

missed conceptions

*Assisted reproduction
is helping many couples
have the babies they long for*

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ILLUSTRATIONS BY CLAUDIA NEWELL

When Daina and Stephen of Toronto got married in 1992, they were looking forward to starting a family right away. And they had no reason to think it would be anything but a breeze. Daina had just turned 30, Stephen was 40, and they were both in prime health. But as time passed without a pregnancy, they realized things weren't working out according to plan. "There was just nothing happening," recalls Stephen.

Still, the couple didn't worry much at first. "We thought it was probably a good thing, because we were still in the beginning phase of our marriage," says Daina. "Neither of us felt any real urgency."

Months turned into years. They tried using basal temperature readings and ovulation predictor kits to pinpoint Daina's fertile period — still no luck. That's when, Stephen says, "the darker thing started to loom." They began to think they might be infertile. In 1999, after seven years of trying, the couple finally got a referral to a fertility specialist. And so the gruelling tests and treatments began. "It takes a huge emotional toll because you feel like such a failure," says Daina.

Daina and Stephen are among more than 250,000 Canadian couples who struggle with infertility. In fact, up to 15% of couples cannot conceive naturally after a year of using no birth control. Although the figures vary, the root causes of infertility break down roughly as follows. In about 20% of cases the underlying causes can be identified as residing with the man; in about 30%

with the woman; and in about 30% with both partners. "In an additional 20% or so, infertility is unexplained and has no identifiable root cause," says Dr. Derek Bochinski, a urologist at the University of Alberta Hospital in Edmonton.

After tests, it was clear that both Daina and Stephen had fertility challenges. Stephen's sperm were somewhat less than Grade A, and Daina had now entered her late 30s, a time when fertility has naturally declined. So, to boost their odds of pregnancy, their specialist recommended that they proceed to in vitro fertilization (IVF). This is a process that uses hormones to stimulate the ovaries, harvests several mature eggs, fertilizes them in the lab with the father's sperm, grows them into early embryos and then implants one or more embryos in the mother's uterus for gestation. He also recommended using intra-cytoplasmic sperm injection (ICSI), a procedure in which a single sperm is injected into an egg in the lab. Again, the egg is grown into an early-stage embryo and then implanted in the uterus.

These did not work. Around this time, Daina was also diagnosed with endometriosis, a condition in which tissue similar to that lining the uterus grows in the pelvic cavity outside of the uterus. Endometriosis can affect fertility if obstructive scarring develops, so Daina underwent surgery to remove the scar tissue. Still no pregnancy. "After the fourth failed round of IVF, everybody was stymied as to why," says Stephen.



“It just became such a stressful thing to be doing,” adds Daina. “I felt a certain amount of grief every time I went. A lot of it had to do with my hormones being all over the place.” Like many women undergoing fertility treatments, she was taking powerful hormones to stimulate the production of several mature eggs at once and to help a pregnancy “take.”

Are Daina and Stephen symbolic of a growing problem in North Americans? Although there’s been speculation that environmental toxins such as those in pesticides, car emissions and plastics may be having an effect on our birth rate, there’s no clear evidence that these are causing a rise in infertility. What is clear, however, is that women who postpone having children often end up facing “age-related infertility.”

“Women may tend to delay giving birth until after they’ve developed their careers, and this is a major and increasing problem,” says Dr. Hananel Holzer, a fertility specialist at the McGill Reproductive Centre in Montreal. “By their 40s, their fertility has considerably decreased.”

Daina and Stephen’s fifth attempt at IVF was probably the most emotionally trying. As before, Daina had been hormonally prepped to produce a number of mature eggs. But when Stephen produced his half of the bargain, he was shocked at the analysis. His sperm count had suddenly plummeted to zero. His left testicle had developed a blockage in the vas deferens — the tube that transports the sperm from the testes to the penis.

The blockage would be surgically corrected, but in the meantime, what to do with Daina’s eggs? The year was 2003, and cryopreservation (freezing) of unfertilized eggs was still under development. But the couple was lucky. Their Toronto clinic had been refining a process of slow freezing that just might work. They quickly agreed to try to preserve Daina’s 10 precious harvested eggs. Although only one egg eventually survived the thawing and fertilizing process almost a year later, that single embryo turned out to be all the couple needed. Amazingly, the pregnancy stuck. Their beautiful, robust daughter was born in July 2005 — but only after they had spent more than \$50,000, not counting the drug costs covered by Daina’s work health plan.

“It was just an unbelievable miracle,” says Stephen, who still keeps the petri dish that once cradled his baby girl. Daina agrees. “We feel blessed,” she says.

With new technologies, it’s now possible for many couples to achieve their own miracles. “But success rates depend on the cause of infertility,” warns Bochinski. “While some couples have no chance of conceiving, others have an 80% to 90% likelihood of pregnancy.” Adds University of Saskatoon fertility specialist Dr. Roger Pierson, “Bear in mind that the actual live birth rate can be 8% to 10% lower than the pregnancy rate, depending on the type of fertility problem and the mother’s age.”

Read on for some of the stumbling blocks and how modern reproductive science is getting around them.

Men

POOR SPERM QUALITY

The sperm are simply not up to the job — either from some known but non-correctable cause or for an unknown reason.

Test A semen analysis measures the count, quality and motility of the sperm.

Treatment Various assisted-reproduction technologies can help a man with poor sperm increase his chances that one of his sperm cells will fertilize an egg. These include IVF, sperm washing and intrauterine insemination (IUI), a technique in which sperm are washed to separate high-quality sperm from their dead or slow-moving brethren and inserted directly into the uterus. The newest technique is ICSI (see p. 36). “Essentially, all you need is one viable sperm for success with ICSI,” says Bochinski. “We’re still pretty excited about that.”

Bottom line Depending on the woman’s age, Canadian fertility clinics claim a 40% to 60% pregnancy rate for IVF and a 40% success rate for ICSI.

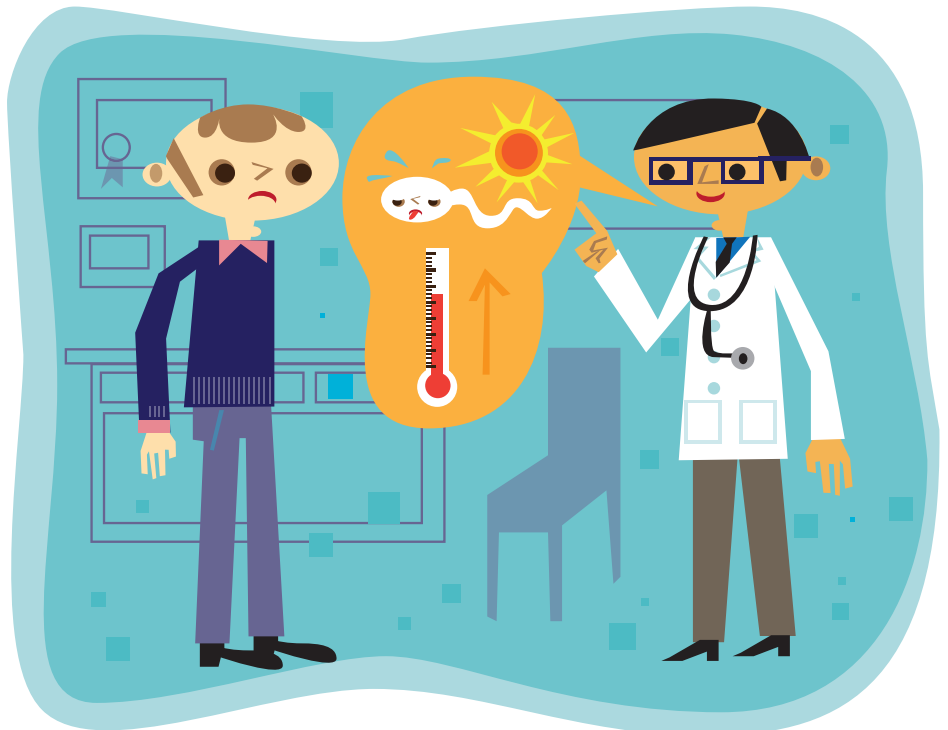
VARICOCELE

A clump of enlarged and dilated veins inside the scrotum, a varicocele is the most common surgically correctable cause of infertility in men. Think of it as a varicose vein in a very sensitive area. There are several theories as to why a varicocele can put a damper on fertility, but it’s generally thought to act like a miniature radiator to increase the temperature in the testicle. The excess heat decreases sperm production and motility.

Test Most of the time, a varicocele can be felt during a physical exam. If the exam is inconclusive, an ultrasound of the scrotum may be required.

Treatment Varicoceles can be corrected with surgery to tie them off and divert blood to normal vessels or with embolization, in which tiny coils are injected through a catheter to block blood flow to the dilated veins.

Bottom line Varicoceles can be fixed, but that doesn’t always translate into a pregnancy. The conception rate after treatment is 30% to 50%.



OBSTRUCTION

Congenital defects or obstructions that develop later — such as scarring from sexually transmitted infections, biopsies or hernia repairs — can block the sperm’s passage anywhere along their journey through the male reproductive system.

Test A semen analysis may show a very low sperm count and a low volume of seminal fluid. A physical examination or a transrectal ultrasound can also locate an obstruction.

Treatment Often the blockage can be bypassed with microsurgery, allowing the sperm to flow freely again.

Bottom line Success depends on where the obstruction is. The closer the blockage is to the testicle, the more complex the fix and the lower the success rate. Pregnancy rates range roughly from 40% to 60%.

HORMONAL IMBALANCES

Caused by glandular disorders, these imbalances impair sperm production and quality and can reduce a man's sexual desire. They include high levels of prolactin, a hormone that is elevated in nursing moms and suppresses male hormones.

Test Semen and blood tests.

Treatment Sperm production is sometimes restored with hormone therapy or drugs that stimulate production of the brain chemical dopamine, which blocks prolactin.

Bottom line Sperm can be restored in about 60% of men, and the pregnancy rate is about 40%, barring other fertility problems, says Dr. Peter Chan, director of male reproductive medicine at McGill.

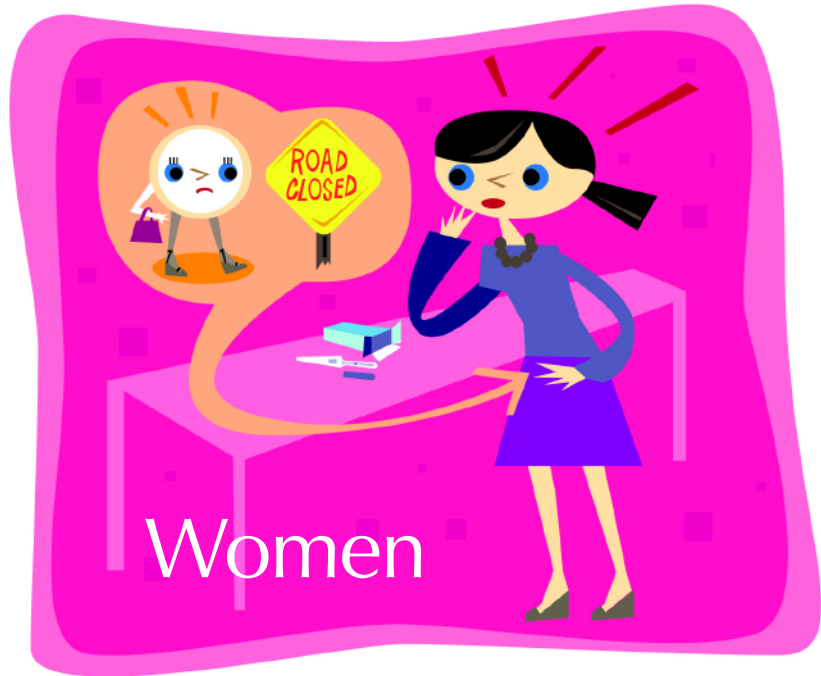
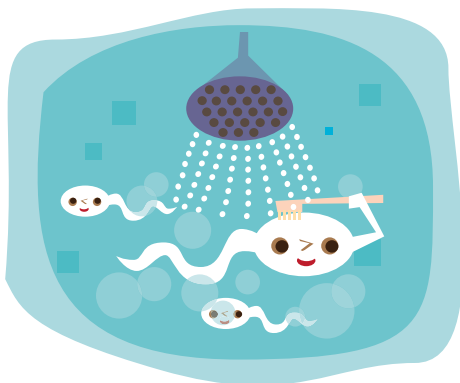
IMMUNOLOGICAL INFERTILITY

Although this is a controversial area, it is thought that some men produce autoantibodies to their own sperm, because of prior infections in, or blows to, the testicles. These may cause sperm to stick together and reduce their ability to reach and penetrate the egg.

Test Semen and blood tests.

Treatment Sperm can be washed in the lab to remove the interfering antibodies, then injected into the woman's uterus.

Bottom line The pregnancy rate falls in the 15% to 20% range.



OVULATION DISORDERS

Absent or infrequent ovulation can be due to hormonal abnormalities, polycystic ovarian syndrome or previous cancer treatments.

Test The doctor takes a history to find out if menstrual patterns have been atypical. Other tests include ultrasound to determine the number of follicles in the ovaries, hormone tests and a physical exam to identify the signs of hormonal disorders, such as weight gain or atypical hair growth.

Treatment A heavy woman may be advised to lose weight. Other treatments entail oral drugs such as clomiphene (Clomid) or hormone injections to jump-start ovulation. The next step might be IVF (see p. 36) or in vitro maturation (see "New Directions," p. 40).

Bottom line Pregnancy rates are as high as 40% to 60% with IVF and 40% with ICSI.

MECHANICAL PROBLEMS

Blockages in the Fallopian tubes can prevent the egg from reaching the uterus for implantation. Sources of obstruction include endometriosis (see p. 36), which can cause blockages around the woman's reproductive organs and in the Fallopian tubes, where fertilization usually occurs and through which the eggs travel from the ovaries to the uterus.

Test In a hysterosalpingogram, dye is injected into the uterus and observed on an X-ray to see if it flows easily through the Fallopian tubes. A similar test can be done with ultrasound. If other tests are not conclusive, the next step might be a laparoscopy, a look inside the pelvis with an imaging device containing a tiny camera.

Treatment Microsurgery to clear the Fallopian tubes may help improve fertility, but success rates will be higher if IVF is also used.

Bottom line Pregnancy rates are as high as 40% to 60% with IVF and 40% with ICSI.

IMMUNOLOGICAL INFERTILITY

Again, a controversial and unproven area, but researchers have speculated that a woman may develop antibodies to her partner's sperm, thereby immobilizing or killing them.

Test In the past, women often underwent post-coital analysis, a test in which, several hours after intercourse, sperm removed from the woman's cervix are examined to see how many are alive and mobile. Blood tests might check for anti-sperm antibodies. Nowadays, when standard tests are normal, women are not usually tested for immunofertility but treated as if they had unexplained fertility (see below).

Treatment "The norm now is to proceed to IVF/ICSI as quickly as possible," says Dr. Roger Pierson, chair of the communications committee of the Montreal-based Canadian Fertility and Andrology Society. "This reduces the frustration for patients. And today, with people waiting much longer before trying to conceive, it's very important to move quickly."

Bottom line High pregnancy rates with IVF/ICSI/IUI — more than 60% in women under age 35.

IDIOPATHIC (UNEXPLAINED) INFERTILITY

There's a lot we still don't know about the complex combination of factors affecting fertility. For instance, women with endometriosis have lower rates of pregnancy even when their tubes are not blocked, and it's not understood why. And in other cases, for some unknown reason, perfectly normal-looking sperm cannot penetrate the egg.

Test The diagnosis is by exclusion. Standard tests come out normal.

Treatment Any treatment that can help the sperm meet up with the egg: IUI, IVF or ICSI.

Bottom line Cases of unexplained infertility have very high rates of success, says Holzer. In women younger than 35, the success rate is more than 60% per treatment, even if the couple may never know what caused their infertility. "In the end, they may not care," he says.

For more information on infertility, go to <http://cfas.cfwebtools.com>. 

New Directions

In Vitro Maturation (IVM)

This new procedure is proving to be a lower-risk, lower-cost way of harvesting eggs than IVF. With IVM women avoid the pain of hormone injections and their side effects such as abdominal discomfort and headaches. In IVM, immature egg follicles are collected, matured and fertilized in the lab. The McGill Reproductive Centre in Montreal has pioneered this method, reporting a promising 35% pregnancy rate, and is now teaching it to other centres in North America. This procedure is suitable for patients with polycystic ovaries.

Cryopreservation

Freezing sperm and embryos has been around for a while. But the successful freezing of eggs, which are more fragile, has long stumped fertility specialists. Recent worldwide developments in slow and fast methods of freezing have meant new options for

women who want to postpone motherhood but still have younger, healthier eggs available when the time is right. These techniques allow them to preserve either their eggs or their ovarian tissue. Egg freezing is a particular blessing for cancer patients who yearn to be moms one day but undergo radiation and chemotherapy that may leave them sterile.

McGill University's Dr. Hananel Holzer has helped many women with cancer to bank their eggs this way. "It gives them hope, and this hope alone may help them in the struggle to overcome their cancer because they know they've done something to preserve their fertility," he says. "I consider this the most important part of my work."

