

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 re-emerge 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.