



# Sugar Treatment for Infertility

by **HEATHER SMITH THOMAS**

Bacterial uterine infection is a leading cause of infertility in mares. The infection and inflammation of the uterine lining (endometritis) can interfere with the establishment of pregnancy, or may even leave the uterus so scarred that it cannot maintain pregnancy even if the conceptus does manage to attach and begin to grow.

Mares with uterine infections are generally treated with expensive and lengthy courses of antibiotics. These sometimes help but often they don't. Researchers have been trying

to find other ways to treat endometritis, since extensive use of antibiotics can often be counterproductive.

One very promising area of research has been the use of sugar to treat endometritis. At Southern Illinois University's Carbondale Laboratory, researchers led by Dr. Sheryl King have been incubating equine uterine tissue, working with four types of bacteria that most often cause uterine infections. They then treated the infected tissues with a plant-derived sugar called mannose.

This special sugar is supplied by Sigma Chemical

Company for experimental use. Mannose is a monosaccharide (a simple sugar, the monosaccharides are colorless, crystalline substances with a sweet taste and are a combination of carbon, hydrogen and oxygen—the hydrogen always having twice as many atoms as the carbon and oxygen). Mannose is produced by the oxidation of mannitol

(a six-carbon sugar alcohol widely found in plants and fungi) and is similar to dextrose in its general properties. Mannose is easily prepared, chemically, by hydrolyzing the vegetable ivory nut (the fully ripe, ivory-like seed of the South American palm, *Phytelephas Macrocarpa*).

According to Dr. King, the test tube experiments with uterine tissue worked

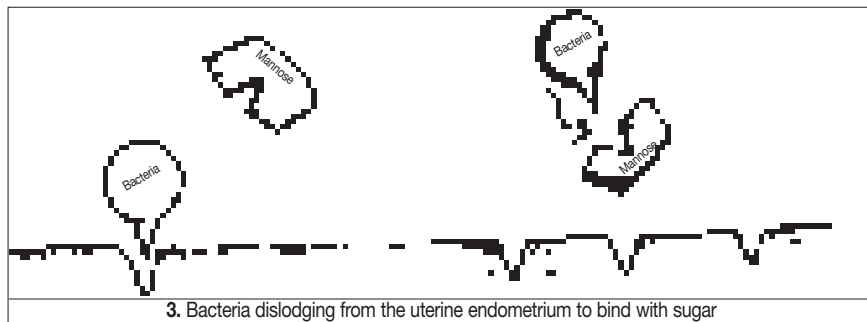
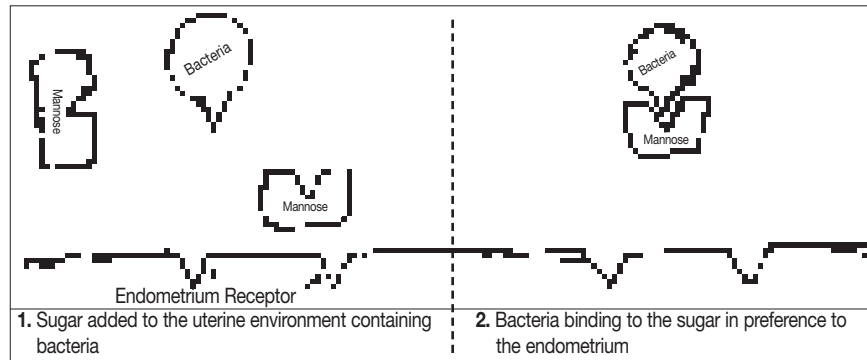
uterine tissue. The bacteria do not attach to the uterine lining because the mannose is more readily available. Sugars mimic the structure of the receptor cells in the uterine lining (the physical features on a cell's surface where other chemical substances can attach, such as hormones or antigens). These are the same cells where the bacteria would ordinarily invade and attach.

As Dr. King clearly explains, the chemical structure of the sugar (one region of it, at least), "is similar enough to the chemical structure of the bacterial receptor (binding site) on the uterine lining that it can

attract and bind bacteria." Once bound to the sugar instead, the bacteria-sugar complex cannot bind to the uterine lining. So, putting sugar (mannose) into the uterus attracts the bacteria to the sugar molecules and it binds to them instead of the uterine lining. As a result, the sugar-bound bacteria can then be flushed out of the uterus. "The mannose competes with the uterus for

binding of bacteria—it therefore prevents bacterial attachment," she says, "and it can also attract bound bacteria"—bacteria that have already attached to the lining away from the uterus.

Thus, when treated with mannose, the uterine tissue in the test tubes were able to withstand infection since the cell's chemical "docking stations" were left empty, due to competition from the sugar. As Dr. King says, the mannose is a "competitive inhibitor" competing with the uterine receptor sites. "The bacteria can



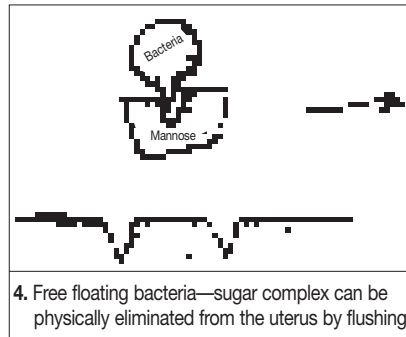
hitch to the uterus or to the sugar," she adds.

She states that in the research tests, the mannose worked well on four types of bacteria that commonly infect mares, preventing the floating bacteria from adhering to the uterine tissue. And in the one bacteria that was further tested, the sugar treatment could also cause already attached bacteria to let go—the mannose dislodged the bacteria that were already latched on.

During 1995 and 1996, the research team started trying the sugar treatment on mares. The theory behind this type of treatment was that the mannose would protect the uterine lining and the bacteria could be naturally flushed out of the mare's reproductive system before they had a chance to attach. But in practice, the problem is not quite that easily solved. As Dr. King explains, "the mare's immune system is kicking in and complicating our determination of just how well the mannose works, compared with Mother Nature alone."

But the researchers are not

deterred—they are working on ways to get around this problem. They are encouraged by the fact that when healthy mares are given an infection (for experimental purposes) and then flushed with the sugar solution, their follow-up cultures come up negative



(Illustration drawn from a sketch provided by Dr. Sheryl S. King, Southern Illinois University)

(they are clear of bacteria). By contrast, the mares who are flushed with ordinary saline solution after experimental infection then culture positive—indicating that the bacteria have been able to become established in the uterus.

The field experiments with brood-

mares are continuing, and the research team is still excited about the possibilities of using mannose in the future treatment of endometritis. As Dr. King concludes, this sugar treatment has much potential, not just for treating uterine infections in mares, but also for other types of medical problems. "It would probably work on most mucosal systems," she says, fighting infection in other tissues. It could also be used in humans.

This type of treatment could be a real breakthrough in the search for alternatives to antibiotics. The overuse of antibiotics has often contributed to the growth of antibiotic-resistant strains of bacteria, and the more we can get away from this problem, the better off we will be. Dr. King and her co-workers are encouraged by their work with mannose, feeling strongly that this may be a way to augment or replace antibiotic therapy. This could make treatment of uterine infections in mares not only less costly, but also more effective.