

## More ways mother's milk fights disease

For decades, pediatricians have touted the advantages of breast-feeding. Not only does it promote mother-infant bonding, they argue, it also transfers many of a woman's disease-fighting antibodies to her baby.

But microbiologists have long suspected there was more to the story. Reporting in Atlanta at Experimental Biology '95, several teams confirmed this week that mother's milk indeed delivers not just antibodies, but a battery of additional infection-fighting agents.

Among them are retinoic acids, a family of vitamin A derivatives. Charles E. Isaacs and his colleagues at the New York State Institute for Basic Research on Staten Island infected cultures of cells with a herpesvirus, then measured how rapidly the virus colonized untreated cultures and cultures treated with beta-carotene, retinoic acids, or one of several other vitamin A derivatives in breast milk.

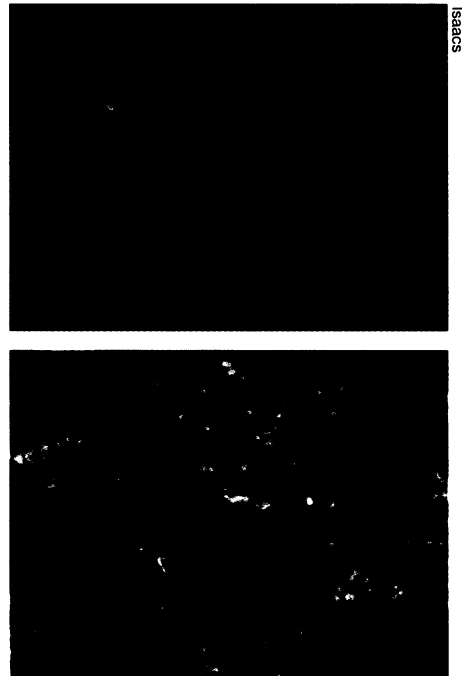
Only the retinoic acids conferred any protection. After 48 hours, two types had each reduced the rate of viral colonization to one-hundredth that seen in unpro-

tected cells; another reduced it to a ten-thousandth of the unprotected rate.

Isaacs emphasizes that the retinoic acids don't kill herpes. His group selected this virus to model the likely responses of many others. "But by slowing down the rate of viral replication, you're helping the immune system," he notes. "With retinoic acid in your body, you might only have to fight 50 virus particles instead of 50,000 or 100,000."

Olle Hernell of the University of Umeå, in Sweden, and his coworkers focused on *Helicobacter pylori*. This bacterium, responsible for many stomach ulcers in adults, can also infect children.

Earlier research had shown that certain glycoproteins — carbohydrate-carrying proteins — can inhibit the ability of this bacterium to attach to the stomach lining. The researchers therefore tested the glycoprotein kappa-casein, one of the two primary proteins in breast milk, in cultures of the mucus-secreting cells that line the stomach. They found, notes coauthor Bo Lönnnerdal of the University of California,



*Herpesvirus, denoted by green fluorescence, has a hard time taking over cells protected by retinoic acid (top). Over the same time period, virus overwhelms unprotected cells (bottom).*

## Tamoxifen derivative shrinks mouse tumors

To treat breast cancer, which afflicts 1 in 10 U.S. women, physicians often use tamoxifen, a drug that blocks estrogen's stimulation of breast tumors.

In addition, scientists are evaluating tamoxifen as a potential protective agent for healthy women who have an elevated risk of breast cancer.

But tamoxifen produces side effects. It increases the risk of uterine and endometrial cancer, can cause hot flushes, and can disturb the central nervous system, triggering depression, irritability, and short-term memory loss.

To lessen these side effects and boost the drug's therapeutic powers, scientists have developed a tamoxifen derivative that is proving effective in fighting tumors in animals, says Marcus E. Brewster, a chemist at Pharmos Corp. in Alachua, Fla.

Speaking at last week's meeting of the American Chemical Society in Anaheim, Calif., Brewster described the design and synthesis of the new anticancer agent, tamoxifen methiodide. The compound dissolves more easily in water, he said, which impedes its ability to enter the brain's fatty tissues and disturb the central nervous system.

In collaboration with researchers at the Weizmann Institute of Science in Rehovot, Israel, Brewster and his colleagues are testing the tamoxifen derivative in rodents.

Results show that the new drug did not infiltrate the brains of rats. Cancerous tumors shrank in 90 percent of the

mice tested and in 40 percent grew too small to measure Brewster reports.

"A chemical modification of the tamoxifen molecule designed to decrease its entry into the brain resulted in improved tissue selectivity," Brewster says.

As well as blocking estrogen stimulation of breast tumors without disturbing the nervous system, the new molecule has unexpected benefits — it strengthens bones without overstimulating the uterus.

This reaction occurs because, unlike tamoxifen, the new molecule does not fit well into the uterus' estrogen receptors, says Brewster. Therefore it does not upset uterine tissues and cause cancer.

On the other hand, Brewster and his colleagues report, the tamoxifen derivative does fit well into the estrogen receptors of bones, stimulating growth and perhaps helping to prevent the onset of osteoporosis.

Women who take tamoxifen to prevent breast cancer should not have to suffer "hot flushes, depressions, and cognitive decline," Brewster says. "Breast cancer patients as well could benefit from a better quality of life if these side effects are prevented."

The new drug "appears to offer a breast cancer treatment and prevention alternative with the benefits, but without many of the limitations, of tamoxifen," he concludes.

Trials of tamoxifen methiodide in women may begin before the end of the year.

—R. Lipkin

Davis, that "*H. pylori* didn't attach."

In the gastrointestinal tract of children receiving kappa-casein from mother's milk, Lönnnerdal now suspects, the bacteria "would also wash out instead of attaching — and therefore become harmless."

Although cow's milk contains even more kappa-casein than breast milk, the bovine form "doesn't have any effect whatsoever on the virus," Lönnnerdal says. Why not? Because the cow's glycoprotein has a different carbohydrate.

Breast milk also contains large quantities of interleukin-10 (IL-10), an immune system molecule that inhibits inflammation, report Roberto Garofalo and his colleagues at the University of Texas Medical Branch in Galveston in the April PEDIATRIC RESEARCH. Inflammation is one way the body fights infection. But sometimes the body fights too aggressively, and healthy tissue succumbs. Indeed, one reason gastrointestinal disease can be so devastating to infants is that the inflammatory process tends to get carried away.

At the meeting, Garofalo described preliminary data suggesting that newborns do not produce IL-10 as effectively as adults. He says that may help explain the significance of another of their findings: that colostrum, the fluid that precedes breast milk, contains the most IL-10.

The emerging picture indicates that mom's milk offers a host of beneficial chemicals that probably work in concert with antibodies to protect babies from life-threatening infections.

—J. Raloff