Investigating Infertility

Clue In to Scientific Advances in Infertility Treatments and Patients' Mental Health Needs

By Mark Harris

For many people, pregnancy and childbirth is a life-changing event that brings joy, fulfillment, and purpose, along with new challenges and responsibilities.

For some, however, the goal of becoming pregnant and giving birth can involve frustration and disappointment due to an inability to conceive or maintain the pregnancy. Unfortunately, infertility is common. Infertility affects about 1 in every 6 people of reproductive age worldwide, according to the World Health Organization.[1] In the United States, approximately 1 in 7 women ages 15–49 have trouble getting pregnant or sustaining a pregnancy.[2]

Infertility is a complex topic, and experts in reproductive medicine want the public to know that experiencing it is more than an inconvenience.[3] In fact, infertility is a serious health condition. Fortunately, modern medicine can do a great deal to treat infertility and support individuals and couples on their journey to pregnancy and childbirth. For patients facing infertility, their family-building hopes begin with a careful medical evaluation by a reproductive health specialist.[3]

"A really important thing to know is that infertility is a disease and affects a lot of people—approximately 15% of couples," says Evelyn Mok-Lin, MD, a reproductive endocrinologist and medical director of the Center for Reproductive Health at the University of California, San Francisco (UCSF). "This is an underestimate, as this does not include many others who require assistance in order to conceive, including single people and same sex couples. The American Society of Reproductive Medicine recently expanded the diagnosis of infertility to include anyone who cannot conceive on their own. The infertility evaluation includes [a] review of the medical history, including one's menstrual cycle regularity, and an assessment of hormones, fallopian tubes, and sperm. Depending on the reason for infertility, there are several advanced assisted reproductive technologies—ART—that we can utilize to help the patient conceive."

To note, while in same-sex couples or independent individuals infertility may not involve underlying biological disease, for purposes of diagnosis and to ensure equitable access to care, the American Society for Reproductive Medicine also recognizes infertility as a condition or status requiring medical intervention.[4]

"Any couple that has been trying to conceive for 12 months—or six months if over 35 years old—should be referred for an infertility workup," explains Dr. Mok-Lin. "Additionally, any patient who has high risk [factors] for infertility, including endometriosis, significant prior abdominal or pelvic surgery, or pelvic inflammatory disease, should be referred early. Anyone who is diagnosed with cancer or a medical condition that requires treatment that may affect their fertility—chemotherapy, radiation, ovarian surgery, gender affirming therapy—should be referred as soon as possible to discuss whether fertility preservation is aligned with their goals."

ART-istic Solutions

As a multidisciplinary field, reproductive medicine is largely led by physicians trained in reproductive endocrinology and infertility, which is a subspecialty of obstetrics and gynecology. The infertility care team can include ob-gyns, who usually provide the initial infertility assessment, as well as urologists, reproductive surgeons, mental health specialists, genetic counselors, primary care providers, nurse practitioners, and other medical personnel.

As a leader in advanced fertility medicine, UCSF's Center for Reproductive Health offers several treatment options and related care. These include in vitro fertilization (IVF), intrauterine insemination (IUI), third-party reproduction (e.g., sperm donation, egg donation, or gestational surrogacy), preimplantation genetic testing, ovulation induction, intracytoplasmic sperm injection, fertility preservation, and other care. The UCSF Center for Reproductive Health also provides specialized LGBTQ+ family building and fertility care.[5]

Since the first successful IVF birth in England in 1978, global use of IVF has expanded considerably. Indeed, as the most common type of ART, IVF is responsible for about 10 to 13 million births since its introduction.[6] In the United States, 95,860 babies were born from IVF in 2023, accounting for nearly 3% of total U.S. births.[7]

Although protocols vary, IVF essentially involves stimulating the ovaries to produce multiple eggs, which are then retrieved and fertilized in a laboratory. The embryos that result are monitored for a time before one or more are transferred to the uterus. The use of IVF is described as more effective for issues such as blocked fallopian tubes, diminished ovarian reserve, and severe male infertility. IVF may also be an appropriate choice when earlier treatments have not been successful.[8]

The main challenges to success with IVF therapy vary. "This can depend on a number of factors, including the reason for infertility, age, ovarian reserve, and their family planning goals," says Dr. Mok-Lin. "The No. 1 predictor of IVF success is the age of the egg, so the main challenge is often the number and quality of the eggs. Age of the sperm is also important, but the sperm's biological clock is more lenient. An IVF cycle takes approximately two to three weeks to complete and involves 10 to 12 days of subcutaneous injections, during which there are ultrasounds and blood draws to track the response. When the follicles are ready, the eggs are extracted via a 30-minute procedure under anesthesia and fertilized with sperm. The embryos are then assessed

The Fertile Window

Those attempting to become pregnant may try to use timing to improve their chances of success:

> The fertile window is the time in a cycle when pregnancy can occur. It is usually the 6 days just before the day of ovulation. Ovulation occurs around 14 days before the next menstrual period, so an individual with a 28-day cycle will ovulate around cycle day 14 (that is, 14 days after the start of their last menstrual period). That means that pregnancy is most likely to happen if intercourse occurs within the 6 days right before the day of ovulation.[15]

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based on [their] appearance and could also be biopsied for genetic testing."

Among other infertility treatment options, IUI is a less invasive—and less costly—procedure than IVF. The insemination procedure involves placing washed sperm directly into the uterus. In many instances, IUI can be the first treatment approach for couples with unexplained infertility, mild male factor infertility, and patients using donor sperm.[5] Other techniques can include injecting sperm directly into the center of an egg (i.e., intracytoplasmic sperm injection), freezing eggs or embryos for later use, and using a female surrogate to carry a pregnancy.[9]

Polycystic Ovary Syndrome

One common cause of infertility is polycystic ovary syndrome (PCOS), which affects up to 15% of women of reproductive age. The condition is related to a hormonal imbalance that occurs when the ovaries produce an excess of hormones called androgens. Symptoms of PCOS may include irregular menstrual periods, excess hair growth, obesity, acne, and more. PCOS can also increase the risk for diabetes and high blood pressure.[14]

Treatment for PCOS is based on the patient's symptoms, medical history, overall health, and whether they wish to get pregnant now or in the future. For those who want to get pregnant, treatment can include medications to induce ovulation, in vitro fertilization, and possibly surgery to remove ovarian tissue that produces androgens. For those who do not plan to get pregnant, treatment includes hormonal birth control, an intrauterine device, medications to block androgens, insulin-sensitizing medication, and lifestyle recommendations for nutrition and weight management.[14]

No Two Cases the Same

How do reproductive health specialists determine the most appropriate treatment plan? "The biology of reproduction is complex, and the diagnostic workup for infertility is limited," says Emily Jungheim, MD, medical director of the Northwestern Medicine Center for Fertility and Reproductive Medicine in Chicago. "Also, patients have different perspectives on what treatments they are comfortable with. There is often variability in resources patients have for treatment—not everyone has insurance coverage for infertility treatment, and patients' desired outcomes differ—some patients focus on parenthood, whereas others plan ahead for future children. Navigating all of this requires an individualized approach. Reproductive health specialists work in partnership with patients through their diagnostic and care journeys while staying grounded in science."

New patients can expect care tailored to their unique medical story, goals, and concerns. "At Northwestern, we take a holistic approach, starting off with understanding the patient's medical history and their reproductive goals and then moving to diagnostic testing," explains Dr. Jungheim. "Once we have the results of the diagnostic testing, we discuss treatment options and anticipated outcomes. We have a collaborative team of physicians rooted in gynecology and urology, advanced practice providers, nurses, embryologists, andrologists, and health psychologists who work together to address the patient's needs along the way. We incorporate additional resources and team members as needed, including support for mental health, high-risk obstetrical subspecialists, minimally invasive surgeons, nutritionists, pharmacists, and others. No one journey is the same, but our team is flexible, resourceful, responsive, and always rooted in science."

Various factors might influence treatment choices. "ART is an excellent first-line treatment for patients with blocked fallopian tubes, those with very low sperm counts, or for patients who have heritable genetic diseases they are trying to prevent in their children," says Dr. Jungheim. "It's also often first-line for people who have cryopreserved oocytes, for those who need help from a third party [such as] a gamete donor or gestational carrier to have a child. For others, IUI is often a good place to start. If IUIs are not successful after a certain number of tries, it suggests there may be some unidentifiable factor … precluding pregnancy. IVF may [then] be a good option to move to."

While complex, IVF represents a highly effective treatment for infertility, remarks Dr. Jungheim. "When it comes to IVF, we need three things for it to work: eggs, sperm, and a normal uterine cavity," she says. "The number of eggs we can get in one oocyte retrieval and the age of the oocyte source are the primary predictors of a successful IVF cycle. When it comes to trying to conceive without assistance, we get one chance per month. If someone is doing IVF and we get 12 eggs, that's like a whole year of trying to conceive. I've found that posing it this way helps patients understand how successful IVF can be. The number of eggs we can get in one IVF cycle is limited by a patient's ovarian reserve. So, if someone has a high ovarian reserve—measured by ultrasound and blood work, they often get more oocytes in an IVF cycle than someone with a low ovarian reserve. As far as oocyte quality goes, that is where age comes in. As we get older, our oocytes are less likely to make an embryo with the correct number of chromosomes. If a patient is older but has a high ovarian reserve, IVF can be a good option. Many people think that IVF works 'better' than IUI, but if I cannot get multiple oocytes per retrieval, IVF may not be the best option."

Minding Mental Health

Whatever treatment approach is followed, health care providers must be sensitive to the emotional toll infertility can have on individuals and couples. "This is so important," emphasizes Dr. Mok-Lin. "Studies have shown that infertility patients experience as much stress as people with cancer. We have three psychologists in our clinic who are available to see our patients. Many also already have an existing therapist and/or psychiatrist with whom we work alongside throughout their fertility journey."

In fact, infertility is often described as one of the most emotionally challenging medical conditions people can face, reports Danielle Melfi, CEO of RESOLVE:

The National Infertility and Family Building Association. "The emotional toll is compounded by feelings of grief, loss of control, and profound isolation—particularly in a society where family building and parenthood are deeply valued and prominently visible," says Melfi. "Because of this intense social-emotional impact, infertility counseling plays a critical role in supporting patients. It's essential that medical providers proactively encourage their patients to seek this kind of professional support as part of comprehensive fertility care."

Chelsea Kramer, LFMT, PMH-C, a Seattle-based licensed marriage and family therapist, notes that infertility can evoke a layered mix of mental health challenges. "Clients can have complex feelings of grief and loss while facing an unknown future," she says. "They can feel like their bodies have failed them. No matter the medical reason for infertility, women are often blamed. Couples often struggle with intimacy and connection as sex can become utilitarian and rigid. Marginalized populations, such as [people who are] disabled, fat, queer, or people of color, may experience discrimination or bias within the medical system. Interaction with the medical system can be traumatic. This time might also bring up past traumas, especially for the birthing person. If patients do conceive, experiences during this time can highly influence their mental health during the perinatal period.

"I use multiple therapeutic approaches with individuals and couples dealing with infertility," says Kramer. "I start with a systemic, trauma-informed lens, understanding each person comes into this situation with a lifetime of messaging around their bodies, gender expectations, experiences, and interactions with the medical system. I use acceptance and commitment therapy and narrative therapy to help clients navigate the complexity of their situations. It's important [that] clients have tools to self-soothe, regulate complex emotions, gain support, and stay connected. Peer support is [also] a highly valuable resource during this time, helping clients know they aren't alone in their struggles."

For many individuals, the experience of infertility can represent a type of "complex trauma," suggests Kramer: "Generally speaking, society doesn't invest in women's health, and thus funding for research around fertility, birth, and reproduction-related health topics is lacking. Individuals and couples dealing with fertility challenges are on a long journey consisting of years of emotional highs and lows. Over time, this emotional roller coaster, along with grief and the level of respectful treatment they receive, can greatly impact their mental health. For many people, this cumulation of stress and loss is traumatic. Viewing it from a trauma-informed lens is important to fully grasp the level of impact this process has on patients."

Counseling services may be especially useful when reproductive treatments are ongoing or prolonged. "Individuals and couples using any form of third-party reproduction services may benefit from therapy," says Kramer. "IVF is what the general population thinks of most often, but typically, once people get to IVF, they've already gone through multiple steps to get there. … It's important to address how this impacts people's individual mental health and their relationships."

Accordingly, Kramer would like to see health systems prioritize psychological care for patients with infertility. "Most individuals and couples facing fertility challenges do not seek out mental health support," she observes. "The health care system could provide more education to patients about the mental health impacts of fertility challenges and treatments. Some clinics have in-house mental health services, but those are often overtaxed. Education, resources, and referrals can be made part of the preventive treatment. Add regular mental health screenings for patient appointments, such as the PHQ-9 [patient health questionnaire] and the GAD-7 [generalized anxiety disorder]. Setting patients up for success during fertility challenges can benefit them in the immediate term, while also supporting their success when or if they do have a child in the future."

Of course, reproductive health issues also impact diverse populations. As such, Kramer emphasizes the importance of reproductive health providers providing equitable, inclusive care to meet the unique needs of all their patients. This includes LGBTQ+ patients who can face unique family-building challenges.

"Most LGBTQ+ people seeking third-party reproduction services aren't infertile," notes Kramer. "They probably don't have the egg or sperm needed to conceive. In my experiences with clients, they often feel like fertility clinics aren't 'for' them because of the way the questions are asked and the processes for care. Many LGBTQ+ patients feel the oppressive weight of heteronormative practices throughout the process. Any marginalized group—disabled, fat, low socioeconomic status, person of color, queer, single people—tends to have more difficult experiences when dealing with the medical system. Inclusive language, processes, and physical access are important to make sure all patients can have a safe and effective experience."

Magnifying the Meaning

The American Society for Reproductive Medicine offers a definition for *infertility*:

> "Infertility" is a disease, condition, or status characterized by any of the following:
>
> - The inability to achieve a successful pregnancy based on a patient's medical, sexual, and reproductive history, age, physical findings, diagnostic testing, or any combination of those factors.
> - The need for medical intervention, including, but not limited to, the use of donor gametes or donor embryos in order to achieve a successful pregnancy either as an individual or with a partner.
> - In patients having regular, unprotected intercourse and without any known etiology for either partner suggestive of impaired reproductive ability, evaluation should be initiated at 12 months when the female partner is under 35 years of age and at 6 months when the female partner is 35 years of age or older.[13]

Male Infertility, Investigated

Nearly 30% of infertility cases are related to male issues.[16] Researchers have identified several possible causes that contribute to male infertility[16]:

- Environmental
  - Pesticide and chemical exposures
  - Drug use
  - Radiation
  - Pollution
- Medical
  - History of prostatitis or genital infection
  - Mumps after puberty
  - Hernia repair

Searching for Mental Support

A significant corollary to the emotional challenges of infertility is the sense of social isolation patients may potentially experience. As a national advocacy organization, RESOLVE strives to support those who want to build a family with a range of social and community resources.

"In addition to clinical counseling, peer support is a vital resource for many people," says Melfi. "Connecting with others who share similar experiences can reduce feelings of isolation and create a sense of community, understanding, and validation that is difficult to find elsewhere. RESOLVE's nationwide network of peer-led support groups is designed specifically for this purpose. After participating in six sessions, 85% of attendees report feeling more in control of their infertility—a powerful indicator of the value of mutual support."

As Melfi explains, RESOLVE's support groups are led by trained volunteers who complete an onboarding process reviewed by mental health professionals. In turn, volunteers receive ongoing training and access to resources to help facilitate effective group leadership. "Through this model, RESOLVE serves more than 2,000 individuals every month, offering free, accessible, and compassionate peer support to anyone struggling with infertility," reports Melfi.

Thus, primary care providers and frontline medical staff have a crucial role to play in supporting patients experiencing infertility. "Because patients often first raise concerns in a general medical setting, providers have a unique opportunity to offer compassionate, informed guidance that sets the tone for the patient's entire family-building journey," says Melfi. "Many patients feel shame, guilt, or fear when discussing infertility. Asking gentle, nonjudgmental questions and normalizing their concerns can help patients feel seen and heard. Simple statements like 'Many people experience challenges getting pregnant—if that happens to you, you're not alone, and support is available' can go a long way in reducing stigma. Advice like 'Just relax' can be dismissive and blame the patient for their infertility. Stress does not cause infertility, but infertility causes stress."

Following Leads

Medical assistants often play a crucial role on the reproductive health team, assisting reproductive endocrinologists and other providers with many essential tasks, procedures, and patient care responsibilities. This can also include work in specialized areas such as genetic counseling.

In many instances, genetic counseling services can help identify factors that may be causing or contributing to infertility or issues such as recurrent miscarriages. Also, genetic screening can identify hereditary risks to future children, helping couples avoid passing on a genetic condition to their child.[9]

"Our genetic counseling team sees anyone who is pregnant or who is trying to get pregnant," says Christine Hricak, CMA (AAMA), a genetic counseling assistant with LVPG Maternal Fetal Medicine at Lehigh Valley Health Network in Allentown, Pennsylvania. "The counselors advise our patients about risk factors in pregnancy—whether it's an issue like an abnormal [obstetric] ultrasound and how that could affect the pregnancy, [lack of success] trying to get pregnant, risks of age-related pregnancy, and other issues."

In Pennsylvania, genetic counselors are licensed health care providers with a master's degree from an accredited genetic counseling program.[9] As a medical assistant, Hricak herself has additional training as a genetic counseling assistant from Johns Hopkins Medicine. As such, her clinic responsibilities include contacting patients before appointments to discuss their history, tracking down laboratory and family medical records, coordinating blood tests for pregnant people, and other responsibilities.

The needs of those who seek genetic counseling can vary, reports Hricak: "A female-male married couple might be interested in having a workup to see if they carry any of the same genetic conditions, so we will talk to them about genetic carrier screening. Do they carry a genetic condition that could be a cause of why they're not getting pregnant or having multiple pregnancy losses? We also make sure that they're not related in any way. It's a matter of how much information the patient wants. Sometimes, a [patient] just wants to start with carrier screening for herself. We can offer something as simple as a [screening] panel that looks at a few genes, like cystic fibrosis, to panels that would test 700 different genes."

IVF, When and Why

Situations that might be aided by IVF include the following:

- Absent fallopian tubes or tubal disease that cannot be treated successfully by surgery
- Endometriosis that has not responded to surgical or medical treatment
- A male factor contributing to infertility, in which sperm counts or motility are low but there are enough active sperm to allow fertilization in the laboratory
- Severe male factor in which sperm must be obtained surgically
- Unexplained infertility that has not responded to other treatments
- Genetic diseases that result in miscarriage or abnormal births[8]

Resources

UCSF Center for Reproductive Health
https://crh.ucsf.edu

Northwestern Medicine Center for Fertility and Reproductive Medicine
https://fertility.nm.org/providers.html

RESOLVE: The National Infertility and Family Building Association
https://resolve.org

Chelsea Kramer Therapy
https://www.chelseakramertherapy.com

The extent of the genetic testing patients may want can also depend on their insurance coverage. “If insurance doesn’t cover our services or there is a high deductible, it can still be $200 or $300 out of pocket for patients,” notes Hricak. “For this reason, sometimes the [patient] wants to start with herself, and if she comes back [as] a carrier of any condition, we will test [their partner] for just those conditions. But sometimes we would order tests for both of them at the same time.”

When do patients typically undergo genetic counseling? “In a perfect world, if someone goes to their ob-gyn and says they want to come off birth control because … over the next year they want to start to have a family, that would be the best time for genetic counseling,” observes Hricak. “But usually, it happens when they’ve had several miscarriages or they’ve been trying for more than a year to get pregnant. Age is also a factor. This is because it’s harder to get pregnant as you get older.”

Working in genetic counseling, Hricak agrees that an empathetic nature can go a long way in patient care. “These [people] want to have children, and there are a lot of hardships with this when they can’t,” she notes. “When you see people [who] really want to get pregnant, and they’re going into their third or fourth loss and were really hoping for this one to work out, it is so important to have empathy and a caring nature.”

Looking to the Future

Over the years, advancements in IVF and ART technology and procedures have made infertility treatment safer and more successful.[8] Of course, the decision to pursue a particular reproductive health approach is still one that patients should make carefully. Unfortunately, without adequate health insurance, costs for IVF are often prohibitive. Other concerns include state legislative initiatives to limit reproductive rights that potentially threaten access to IVF and other reproductive care.[11] Whatever the concerns, some couples may seek approaches to resolve infertility using more minimal ART or non-ART interventions. The former might include treatments involving “minimal-stimulation IVF” or “natural cycle ART” that use less medication and other approaches than standard IVF.[12]

Further, reproductive health care can encompass counseling on strategies to optimize natural fertility, including advice on sexual and healthy lifestyle practices related to procreation. When a diagnosis of infertility is not definitely established, reproductive health providers may offer informed perspectives on how to achieve a natural, non-medically assisted pregnancy.

All in all, advances in reproductive medicine have dramatically transformed infertility treatment options in recent decades. In doing so, the dreams of millions of individuals and couples to become parents and build a family are now increasingly within reach. ✦

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