectively dilute [any maturing agents] secreted within the epididymis."

What the new data clearly demonstrate, Korach states, is the essential role of estrogen in male reproductive health. Indeed, Sharpe adds, "Suddenly, the idea of 'male' and 'female' hormones begins to look thin."

Hess' team argues that the new data also raise "further concern over the potential direct effects of environmental estrogens on male reproduction and reported declines in sperm counts."

After analyzing 61 studies, Danish scientists reported an apparent downward trend in human sperm counts 5 years ago (SN: 1/22/94, p. 56). Since then, others have challenged their assessment, arguing that the data—collected in different regions, over different times, and using different criteria—are not comparable.

Not so, concludes a major reanalysis.

"I think we were the only group that actually got all of the original data," says Shanna H. Swan of the California Department of Health Services in Emeryville. Her group analyzed the data using a series of alternative statistical techniques to see if the decline originally reported was an artifact of the way the data had been analyzed.

In the just-published November ENVIRONMENTAL HEALTH PERSPECTIVES, Swan's team reports that all its analyses show a decline in sperm counts since 1970 for men in Western countries. Indeed, Swan observes, the statistical representations that best fit the data detected an even stronger drop than the Danes had reported.

The new declines average more than 1 percent annually—or about 1.5 million sperm per milliliter per year in the United States and 3 million sperm per milliliter per year in Europe. *—J. Raloff*

Herpesvirus linked to multiple sclerosis

Compared to other babyhood diseases, roseola is mild. More than 9 out of 10 infants get it, running a fever, developing a rash, and usually recovering quickly.

Now, research shows that the herpesvirus that causes roseola can reemerge years later in people with multiple sclerosis, a nerve disease characterized by muscle weakness, vision problems, and paralysis. Some scientists suspect that this virus somehow triggers the disease.

Roughly 350,000 people in the United States have multiple sclerosis, which usually strikes between the ages of 20 and 40. It often begins as an off-and-on disease, with symptoms repeatedly appearing and disappearing. The disease eventually progresses to a downward spiral.

Many scientists believe that multiple sclerosis arises from a combination of factors that has not yet been established. Genetic makeup seems to predispose some people to the disease (SN: 9/16/95, p. 180). Researchers also suspect that it results from an autoimmune reaction in which the body's immune cells attack myelin, the sleeve of tissue that surrounds nerve cells. At sites in the brain where the myelin has been attacked, patients develop lesions—also called plaques or scleroses. Over time, many scleroses form, giving the disease its name.

Scientists don't know how the process starts, however. Suspecting that viruses play a role, several groups of researchers have investigated the herpesviruses in recent years. Some detected evidence of the roseola virus, or human herpesvirus 6 (HHV-6), in brain tissue taken from deceased multiple sclerosis patients.

In the first part of the new study, researchers at the National Institute of Neurological Disorders and Stroke in Bethesda, Md., analyzed blood from 102 volunteers: 36 people with multiple sclerosis; 31 people with various other neurological diseases, including Parkinson's; 21 people with other inflammatory illnesses, such as lupus, which is also an autoimmune disease; and 14 healthy people. The researchers found antibodies to HHV-6 in two-thirds of multiple sclerosis patients in the recurrent stage of the disease.

Another test found that 15 of 50 multiple sclerosis patients harbored DNA from the replicating virus itself, says Steven Jacobson, a viral immunologist at the institute and a coauthor of the report, which appears in the December NATURE MEDICINE.

Both findings were curious. First, the antibodies were the sort that a body produces in the throes of a battle against the virus, not "memory" antibodies that circulate routinely in the body, awaiting a call to action, Jacobson says. The only other study participants to show high concentrations of these antibodies were two of the patients with lupus and a patient with another inflammatory disease.

In the second part of the study, the researchers detected no active DNA from HHV-6 in anyone other than multiple sclerosis patients.

Preliminary evidence from an ongoing study shows that HHV-6 protein is present in areas of the brain where myelin is being destroyed—but not in healthy areas of the same patient's brain, Jacobson says.

"This is very interesting and potentially important work, but it leaves a conundrum," says David A. Hafler, an immunologist and neurologist at Harvard Medical School in Boston. "Is HHV-6 really involved [in the cause of multiple sclerosis], or is it just a consequence of the disease?" The evidence doesn't resolve this question, but the study adds to the growing school of thought among scientists that viruses are somehow involved with multiple sclerosis, Hafler says.

Jacobson agrees that no one knows what causes the debilitating disease, but he says that herpesviruses make fitting suspects. These viruses attack the nervous system and typically lie dormant for long stretches—just as multiple sclerosis does. "We know this is a latent and persistent virus," Jacobson says.

In any case, the findings convincingly show that many multiple sclerosis patients have an HHV-6 infection, says Byron H. Waksman, an immunologist at New York University.

The new study may provide evidence that HHV-6 acts to maintain, rather than cause, multiple sclerosis lesions, Waksman says. Either way, the long progression of multiple sclerosis may remain a puzzle even after the role of the virus is understood, he says. *—N. Seppa*

Tracking a black hole eruption

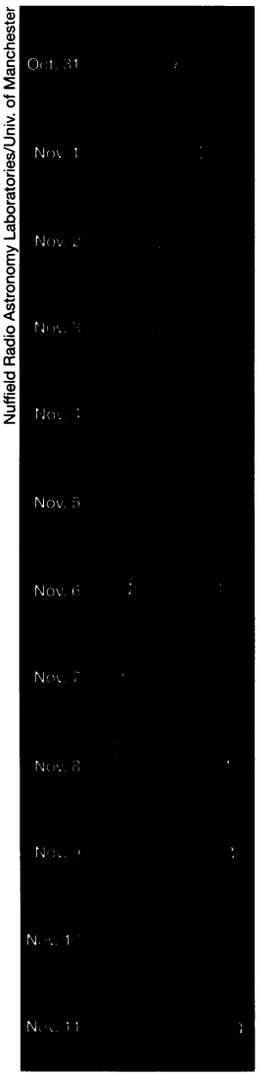
On Oct. 29, astronomers around the world were alerted that a massive, compact body 40,000 light-years from Earth was once again shooting off fireworks. Within 2 days, scientists had trained an array of radio telescopes on the object, a suspected black hole partnered by an ordinary star.

For 2 weeks, the telescopes tracked the evolution of two oppositely directed jets of radio-emitting gas spewed by the black hole system, known as GRS 1915+105. Each jet races at 90 percent of the speed of light. Because one of the jets points toward Earth, it appears to move twice as fast as this cosmic speed limit.

Astronomers had previously observed superluminal motion of material expelled by GRS 1915+105, notably during a giant outburst 3 years ago (SN: 9/3/94, p. 150). The network of telescopes employed during the most recent event, however, tracked the activity closer to the black hole than ever before—within about 400 light-years, says Thomas W.B. Muxlow of the University of Manchester in England. He and his colleagues announced their findings this week.

Known as MERLIN (multi-element radio-linked interferometer network), the telescope array consists of six detectors spread across England, working in concert to create radio images sharper than the Hubble Space Telescope can generate in visible light. Other arrays, even larger than MERLIN, can home in on smaller objects but can't detect such faint emissions, Muxlow notes.

GRS 1915+105 is called a microquasar because its stream of X rays and blasts of radio-emitting gas resemble a scaled-down version of the action of quasars in faraway galaxies. By monitoring this nearby source, "we can apply [what we learn] to much more distant objects in the universe," says Muxlow. *—R. Cowen*



Nuffield Radio Astronomy Laboratories/Univ. of Manchester

False-color radio images (red denotes the most intense emissions) track gas blobs shot from a suspected black hole. The blobs at left are approaching Earth and seem to move faster than light. Gas in the most recent image has two-hundredths the brightness of that in the earliest.

Corroded planes turn paint pink

Airplanes get rained on, baked in the sun, and attacked by the wind—onslaughts that corrode metal and ultimately compromise safety. Detecting corrosion can be a tedious job for maintenance crews, since many imaging techniques work only on one small area of a large aircraft at a time.

Now, researchers are developing a way for airplanes to signal to their crews when it's time for repairs. At a meeting of the Materials Research Society in Boston this week, Gerald S. Frankel of Ohio State University in Columbus described paints that change color if the underlying metal becomes corroded.

The paints, created by Frankel and his colleague, Jian Zhang, detect changes in acidity and alkalinity, measured as pH. When water and air attack some metals, the resulting electrochemical reaction produces ions that increase pH.

One of the paints consists of a clear acrylic coating mixed with phenolphthalein, a chemical that turns from colorless to red above a given pH. Frankel and Zhang made test samples by covering pieces of an aluminum alloy with the special coating and a top layer of plain acrylic.

Passing a current through the samples stimulated the electrochemical reaction, and visible pink spots popped up. Later, Frankel says, "we will probe with electrochemical and other techniques to prove there is corrosion happening locally." From these measurements, the researchers calculate that the phenolphthalein coating could detect pits less than 15 micrometers deep.

The team has also looked at acrylic mixed with a compound that fluoresces under ultraviolet light when above a particular pH. By measuring the emitted light with a spectrophotometer, Frankel says, the researchers may be able to quantify the color change and thus the extent of corrosion.

The color change method, says William M. Mullins of Technical Management Concepts at Wright-Patterson Air Force Base in Ohio, is a "very clever idea. You could walk down the vehicle and see there's a pink spot. It would be very nice to be able to do that without actively going in with an instrument."

The new method would be especially useful for detecting the most troublesome corrosion, which is concealed around rivets and in the joints where sheets of metal overlap, says Mullins, who uses ultrasound to map out and model corrosion on the surface of materials.

Only clear coatings will work, but that limitation on airplane appearance may not matter if the coatings are used in hidden places, Frankel says. *—C. Wu*