MAYBE BABY

Patients travel from as far away as Europe to visit Attila Toth, MD, a physician in New York who claims his extreme treatment will help infertile women conceive. Couples are going home with babies, but doctors think his methods are far from sound. *Sarah Elizabeth Richards explores*

For 10 days straight in the summer of 2010, Samantha*, a lawyer from Greenwich, Connecticut, and her husband came into New York City to visit the office of Attila Toth, MD, a fertility specialist who thought he could solve the mystery of why, at age 28, she couldn't get pregnant.

On the first morning, Toth put in their arms IVs that delivered an antibiotic that they each carried around in a fanny pack for the entire 10 days. He then threaded a catheter into the pinpoint opening of Samantha's cervix so that, for the next hour, a cocktail of four antibiotics, the steroid Medrol, and a large dose of the yeast-infection medication Diflucan could wash out her uterus. The first two mornings, Samantha suffered excruciating cramps from these daily washes, but by the third, the pain had subsided, and she settled into a routine of watching *Dr. Phil* on the examining-room television until Toth returned to remove the catheter and insert a paste containing a fifth antibiotic that would be absorbed into her body for the next 24 hours. Meanwhile, every other day Toth gave her husband a painkiller and then injected antibiotics through his rectum and into his prostate; twice Toth also injected his seminal vesicles. After their last visits, Toth gave the couple prescriptions for still two more antibiotics that they'd take for a month.

When their treatments were over, Samantha and her husband returned to see Toth, who declared them both "clean," by which he meant they were free of *Chlamydia trachomatis*, a bacterium that can cause infertility in women and has been linked to recurrent miscarriage, premature labor, ectopic pregnancy, and pelvic inflammatory disease.

Outside of Toth's office, such an elaborate antibiotic assault on chlamydia is practically unheard of. The standard treatment—which health officials say is at least 97 percent effective—is a seven-day course of the antibiotic doxycycline or a single dose of azithromycin. But Toth thinks chlamydia is far harder to detect and treat than most doctors do. In fact, he thinks it may be responsible for a substantial portion of the one third of infertility cases that doctors now classify as "unexplained."

Toth, 72, came up with the idea of administering intrauterine washes (also known as lavages) to patients in the late 1970s after learning about the horse breeder who successfully put the racing legend Secretariat to stud. The breeder would flush out the uteruses of mares with antibiotics to kill the microbacteria that could interfere with conception. Why couldn't humans benefit from such a therapy too? Toth thought. In 1977, he started testing infertile couples for a little-studied bacterium called mycoplasma that had been linked to infertility. He

*Name of patient has been changed

Jena Cumbo/Getty Images

gave men who tested positive an oral antibiotic, and many of their wives soon became pregnant, Toth says.

Around this time, public health officials were becoming increasingly concerned about chlamydia, and his boss at New York Hospital suggested he look into it. "He said, 'That's far more important and can do much more damage to the reproductive tract'" than mycoplasma, Toth recalls. Pictures of this were telling: scarred and blocked fallopian tubes, uterine adhesions, blocked epididymides (the coiled ducts that collect sperm). "I thought, This is destroying people's anatomy," he says.

At first, Toth treated people who tested positive for chlamydia with a conventional dose of oral antibiotics. But when cultures from his patients continued to show traces of the bacteria, he lengthened the time to four weeks. He added another antibiotic. Then he doubled the duration of both medications to eight weeks. "The longer they took them, the faster they got pregnant," he says. In the early '80s, he introduced IVs for men and women; patients would cluster in his office basement while they were hooked up to the then primitive machines and call themselves the "IV League." By the late '80s he had refined his regimen further, introducing the uterine lavages; five years ago he added prostate injections.

Toth, a man whose bear-hug personality endears him to his patients, now sees some 150 couples a year for infertility, a third of whom, he estimates, are referred by gynecologists, urologists, or fertility specialists who are at a loss as to how to help them. Gideon G. Panter, MD, a Manhattan-based gynecologist and infertility specialist, has sent Toth 40 to 50 patients, he says, and "always with the same story," of unsuccessful IVF cycles, including one couple who traveled from Europe after four had failed. "Toth has been saying this stuff for 20 years," Panter says. "But fertility medicine is big business. Doctors don't stop to think, Wait! My patient's IVF cycle failed twice. Something else must be going on. Toth's treatments cut into the economic overhead of infertility treatment. He's ahead of his time."

Toth claims women who complete his treatment have easier pregnancies and healthier babies. "Give me a germ-free uterus and germ-free sperm, and I will make you a better baby!" he says.

After finishing medical school in Hungary in the late '60s, Toth emigrated to the U.S., where he received a fellowship at the Cleveland Clinic and finished a residency in pathology at The Mount Sinai Hospital before opening up a private practice at New York Hospital in 1977. Fifteen years later, he moved his practice to the Upper East Side townhouse where he remains today. A tall man with a mustache, a full head of sandy brown hair, and a thick accent, he avoids conferences and has published infrequently. He says he encountered such cynical resistance from the medical community early in his career that he retreated to his office and relied on his evangelistic patients' word of mouth to grow his practice. "I just became frustrated by the lack of interest in the role of infections on fertility, no matter what ideas I put forward," he explains. "So I treat my patients according to my best understanding, and my reward is seeing them get pregnant."

According to the Centers for Disease Control and Prevention (CDC), chlamydia rates have been climbing steadily over the past 20 years, with some 1.3 million new infections reported in 2010. Gail Bolan, MD, director of the CDC's Division of STD Prevention, says that number actually represents only the "tip of the iceberg," because most people are not aware they are infected and do not seek testing; she estimates the number of new infections each year is closer to 3 million. The most common symptoms for women—which typically appear one to three weeks after exposure to the bacteria—are abnormal vaginal discharge and burning during urination. But as many as 70 percent of infected women are asymptomatic. The CDC has responded by recommending stepped-up screening efforts, especially for sexually active women 25 and under (who are the most vulnerable group) or women who have several sexual partners or who have a new one.

Chlamydia works, according to the prevailing theory, by invading cells and then multiplying inside them until the cells rupture, allowing the bacteria to spread. It can also "hide" within a cell, however, not actively replicating ("It's trying to trick the body into thinking that it's not there," says Allison K. Rodgers, MD, a reproductive endocrinologist at Chicago IVF and an expert on chlamydia screening), and it's unclear whether in this state it does any damage. But regardless of whether it's spreading, the bacteria can be detected with a standard test and then eliminated with a quick round of antibiotics.

Or so just about everyone besides Toth believes. He insists that these short courses kill only active bacteria—not those that hide. He thinks this low-lying chlamydia might be inflaming the uterus and making it difficult for an embryo to attach and grow. His treatment is long enough, he says, that when the cells finally become active and erupt, antibiotics are still in his patients' systems. The steroid in the lavages and prostate injections suppresses the immune system and activates the bacteria. "That's the trick," he says. "I'm waking up the dormant chlamydia. The steroids tease them out, and the antibiotics that are already sloshing around in there kill them."

The response from Margaret R. Hammerschlag, MD, an infectious-disease specialist at SUNY Downstate Medical Center, to Toth's ideas and treatment is common: "This is ridiculous. This isn't good medicine. Chlamydia is easy to diagnose and easy to treat."

"It's as if you've got a sore throat and they cultured strep and put you in the hospital for seven days. You'd be like, 'Really?'" says William B. Schoolcraft, MD, medical director of the Colorado Center for Reproductive Medicine in Denver.

"[Toth] believes that large doses of antibiotics are effective against everything," says John E. Buster, MD, a fertility doctor at the Women & Infants Hospital in Providence, Rhode Island. "But it's never been proven. It's never been subjected to rigid peer review."

Toth recently examined the cases of 63 couples he treated between 2006 and 2009 who'd failed to get pregnant with IVF. After both partners completed his treatment, 12 women became pregnant on their own. Twenty-three underwent another round of IVF, and of those, 17 delivered babies. Taken alone, those numbers are impressive, since the live-birth rate for IVF after one failed cycle ranges from 2 to 35 percent, depending on a woman's

age. But one of the problems with judging the overall effectiveness of Toth's treatment is that he lost track of the 28 other couples in his sample.

Which is why such retrospective reviews of one's own work hold little sway in the medical community. It's too easy to cherry-pick your patients. And the results don't necessarily prove that your treatment made the difference. It's possible, says James A. Grifo, MD, PhD, program director of the NYU Fertility Center, that the next round of IVF treatment would have worked anyway.

There's enough that we don't know about the science of infertility that entirely dismissing Toth's narrative of lurking chlamydia is difficult—especially if you're among the 10 percent of women in the U.S. who can't conceive. It's easier to endure all those antibiotics than face the fact that your inability to get pregnant might be outside your control. Why not have antibiotics "wash" your womb in preparation for the baby that will soon grow there? (One woman wrote on a Yahoo! message board for patients under Toth's care, "I felt the lavages were the best part. I had never felt so clean in my life!") Toth warns that his treatment may cause exhaustion and the rare yeast infection (Samantha felt run-down, and on the message board, several other women complained of flu-like symptoms, diarrhea, and a metallic taste in their mouth), but he also says that women who complete his treatment have easier pregnancies and healthier babies. "Give me a germ-free uterus and germ-free sperm, and I will make you a better baby!" he says.

Six months before visiting Toth, Samantha and her husband saw New York fertility specialist Sami S. David, MD. Samantha had been having a brownish blood discharge for up to a week before her period for several cycles, but her ob-gyn had said it was normal. David ruled out chlamydia but found that both partners tested positive for ureaplasma, another asymptomatic bacterium that can damage a woman's reproductive tract and a man's sperm count. He prescribed a two-week course of the antibiotic doxycycline, then, when they still tested positive, a week's worth of azithromycin. After a third test showed the couple was still infected, David threw his hands up and referred them to Toth.

Toth thought that ureaplasma was only part of the problem. As usual, he suspected chlamydia, even though David had used a CDC-recommended test that detects chlamydia's DNA and is accurate more than 90 percent of the time. Toth says the majority of his patients have had negative test results, but he finds chlamydia in at least 60 percent of them. He worries about the standard test's accuracy, especially given that there's evidence from abroad that chlamydia might be mutating and exhibiting different markers than the CDC screen looks for. In 2006, Swedish health officials were puzzled when chlamydia rates were markedly lower in some counties, until they realized certain DNA tests had failed to detect a new chlamydia variant that had recently emerged. Toth says he gets more reliable results using a direct fluorescent antibody test, which looks at cells collected with a small bristle brush from a woman's cervix or a man's urethra, because it can detect some 16 strains. But the antibody test must be done by hand and takes an hour to examine. By contrast, the DNA test employs machine analysis.

The antibody tests confirmed Toth's hunch: Both partners were indeed infected. Toth believed that the bacteria had irritated the lining of Samantha's uterus, causing it to prematurely thicken and shed every month before the arrival of her period. Although Samantha's husband hadn't experienced any of the common male symptoms (such as discharge or burning at the tip of his penis), he not only risked developing testicular and prostate infections if he wasn't treated, but he was also likely to reinfect her.

A few months after their treatment, Samantha was pregnant. But because chlamydia can flourish in the uterus during pregnancy (the body shuts down the immune system so it doesn't reject the fetus), Toth prescribed Samantha a cycle of oral antibiotics every two months to prevent any "straggler" bacteria from infecting the baby. Last year, after receiving a final antibiotic IV during her C-section delivery, Samantha gave birth to a robust baby girl. Toth's total bill: $16,600, of which the couple's insurance covered only half.

Although health officials have repeatedly warned about the risks of taking too many antibiotics, which could lead to superbugs that can't be treated, many doctors concede there are actually few risks to women taking so many drugs during Toth's regimen. "I am against inappropriate antibiotic use, but it's really a spit in the ocean compared to all the antibiotics prescribed for colds and fevers," says Sandra Arnold, MD, a pediatric infectious-disease specialist at the University of Tennessee Health Science Center who has written on the dangers of antibiotic misuse. "The likelihood that a person getting this treatment would develop infection with highly resistant bacteria is very small."

Certainly Toth isn't the only doctor who believes in the power of antibiotics. "Surgeons love to sprinkle antibiotics on things," says Arnold. "If they open up your chest, they like to flush your chest with them. Orthopedists sometimes put them into bones they're mending, but we have no idea whether they work." Researchers have explored the promise of antibiotics to treat infections that cause premature labor, or to soothe inflammation that may contribute to coronary heart disease. It's standard practice at many fertility clinics for doctors to give couples a course of oral antibiotics during an IVF cycle to prevent bacterial infections that could interfere with implantation of embryos.

And, of course, Toth wouldn't be the first doctor people thought was crazy who turned out to be right. J. Robin Warren and Barry Marshall were routinely dismissed when they suggested that stomach ulcers were caused by bacteria rather than late nights at work or too much Tabasco sauce. In 2005, they were awarded a Nobel, and today ulcers are routinely treated with two antibiotics plus an acid blocker. As Charles M. March, MD, a reproductive endocrinologist in private practice in Los Angeles, points out, "[Toth] is controversial, but I have patients who swear he walks on water because they went home with a baby."

"It's not that no one wants to believe him. They just want better data," Grifo says. Toth recently approached him about doing a study, but Grifo declined. To have credibility, they would need to conduct a classic randomized controlled trial in which half of patients received the antibiotic treatment and the other half received a placebo before undergoing an IVF cycle. "Don't underestimate how difficult it is to do these studies," insists Grifo. "It's such an invasive procedure, especially for men, that it's hard to get patients to sign up." But Grifo concedes, "Toth might be onto something. It may be that a small subset of patients need his treatment, but that needs to be determined." Which is perhaps why he has not entirely ruled out working with Toth in the future.

Andrew Toledo, MD, a fertility doctor and chief executive officer at Atlanta's Reproductive Biology Associates, the largest fertility clinic in the Southeast, first heard about Toth from his patients in 1998 and has so far referred 20 to him. These are women at the ends of their ropes, who have endured multiple tests and treatments. Their embryos don't thrive. "When they come back to me, nine times out of 10, they get pregnant and stay pregnant. I can't blow that off," says Toledo. "People thought it was voodoo. But I think more and more of us think there has to be something to it. Now I tell my unexplained cases, 'There's this doctor in New York City….'"