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Experimental immunotherapy offers hope for recurring miscarriages

By Adrianna Barton
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But detractors claim it's costly, risky and not clinically proven

A miscarriage at age 30 was so traumatic for Mary Musollari that she waited two years before trying to conceive again. Although she had no trouble getting pregnant, once again, in the seventh week, her unborn baby perished.

"It was devastating," she says. "You just blame yourself."

After her second loss, she became a patient of Carl Laskin, a specialist in reproductive immunology at LifeQuest Centre for Reproductive Medicine in Toronto.

In her blood, Dr. Laskin found high levels of antibodies associated with blood clotting and pregnancy loss. He prescribed low-dose aspirin and a blood thinner for Ms. Musollari to take in her third pregnancy.

At last, a six-week ultrasound revealed what she'd longed for - a healthy baby with a strong heartbeat.

Ms. Musollari credits the treatment for the birth of her daughter Emily, now 2.

For a woman with antibodies that interfere with pregnancy, she explains, there's no such thing as "good luck."

The notion that a woman's immune system can create a hostile environment for an embryo or fetus is a basic principle of reproductive immunology, a field immersed in controversy as well as hope.

Although it isn't new, reproductive immunology made headlines last month when a woman in the United Kingdom, who had suffered 18 miscarriages, gave birth after receiving immune therapy. According to her doctor, Hassan Shehata, 33-year-old Angie Baker had high levels of natural killer cells that attacked her embryos as a foreign body, a problem he treated using a corticosteroid before conception.

Ever since the news came out, the phone at his miscarriage clinic in the London area has been ringing off the hook, Dr. Shehata says. "It's been mad."

But experimental treatments, including corticosteroids and injections of antibodies derived from human blood, can involve health risks. And most forms of immunotherapy for recurrent miscarriage are unproven in randomized

controlled trials, experts say.

In fact, research suggests that one of the most effective treatments for repeat pregnancy loss may be attentive medical care - in other words, TLC.

Dr. Shehata is well aware that immune therapy is the dark horse of reproductive medicine. "A lot of people still don't believe in it," he says.

Clinical data is thin because it's tough to recruit women who are racing against the biological clock, he says. "No one wants to be in the placebo group."

Using experimental therapies, Dr. Shehata says, his clinic has an 80 to 85 per cent success rate in treating recurrent miscarriage on the first attempt.

Elsewhere, too many doctors blame early pregnancy loss on "pure bad luck," he says.

Recurrent miscarriage - usually defined as three or more consecutive losses - affects about 1 per cent of women who become pregnant.

Immune mechanisms are the culprit in about 50 per cent of these cases, according to Dr. Shehata and data from private clinics such as Reproductive Immunology Associates in the Los Angeles area.

But Dr. Laskin, who runs Canada's largest recurrent miscarriage program, says he is skeptical of the figure. "That's way too high."

A Canadian study found that 15 to 20 per cent of recurrent miscarriages had an immune factor, notes Sony Sierra, spokesperson for the Society of Obstetricians and Gynaecologists of Canada.

Immunotherapy is still an emerging field, however. And couples desperate for children are far too willing to spend thousands of dollars at private clinics for treatments that aren't proven, Dr. Sierra adds.

"I've had patients go to the States and come back with literally full binders of test results that have been ordered on every single circulating antibody," she says. The problem is, "there's no link between 99.9 per cent of those antibodies and what results in recurrent miscarriage."

At the Alan E. Beer Center for Reproductive Immunology and Genetics, north of San Francisco, fees range from \$600 (U.S.) for an initial consultation to \$3,500 for a single infusion of intravenous immunoglobulin G (IVIg), a blood plasma product often used multiple times in a pregnancy.

But in clinical trials so far, neither IVIg nor corticosteroids have proven to be effective treatments for recurrent miscarriage.

Although many clinics report high live birth rates, their success may be unrelated to experimental therapies, says Dr. Sierra, who studied recurrent miscarriage in Vancouver with Mary Stephenson, founder of the pregnancy loss clinic at B.C. Women's Hospital.

"We found that providing just monitoring and a lot of handholding through the first trimester gave us a 71 per cent live birth rate," Dr. Sierra says, adding that Scandinavian researchers have published similar findings.

Using expensive treatments such as IVIg for recurrent miscarriage makes little medical or financial sense, says Dr. Stephenson, now director of the University of Chicago's recurrent pregnancy loss program. "It can bankrupt patients."

Instead, she says, the focus should be on testing after each miscarriage for the most common cause of pregnancy loss - random chromosomal error.

"Until we start doing that routinely, patients are going to be overtreated with whatever medication," Dr. Stephenson says.

In Canada, "baby" aspirin and low-molecular-weight heparin, a blood thinner, are the most widely used and accepted treatments for antibodies associated with clotting and recurrent miscarriage.

But even these medications may be no better than a placebo, according to Dr. Laskin, who has done clinical trials on these and other immune treatments since 1980.

"There are times I think I could put chicken entrails under the chairs of my waiting room and we'd be successful."

Nevertheless, Ms. Musollari is convinced that aspirin and heparin helped turn her history of miscarriages around. Now six months' pregnant with her second child, Ms. Musollari says she is confident her last trimester will go well under Dr. Laskin's care.

But she wishes she had known years ago that miscarriages were treatable with medication, she says. "It just makes me mad that I didn't do this before."

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