NARRATIVE MEDICINE

Fertility Treatments: Increasingly Successful, Difficult to Access

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Healers have been treating infertility as a medical problem for millennia. Texts from traditional Chinese medicine, Ayurvedic practitioners,[1] and ancient Greek and Egyptian physicians document therapeutic approaches,[2] while archeologists have found ancient statues among the remnants of early civilizations. Many of these statues are postulated to represent fertility goddesses, including that of the Venus of Willendorf (see Fig. 1).

Our understanding of the biology of human conception has only come to fruition within the last 100 years. While Naegele's rule to estimate the date of anticipated birth — using the last menstrual period — was first published in the 1700s,[3] ovulation and its timing within the menstrual cycle was not described until the 1920s.[4] The fertile window was further described and defined in the 1990s.[5]

Like patients who must negotiate other specialized fields of health care, patients who have infertility face practical concerns that stretch beyond biology and physiology. Over the past 100 years, advances in the field of reproductive medicine have been concurrent with the development of birth control methods and overall delayed childbearing, as well as a patchwork availability of insurance and access to needed health care.

And while we have an improved understanding of reproductive biology, the inability to conceive has continued to carry the stigma of being "a woman's problem." Couples who know better may still feel ashamed that the ability to conceive reflects the strength of their relationship or sex life.

These stigmas may be compounded by a broad lack of recognition by authority figures as well as the lay public. The World Health Organization did not recognize infertility as "a disease of the reproductive system" until 2009. The American Medical Association only formally recognized infertility as a disease at its 2017 annual meeting, nearly 40 years after the first birth using in vitro fertilization (IVF) and 50 years after the Food and Drug Administration (FDA) approved the use of clomiphene citrate. Although our ability to help patients has dramatically increased, this ability has come with economic costs, bringing into focus questions about how patients can access treatment and who decides which treatments are covered by insurance.

Worldwide, different systems of payment for health care include nationalized medicine with primarily government-funded insurance, private-insurance models, and fee-for-service care. In the United States, health insurance has evolved as a quilt of these options and for many includes employer-based benefits initially designed to recruit and retain a Great Depression-era workforce.[6] However, because insurance coverage has developed in this manner in the United States, wide geographic and social discrepancies exist regarding which treatments are covered and who has access to that care.

Some U.S. state legislatures have prioritized access. Although injectable fertility medications — made with purified urinary gonadotropins from post-menopausal women — became available in the 1960s,[7] the real game-changer for infertility was IVF. The first IVF baby, Louise Brown, was born July 25, 1978, in England, and three-and-a-half years later, Elizabeth Carr was the first IVF baby in the United States. Shortly after these success stories, nine U.S. states — Arkansas, California, Hawaii, Massachusetts,

Fig. 1. Statue of the Venus of Willendorf, estimated to have been carved more than 29,000 years ago.
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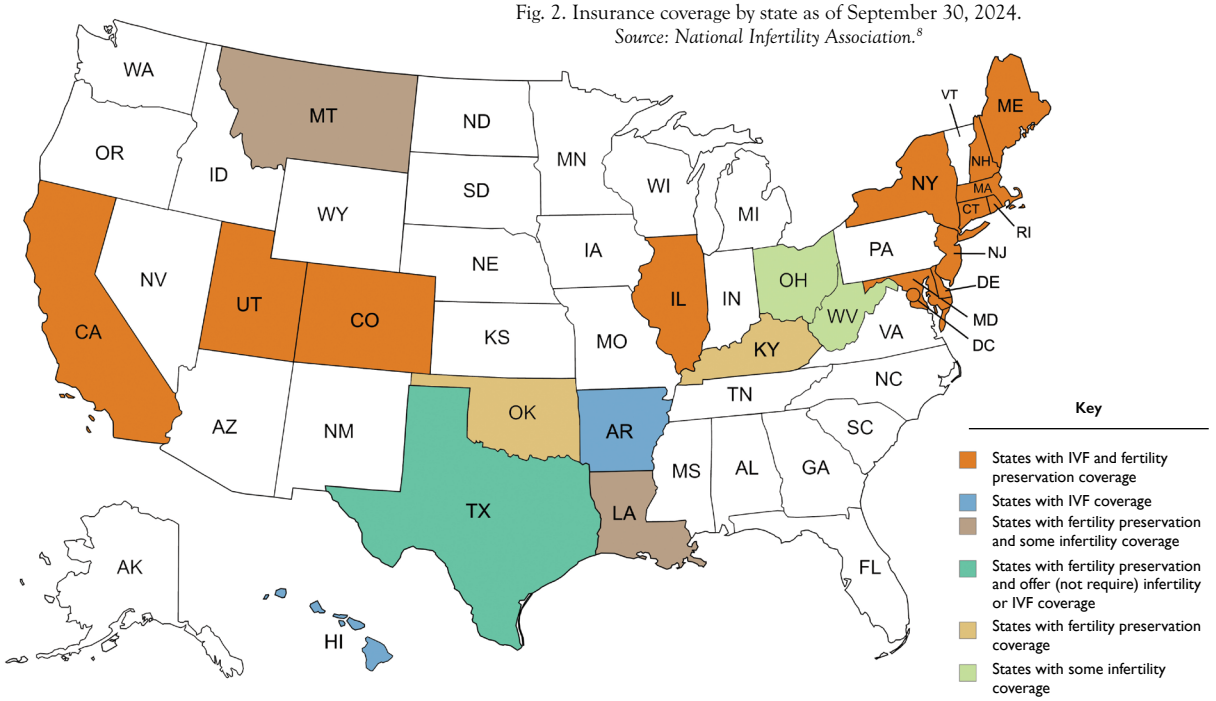
Fig. 2. Insurance coverage by state as of September 30, 2024.
Source: National Infertility Association.[8]



Maryland, Montana, Rhode Island, Texas, and West Virginia — developed mandates that insurance make infertility treatments available.[8] However, the amount of coverage and types of treatments covered were and remain markedly variable among U.S. states.

When IVF techniques were first being employed, the success rates were low and the treatments were far more invasive than they are today. Oocytes were originally retrieved laparoscopically, and the monitoring of the developing follicles containing the oocytes was rudimentary without transvaginal ultrasound, which was not developed until the late 1980s. Low rates of success and a limited ability to cryopreserve additional embryos necessitated that practitioners often transfer more than one embryo for patients who accepted the risk of multiple gestation.

As IVF became more successful, the rate of higher order multiple births — triplets, quadruplets, etc. — increased, climbing from a baseline of less than 45 per 100,000 births in 1980 to a rate of 193 per 100,000 births in 1998.[9] As a result, in 1998, the Society for Assisted Reproductive Technology (SART) and the American Society of Reproductive Medicine (ASRM) published guidelines to address the rising rates of multiple gestation pregnancies; the rate has dropped consistently since 2003.[9] The most recent iteration of these guidelines strongly recommends transfer of a single embryo for all favorable patients, including patients with chromosomally normal embryos across all age groups.[10]

Improvements in laboratory techniques within the field of embryology and the overall efficiency of IVF cycles have contributed to increased success rates. Nationally reported data for 2021 — the most recent year with complete statistics — show that more than 82% of patients up to age 37 years who proceed with an egg retrieval will have extra embryos available for cryopreservation.[11] Using current protocols for embryo cryopreservation, greater than 95% of embryos will survive the freezing and warming process. For most patients, this translates to having more than one chance at achieving pregnancy from a single egg retrieval.

The cumulative success rates with single embryo transfer, particularly for patients with a favorable prognosis, are excellent. Nationally, the 2021 SART report indicates that a new patient presenting to an IVF clinic has a 65% of livebirth for women under 35 years old and remains as high as 41% for women ages 38-40 years.[11]

Lack of insurance coverage and overall costs associated with treatment remain a barrier. Although the process leading up to an egg retrieval is the most costly and arduous aspect of an IVF cycle, patients who want to approach treatment "one embryo at a time" will accrue even greater costs with each transfer than patients who would potentially choose to transfer multiple embryos from a single egg retrieval procedure. Without

insurance coverage for fertility treatments, patients are financially incentivized to transfer more than one embryo; insurance coverage for IVF has been shown to result in a higher rate of single embryo transfer and a lower rate of multiple gestation.[12,13]

Infertility now affects one in six couples, in part due to increasing age at first pregnancy and changes in sperm viability. In 2022, for the first time, the U.S. Census Bureau reported the median age of first birth to be 30 years,[14] a significant increase from the average age of first-time mothers of 21.4 years that the Centers for Disease Control and Prevention reported in 1970.[15] Worldwide, there has been a decline in reported semen parameters over the past 50 years,[16] with urologic experts calling for increased research into male fertility to understand the causes and implications.

As the rate of infertility increases and the U.S. birth rate decreases, providing access to safe and effective fertility care, including IVF, will become even more important.[17] Insurance coverage and access vary from state to state (see Fig. 2). Advocacy may as yet yield coverage for patients who are currently excluded, including cancer patients who need fertility preservation.[18]

Our needs and desires change, and for couples there can be years of desperate hope not to become pregnant, followed by an equally fervent desire to conceive. While some may find that controlling fertility is a polarizing prospect, empowering patients along the road toward desired parenthood may ultimately be seen as dignifying and noble.

I am grateful that the Penn Medicine employees I see as patients have insurance coverage for fertility treatment. I look forward to the day when Pennsylvania will join its neighboring states in mandating access to fertility care.

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