

# New evidence favors breast-feeding

*Three studies point to protective substances in human milk*



Nursing baby benefits from lymphocytes, antibodies, and other proteins it ingests.

**N**ew facts about mother's milk keep turning up that suggest Nature, in instance after instance, is best left to her own devices.

Investigators in Texas, in Göteborg, Sweden, and in Minnesota have recently reported the presence in human milk of lymphocytes, antibodies, and certain proteins that may well play a key role in protecting a newborn baby from immunological or infectious complications. Their findings, outlined below, present another compelling case for breast-feeding, which already has a growing and vocal constituency in the U.S.

## LIVE LYMPHOCYTES: FIRST-LINE DEFENSE

Living white blood cells in a mother's milk were once considered a sign of recent infection. But new studies show that their presence may be essential to her baby's health.

In one such study Dr. Alan E. Beer and his associates at the University of Texas in Dallas found that human milk contains living lymphocytes in concentrations as high as those in blood. Lymphocytes taken directly from the milk are fully active in cell

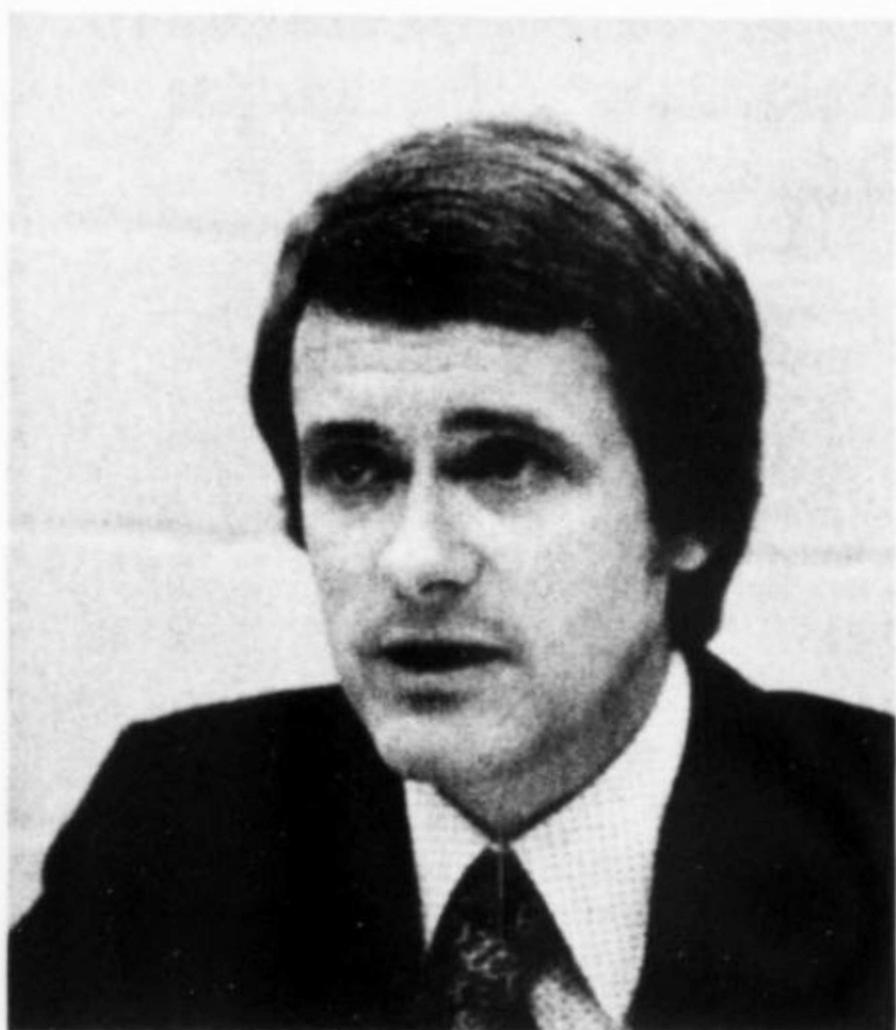
culture, reports Dr. Beer, an associate professor of cell biology, obstetrics, and gynecology at Southwestern Medical School in Dallas. These cells are immunocompetent and able to express delayed hypersensitivity reactions "to tide the infant over as it is exposed to a highly contaminated environment," he told the American College of Obstetricians and Gynecologists meeting in Boston.

Clinicians see the breast as a second placenta, performing a function—the transfer of immune "killer cells" to the fetus—that the placenta may have found too dangerous to complete in utero. A mother's protective antibodies can cross the placenta to the fetus, usually in five times the concentrations existing elsewhere in her body. These protective antibodies persist in the infant for four or five months after birth, on the alert for infection.

"But that's only half the story," the Texas obstetrician observes. "There's about a two-week delay between the time an invader enters the infant and the time his own killer cells go into action." If the baby is being breast-fed, Dr. Beer suggests, the mother's lymphocytes can come to his rescue.

"Here's where we ought to give breast-feeding a second thought," he says. Several unexplained but deadly pediatric illnesses may need to be re-examined in terms of the adoptive immunity apparently conferred by breast-feeding. Killers like sudden infant death syndrome (SIDS) and necrotizing enterocolitis may be basically infectious diseases that take advantage of an immunologically immature infant, he speculates.

"We know that necrotizing enterocolitis, the chief killer of blood-transfused babies, can be prevented if the baby is fed human milk containing lymphocytes. And the incidence of SIDS is known to be much



Dr. Alan Beer says breast milk may confer immunity to some deadly infant diseases.

higher in infants who are not breast fed." He thinks SIDS may well be an anaphylactic response to regurgitated cow's milk.

Previous animal experiments and some new human studies suggest that the immune protection conferred through mother's milk is the last in a chain of immune reactions benefiting the fetus in utero.

"In reproductive biology we have been led to believe that an exaggerated immunologic response by a mother to the foreign tissue antigens of her fetus or placenta might be operational in certain cases of infertility, repeated pregnancy wastage, intrauterine growth retardation, or toxemia," Dr. Beer told his colleagues. But quite the reverse has turned out to be true: If a woman's immune system is normal, the stronger her antigenic difference from her fetus the better its chances for health.

The paradox is best illustrated by rabbit studies in which the University of Texas team sensitized one of a female rabbit's uterine horns against her mate's sperm, and used the other as a control. Invariably, he reports, the number of implantations and the fetal growth rate were much higher in the sensitized horn.

"In fact, anything we've done to prejudice the survival of the fetus by increasing a mother's immune reaction has led to an enhanced rate of

pregnancy," Dr. Beer told MWN. "On the other hand, if we look at women whose immune response was frustrated during pregnancy, such as kidney transplant patients or those with lupus erythematosus or rheumatoid arthritis, they show an increase in toxemia and their fetuses are often small for date.

Microscopic studies of the reproductive process in animals have helped explain this paradox, Dr. Beer told his fellow obstetricians. When a fertilized ovum antigenically dissimilar to the mother is implanted, "the uterus engages in an intense local inflammatory response with all the features of a delayed hypersensitivity reaction," he explains. "This response causes a growth of decidua buffer tissue between the developing placenta and the mother's immune system, which favors formation of a humoral antibody rather than a killer-cell type of immune response." Blocking antibodies are formed, which coat the surface of the placenta and mask it from harmful lymphocytes.

The explanation makes sense to Dr. Karl E. L. Hellstrom, professor of pathology at the University of Washington in Seattle and an originator of the blocking factor concept.

"We know some antigens are better in eliciting a cellular immune response, while others are better in provoking humoral responses, including blocking factors," he comments. "The latter group may well include placental antigens."

## ANTIBODIES MAY BE SENSITIZED IN GUT

One theory by which immunity to enteric pathogens is transferred from mother to child through breast feeding has been advanced by a Texas pediatrician. Specific antibody-producing cells, says Dr. Randall M. Goldblum, are first sensitized in the mother's gut, and home to her breast, where the colostric cells produce secretory immunoglobulin A (IgA) antibodies to her enteric bacteria.

An assistant professor at the University of Texas Medical Branch at Galveston, Dr. Goldblum arrived at that conclusion following a study of precolostrum, colostrum, and transitional milk he did while a fellow at the Institute of Medical Microbiology in Göteborg, Sweden. He reported his findings to the Society for Pediatric Research meeting in Denver.

With his Swedish associates, Dr. Goldblum studied the colostrum of seven normal women. He first determined the amount of antibody against a pool of O antigens from eight commonly encountered *Escherichia coli* strains. Though the team detected small amounts of IgG and IgM antibodies, they found that the anti-*E. coli* antibodies were largely IgA. Large numbers of antibodies were seen as early as two months prepartum, but they decreased rapidly after the first week postpartum, an effect the researcher attributes to simple dilution with milk.

Additional investigation confirmed that most of the IgA produced in the colostrum was of the secretory type, a finding that suggested to Dr. Goldblum and his colleagues that the sensitized lymphocytes had undergone antigen-induced clonal proliferation within the mammary gland or had homed to that organ after they had become sensitized at another site.

To test the latter hypothesis, the Göteborg investigators went straight to the point: They asked three of the volunteer women to swallow "cocktails" of live *E. coli* 083, an unusual but nonpathogenic strain of bacteria, sometime during the last month of their pregnancies.

Typing of *E. coli* in their stools confirmed a short-lived and mild colonization, without symptoms, following each oral immunization. Yet while the investigators saw no change in serum antibody response to the organism, they found cells producing secretory IgA antibodies to the *E. coli* strain in each woman's colostrum within a week after ingestion.

It was the lack of systemic immune response to the bacteria that con-

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#### BREAST-FEEDING *continued*

vinced Dr. Goldblum that antigenemia was not a factor in the appearance of antibody-producing colostric cells.

"It would appear that sensitized cells from a woman's gastrointestinal tract migrate to her breast," he concludes. "Thus colostrum, with its antibodies and antibody-producing cells, may provide a mechanism for transferring to her infant built-up immunity to enteric organisms she has been continually exposed to."

### LACTOFERRIN AS A POTENT GERM-KILLER

Lactoferrin, a protein found abundantly in colostrum, appears to be involved in the killing of bacteria by phagocytes, report two investigators who have been studying its action at the University of Minnesota-Minneapolis Medical School.

The red, iron-binding protein is also secreted in the mucosal tissues of the respiratory, gastrointestinal, and genitourinary tracts; in seminal and cervical fluids, tears, and saliva; and in granular extracts of polymorphonuclear (PMN) leukocytes.

At St. Mary's Hospital in Minneapolis, Drs. Robert S. Dobrin and Beulah Gray collected some 400 cc of colostrum from volunteer nursing mothers, isolated the red protein, and set about measuring its ability to eradicate microorganisms.

Previously, several investigators had tried to figure out the precise germ-killing mechanism of the inflammatory process that occurs when a phagocytic neutrophil engulfs a live bacterium. One bactericidal system consists of halogenation with iodine or chlorine ions induced by hydrogen peroxide in the presence—or absence—of a secretory enzyme, peroxidase.

The system was initially described in the 1960s by Dr. Seymour J. Klebanoff at the University of Washington School of Medicine. He found that the nonenzymatic effect of peroxide-plus-iodide in killing microorganisms was greatly enhanced by catalysis with myeloperoxidase. This green enzyme,

secreted by PMN leukocytes, is thought to explain the bactericidal properties of pus, for example.

The Washington team found that lactoferrin, like myeloperoxidase, had the strongest bactericidal effect when it was used with chloride rather than with iodide as oxidizable co-factor in an acid environment. As Dr. Dobrin told the Federation of American Societies for Experimental Biology in Atlantic City, the peroxide-lactoferrin-chloride system he tried reliably killed 88% of rough-strain *E. coli* B inocula; only 38% of the same strain were destroyed by the nonenzymatic peroxide-plus-chloride control system run at the same time.

The Minnesota team found lactoferrin's molecular weight to be 70,000; Dr. Klebanoff had previously established myeloperoxidase's as 148,000. Lactoperoxidase, also found in human colostrum, milk, and saliva, is close to lactoferrin in molecular weight, but its kill rate is only 63%.

Dr. Dobrin is now a research fellow of the New York Kidney Disease Institute, working jointly at Rockefeller University and Memorial Sloan-Kettering Cancer Center. He notes that lactoferrin performs best at low pH in combination with iron and in a high ionic environment—three prime parameters of the inflammatory process. Therefore he sees the protein as "tailor-made" for a role in neutralizing bacterial infection at the site of inflammation.

Does the high concentration of lactoferrin in colostrum mean a newborn nursing drinks in with his mother's milk a kind of peroxidase-mediated protection against germs, along with the lactic immune antibodies? It's theoretically possible, Dr. Dobrin told MWN, adding that his findings "may have implications for the benefits of breast-feeding."

But he stressed that it's premature even to think of using lactoferrin as a pharmaceutical germicide, antiseptic agent, or diet additive. Rather, his continuing investigation is aimed at gaining further insight into the protective protein's over-all role in the immune defense. ■

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