A Review of Infertility for the Primary Care Provider

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KEYWORDS

- Infertility • Female infertility • Male infertility • Subfertility
- Hypothalamic dysfunction • Diminished ovarian reserve • Fecundability
- Preimplantation genetic screening

KEY POINTS

- Difficulty becoming pregnant is a common phenomenon seen in health care, but it is believed that most cases relate to subfertility rather than infertility or sterility.
- Causes of infertility are vast and varied, can relate to both male and female pathology, and are not definitively identified in approximately one-third of couples presenting with inability to become pregnant when they want to.
- The evaluation of infertility should encompass a work-up of both members of a couple, starting with detailed history and physical examination, semen analysis, and serum hormone studies.
- Considerations regarding management of infertility should address the goals of a couple, financial implication and insurance coverage, and potential need for referral to a reproductive endocrinologist and infertility specialist and should start with least invasive measures.

INTRODUCTION

It is estimated that 1 in 8 couples experience infertility. Experience with infertility is often described as isolating, frustrating, and depressing. Physician assistants can help their patients during this difficult time by providing accurate information and helpful emotional support. This article reviews the definitions of infertility, how to conduct and interpret the infertility work-up, and how to assist patients as they navigate through treatments offered by a reproductive specialist.

DEFINING INFERTILITY

This discussion starts by asking the question, What is normal fertility? The study most commonly referenced was data collected from 5574 couples between the years 1946

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to 1956. It was noted that 50% became pregnant after 6 months and 85% were pregnant by the end of 1 year.[1] Although these data was collected more than 70 years ago, other studies with much smaller sample sizes have shown similar results. It was further calculated that fecundability (ability to become pregnant) is 0.25 in the first 3 months of trying to conceive and drops to 0.15 for the next 9 months. These numbers represent the percentage chance of pregnancy for a healthy couple with no reproductive barriers. One of the most inherent challenges to fertility is that human reproduction is inefficient. The woman produces 1 gamete per month and there is a narrow window of time in which fertilization can occur. Although only 1 sperm is needed, men have millions of gametes at their disposal at any time.

Nonetheless, the timeframe of 1 year without conception has been accepted as the point to begin an infertility work-up in women under the age of 35. Accepting that age is an important contributing factor to infertility, it has been suggested that the work-up can take place after 6 months for women older than 35.[2] These timeframes apply to starting the investigation, not establishing a diagnosis of infertility. Some investigators argue that with the exception of a few diagnoses (premature ovarian failure, nonobstructive azoospermia, bilateral tubal occlusion, Asherman syndrome, or severe müllerian abnormalities), most couples seeking fertility evaluation or treatments are really subfertile, meaning they have a decreased potential for conception rather than a complete inability to become pregnant. Yet, for practical purposes, patients define infertility as the inability to be pregnant when they want to be.

ETIOLOGY OF INFERTILITY

Arriving at a definitive diagnosis for infertility or subfertility can be difficult. Sometimes a work-up identifies several factors contributing to a couple's inability to conceive, or it may reveal no explanation at all. A frequently referenced study offers the following breakdown: male factor infertility attributes 26% of the time; the ovary (premature ovarian failure, diminished reserve, polycystic ovarian syndrome [PCOS], or hypothalamic amenorrhea) accounts for 21% of cases; fallopian tube disorders represent 14% of cases, with 6% related to endometriosis; sexual dysfunction may be responsible 6% of the time; cervical stenosis may represent 3% of infertile causes; and approximately 28% of infertile couples do not have an identified causal factor and are labeled as "unexplained."[3]

EVALUATION OF INFERTILITY

It is important to review examples of advice that are not helpful when a patient seeks evaluation and treatment of infertility or subfertility. Many women who struggle with infertility have heard these words from their health care providers: "You're trying too hard; relax and take a vacation!", "You're young, I'm sure everything is fine.", and "I once had a patient who was told she couldn't become pregnant. She tried multiple treatments that didn't work, then she gave up completely and found out she was pregnant." Stress only contributes to infertility through potential hypothalamic dysfunction, menstrual cycle irregularities, and negative affect on sexual performance.[3] Gametes do not have any cognitive powers to be aware if a couple is trying to conceive or are too focused on conception. A tropical location does not enhance fertility and correlation is not causation. Women of various ages can present with infertility and it can be difficult to predict which are affected.

The first step in the evaluation of an infertile couple starts with a detailed history, including history of previous pregnancy and outcomes of those pregnancies, length of time the woman has been actively pursuing pregnancy, and any fertility awareness