New Study May Redefine High-Risk Sex

Researchers who set out to study mother-to-infant AIDS transmission in monkeys have, much to their own surprise, dragged a nettlesome AIDS question into public view and challenged definitions of "high-risk" sexual activities that have stood since the start of the AIDS era 15 years ago.

The work began with an attempt to determine whether infant monkeys become infected at birth by ingesting blood from infected mothers. That led to a follow-up study suggesting that oral intercourse in humans may be riskier than the anal variety—contrary to a mountain of reports that identify unprotected anal intercourse as the likeliest route to an AIDS-abbreviated life.

The investigators are quick to point out that their findings come from a study of simian immunodeficiency virus (SIV) in macaques, not of HIV, the AIDS-causing virus, in people. Moreover, unlike sex, exposure in the lab does not cause the tiny abrasions that can convey the virus to the bloodstream.

The researchers report in the June 7 SCIENCE that the minimum SIV dose required to infect a monkey by mouth was 6,000 times lower than the dose needed to infect via the rectum. Six of seven full-grown macaques have become infected in this way, say the researchers, who used SIV because monkeys are essentially unaffected by HIV. Two of the six have died of the simian version of AIDS.

Ruth M. Ruprecht of the Dana-Farber Cancer Institute in Boston and her colleagues conclude that "unprotected receptive oral intercourse should be added to the list of risk factors for HIV-1 transmission."

Although researchers at the Centers for Disease Control and Prevention (CDC) in Atlanta acknowledge that "such sexual activity does carry a risk of HIV-1 transmission," they argue in a 1996 supplement to the journal AIDS that the risk "is substantially less than the risk of transmission during unprotected penile vaginal and penile anal sex."

That conclusion arises from studies of the self-reported sexual practices of people have who have become infected. Though imperfect, such studies provide the best information available in humans.

Case reports suggest that 17 people worldwide—three to five of them in the United States—have acquired HIV through oral sex. "I think our animal study should serve as a warning in light of the human case reports that oral sex is not safe sex," Ruprecht says.

"We can agree with that—low-risk doesn't mean no-risk," says Scott D. Holmberg, a CDC epidemiologist who studied one such case. "But we need to be careful about drawing conclusions based on macaque experiments."

Ruprecht and her team became intrigued with the question of oral transmission of SIV when they found that infant monkeys become infected by swallowing blood during birth. The team theorized that newborns lack sufficient stomach acid to disarm the virus.

To test that idea, they dropped SIV on the tongues of three adult macaques, two of which had been given antacids. When, contrary to expectation, all three became infected, the team tested seven monkeys to find the lowest dose of SIV needed to infect the monkeys orally and rectally. The higher efficiency of oral infection was a "surprise because, in humans, anal receptive intercourse has been recognized as the most dangerous activity," says Ruprecht.

It is difficult to establish any link between oral sex and AIDS in humans because it is hard to find people who have only oral sex. Researchers have also found a protein in human saliva called secretory leukocyte protease inhibitor—a natural cousin of the new AIDS drugs on the market—that guards against HIV infection (SN: 2/18/95, p. 108).

Ruprecht and her colleagues have not studied this protein in macaques, nor have they tried to determine whether SIV-infected cells, which shed virus, are as infectious as the cellfree virus they used. Other questions concern the cells that SIV infects and the route by which it enters the monkey's system.

"We need to do a lot more work," Ruprecht says. "We have raised more questions than this study can answer."

— S. Sternberg

'Estrogen' pairings can increase potency

Toxicologist John A. McLachlan and his coworkers made a startling observation 2 years ago: A pair of polychlorinated biphenyls (PCBs) delivered together had up to 20 times the ability to switch the sex of incubating turtles as either of these weak estrogen mimics had when delivered alone (SN: 10/8/94, p. 239).

Now, McLachlan and his coworkers at the Center for Bioenvironmental Research at Tulane and Xavier Universities in New Orleans note even more dramatic synergies among several ubiquitous pesticides. For instance, they had to use 160 times as much endosulfan or 1,600 times as much dieldrin alone to match the estrogenicity of the two combined, they report in the June 7 SCIENCE.

Chlordane offered the biggest surprise. While it exhibits no estrogenic activity on its own, this termite killer proved almost as potent as dieldrin or toxaphene in boosting the estrogenicity of endosulfan. Toxaphene is another weak mimic of estrogen, the primary female sex hormone.

Though dieldrin, toxaphene, and chlordane have long been banned in the United States, traces of all three persist in the environment. Endosulfan remains in widespread use. Steven F. Arnold, a coauthor of the study, says his team focused on these pesticides because of their presence in the eggs of a population of reproductively impaired alligators at Florida's Lake Apopka (SN: 1/8/94, p. 24).

Hormones regulate critical activities in the body by unlocking receptors on and in cells. Estrogen triggers various activities, depending on its timing and the receptor's location, thus making it difficult to evaluate the hormone's effects within a whole animal.

The Tulane-Xavier team therefore inserted a human estrogen receptor into yeast cells, which normally lack hormone receptors. Then they added a chemical response system that turns yellow when the receptor is activated, enabling them to quantify estrogenicity.

Describing the new findings as "quite interesting" and solid, Stephen H. Safe of Texas A&M University in College Station cautions that one should not conclude that all weak environmental estrogens will exhibit similar synergy or prove toxic in animals. However, he adds, "it's certainly worth looking at."

The new data also suggest it may be time "to resurrect" the idea of multiple hormone-binding sites on each estrogen receptor, says S. Stoney Simons Jr. of the National Institute of Diabetes and Digestive and Kidney Diseases in Bethesda, Md., in an accompanying commentary.

Indeed, McLachlan points out, the data suggest that two binding sites exist and that both "would have to be occupied for the synergy to occur." While it's unclear how the pairs of pollutants operate, he says they may act as partial keys that can unlock only one of the sites and only after the pollutants have merged. *— J. Raloff*

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