Keeping mosquitoes healthy for humans' sake

Efforts to stop the spread of mosquito-transmitted diseases usually focus on killing the insects. Although researchers are developing novel techniques for reducing mosquito populations (SN: 4/27/96, p. 270), the bugs and the diseases they carry continue to spread.

So some scientists are taking a new approach—trying to keep mosquitoes free of disease. They hope eventually to genetically engineer the insects to resist viral infections and pass that trait on to their offspring.

A Colorado State University team in Fort Collins took the first step toward this goal by using a piece of RNA to prevent the dengue virus from replicating in mosquito saliva. Mosquitoes treated in this way cannot then transmit the virus.

The dengue virus, carried by *Aedes aegypti* mosquitoes, poses an increasing threat to people living in warm regions from Texas to Asia (SN: 4/6/96, p. 218). Dengue fever causes flulike symptoms in humans, and dengue hemorrhagic fever can kill infants and young children.

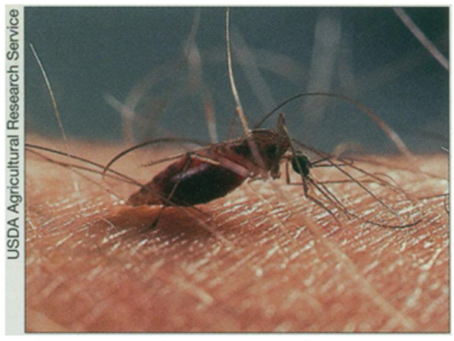
In their study, Kenneth E. Olson and his coworkers attached a small piece of dengue virus RNA to Sindbis, a common virus that has little effect on mosquitoes, they report in the May 10 SCIENCE. They then infected mosquitoes with the engineered Sindbis virus, as well as with normal dengue virus.

The engineered virus replicated in almost all of the mosquitoes' tissues, including their salivary glands. While replicating, the dengue RNA molecules from the engineered virus jammed the replication machinery of the normal dengue, although how they did so remains unclear.

The researchers found no dengue virus in the mosquitoes' saliva. Moreover, when the scientists injected the saliva into uninfected mosquitoes, no signs of the virus appeared.

This is the first successful attempt to confer "intracellular immunity" on an important human pathogen by introducing a foreign gene into an organism, Anthony A. James of the University of California, Irvine asserts in a commentary accompanying the report.

The method appears to have had some success with other mosquito-borne viruses as well. In a study in the April 30 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, Ann M. Powers and other members of the Colorado team report that they halted replication of the LaCrosse virus—which causes encephalitis in children—in *A. triseriatus* mosquitoes. However, the Sindbis virus failed to infect the salivary glands of *A. triseriatus*, so the mosquitoes could still transmit the disease.



An A. aegypti *traversing a hairy arm.*

The scientists hope to use dengue and LaCrosse RNA that interfere with viral replication to meet their larger goal of ensuring that mosquitoes can pass disease resistance on to their offspring.

But "that's quite a big step," notes coauthor Barry J. Beaty.

Researchers have created transgenic mosquitoes using marker genes, but these genes don't alter insects' ability to transmit diseases. They fashioned these transgenic bugs by inserting DNA into mosquito eggs. A new technique now being tested involves inserting DNA into retroviruses, RNA-containing viruses that may integrate the DNA directly into the mosquito genome. — *T. Adler*

Petri dish + hormones = parenthood?

Childless couples pondering in vitro fertilization (IVF) quickly learn that the laboratory is neither an inexpensive nor a congenial place to conceive a baby. Now, a technique being tried in the United States may turn petri dish parenthood into a more tolerable experience that many more couples can afford.

What the new method won't do, scientists say, is turn a gamble into a predictable success—at least for now. Still, Jeffrey B. Russell and his colleagues at the Reproductive Endocrine and Fertility Center of Delaware in Newark, say the technique, called immature oocyte retrieval, promises to reduce the risks, costs, and discomforts of IVF.

In standard IVF practice today, women receive daily injections of powerful hormones for a month or more. The flood of hormones bullies the ovaries into preparing as many as 2 dozen eggs for fertilization, rather than nature's preferred count of one. In about 10 days, doctors nonsurgically suction mature eggs from the ovaries and fertilize them in a lab dish. Fertilized eggs that successfully develop into 32-cell embryos can then be placed in the nurturing warmth of the womb.

The newer procedure, which has been used in mice and cows for a decade and was first tried successfully in humans in Korea in 1992, differs from the current routine primarily in its timing. Rather than hastening maturation of eggs within the ovaries, doctors extract immature eggs from the ovaries and push them to mature outside the body.

Scientists bathe the eggs with tiny doses of powerful hormones, a process that causes the eggs to mature. This spares women the daily hormone injections that contribute $3,000 to the IVF bill—and turn every day into a queasy roller-coaster of mood swings, headaches, nausea, and bloating. Worse, doctors say, the injections may confer a slight risk of ovarian cancer.

"What you're looking at is a revolutionary technique in the human reproductive field," Russell says. "We have the capability to stop giving patients most drugs, to eliminate the long-term risk of ovarian cancer, and to decrease the time involved in doing an IVF cycle by 75 percent, with a 40 percent reduction in cost."

The scientist who pioneered the technique in mice in 1984 concurs. "In time, the technique will improve to where it represents a distinct advantage over earlier techniques in success, safety, and cost," asserts John Eppig of Jackson Laboratory in Bar Harbor, Maine.

If the new method even partly meets such lofty expectations, it promises to attract many more childless couples. Demand for the current procedure in the United States has spawned a $2-billion-a-year industry, despite medical bills approaching $9,000 per attempt and success rates of just 18 percent.

Russell, who described the research on April 30 at a meeting of the American College of Obstetricians and Gynecologists in Denver, produced embryos for six of the first eight patients on whom he tried the new technique. These women had tried standard IVF unsuccessfully a total of 18 times. One woman became pregnant and gave birth to a baby girl.

Although this single birth amounts to a success rate of just 5 percent, Eppig says Russell's record is likely to improve, given time and systematic refinement of his technique.

"As with anything that's revolutionary," Russell acknowledges, "we have to go through a steep learning curve to bring this to where it needs to be."

In mice, Eppig says, about 45 percent of eggs matured outside the body produce healthy offspring. "We have produced hundreds and hundreds of mice this way," he says. "We have yet to see an abnormality." — *S. Sternberg*