

40% of IVF Treatments Are Unnecessary

Analysis by [Dr. Joseph Mercola](#)

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STORY AT-A-GLANCE

- › One scientist believes up to 40% of in vitro fertilization (IVF) procedures may be unnecessary if a woman's low progesterone levels are treated. In response to her own struggle with miscarriages, Amy Galliher-Beckley, Ph.D., designed a urine test for progesterone metabolites she believes will help women avoid IVF
- › Progesterone and estrogen are two important hormones that affect a woman's ability to get pregnant and support a pregnancy. Beckley found she could conduct a simple urine test to evaluate the presence of progesterone metabolites, necessary to develop a healthy uterine lining
- › When there isn't enough progesterone produced and secreted the condition is called Luteal Phase Defect, which affects the menstrual cycle after ovulation and until pregnancy or menstruation. Progesterone may be affected by anorexia, obesity, polycystic ovary syndrome and high levels of exercise
- › Factors over which a woman has control include smoking, eating well and avoiding excessive alcohol. One factor affecting fertility over which a woman does not have control is sperm count, which has declined by up to 60% in North America since 1973

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Your entire body takes direction from your hormones. Hormones are secreted by your endocrine system and are responsible for telling your organs what to do and when to do it.¹ They are essentially chemical messengers that travel throughout your bloodstream,

working slowly over time to affect processes like growth and development, metabolism and reproduction.

Sometimes, these chemical messengers may get out of balance, and this leads to chronic disorders such as Type 2 diabetes, weak bones and infertility.² Hormones may be secreted by your adrenal glands, endocrine-related organs, hypothalamus, sex glands and other organs.³

Progesterone is important to fertility and supporting a pregnancy. It's a steroid hormone secreted by the corpus luteum and then by the placenta if you become pregnant.⁴ In some cases, when couples suffer from infertility, they choose in vitro fertilization (IVF).

This is a complex series of procedures in which eggs are retrieved from the ovaries, fertilized by sperm in a lab and then transferred into the uterus.⁵ One full cycle can take up to three weeks⁶ and cost \$12,000.⁷ In response to her struggles with infertility, Amy Galliher-Beckley, Ph.D.,⁸ co-founded MFB Fertility and the progesterone test Proov.⁹

The Estrogen and Progesterone Relationship

Each of your bodily systems maintains a balance to help you maintain optimal health. Your reproductive system is no different. For a woman, there are several hormones affecting a complex system to mature an egg follicle and release an egg where it travels to the uterus. If fertilized, the egg must implant into the uterus, called the endometrium, where it begins to develop into a baby.

These events are controlled by hormones secreted from several sources in the body. The ovaries produce the eggs and are the main source of estrogen. The adrenal glands sit on top of each kidney and also make a small amount. Estrogen plays a role in physical changes during puberty; it also controls the menstrual cycle, protects bone health and affects your mood.¹⁰

The second hormone essential to fertility is progesterone, a steroid hormone that is first secreted by the corpus luteum. After the egg is released, the corpus luteum is left

attached to the ovary, which functions as a temporary gland.¹¹ These two hormones are controlled by the release of other hormones.

During the menstrual cycle gonadotropin-releasing hormone is secreted from the hypothalamus, triggering the secretion of follicle-stimulating hormone (FSH) from the pituitary gland.¹² This begins follicle development and triggers a rise in estrogen.

Luteinizing hormone (LH), also secreted by the pituitary gland, supports the maturation of the follicle and a trigger to cause the egg to be released. When estrogen levels get sufficiently high it signals a sudden release of LH, around mid-cycle, which triggers a set of events that ultimately release the mature egg from the follicle.¹³

Once released, the empty follicle becomes the corpus luteum, which produces progesterone. The release of progesterone triggers the uterus to develop a highly vascularized bed suitable for implantation of a fertilized egg.

Without fertilization, the corpus luteum begins to degenerate, the secretion of progesterone drops off and menstruation occurs. If pregnancy occurs then the corpus luteum produces progesterone for the first 10 weeks until production is taken over by the placenta.^{14,15}

Not About Getting Pregnant, but Staying Pregnant

As Beckley explains in her interview with Forbes magazine,¹⁶ her test is not about getting pregnant, but rather staying pregnant. Progesterone not only prepares the uterus for the egg to implant; it also protects the endometrium from degeneration and menstruation. While the body is producing high levels of progesterone during a pregnancy, a second egg will not mature.¹⁷

In order to maintain a pregnancy, the corpus luteum must continue to secrete progesterone. This maintains the blood vessels in the endometrium to feed the growing baby. It is in these early weeks that women with low levels of progesterone may have difficulty, both conceiving and developing the right environment for a fertilized egg to grow.

Some women who do get pregnant are at a high risk for miscarriage.¹⁸ The test Beckley developed comes with sticks used in much the same way ovulation and pregnancy tests are used. These sticks measure the amount of progesterone metabolites excreted in the urine. To date, this is the first at-home, over-the-counter test used to evaluate a woman's ability to produce progesterone.¹⁹ Beckley explains:²⁰

"Low progesterone is the number one cause of unexplained infertility. Women who go through IVF protocols all are offered progesterone. If you are not going through IVF, most doctors don't talk about progesterone, they don't offer progesterone, they don't test for progesterone. When your progesterone crashes too quickly, it is called a luteal phase defect."

Luteal Phase Defect Increases Chances of Miscarriage

The luteal phase in a woman's cycle begins after ovulation and represents the second half of the menstrual cycle. The luteal phase is named after the corpus luteum. Luteal Phase Defect (LPD) results in an abnormal endometrial growth that may not support a pregnancy.^{21,22}

While researchers struggle to identify the underlying dysfunction and efficacy of LPD in supporting fertility, experts report women undergoing IVF always have LPD present.²³ LPD is marked with a luteal phase less than 11 days. However, not all physicians believe the condition exists; reliable tests are lacking.²⁴

Beckley developed the Proov urine test to help women identify a reduction in progesterone during their cycle. According to Beckley,²⁵ her test gives women more knowledge about how their body works and provides a foundation for asking their infertility doctors better questions.

The test measures the presence of metabolites in the urine that should increase and remain elevated after ovulation. It may be used to confirm ovulation and confirm levels of progesterone afterward. A single negative test before ovulation followed by a single positive test will confirm ovulation for women trying to get pregnant.²⁶

For women trying to conceive, the test is recommended four days after peak fertility and then for continued testing 10 days past ovulation.²⁷ When questions arise about levels of progesterone to maintain a pregnancy, they recommend testing six days after peak fertility and as needed during the pregnancy since the test should remain positive.

Other Functions of Progesterone

Although LPD has a significant impact on a woman's ability to carry a pregnancy, it is the subject of debate.²⁸ In some cases, the ovaries release enough progesterone but the uterine lining does not respond.²⁹ LPD has been linked to other health conditions, including:³⁰

Anorexia	Endometriosis
High levels of exercise	Obesity
Thyroid disorders	Polycystic ovary syndrome (PCOS)
High levels of prolactinemia (the hormone responsible for breast milk)	

In some circumstances, when these conditions are treated, the LPD resolves.³¹ Later in life, if levels of progesterone decline, a woman's period may become irregular, heavier and longer,³² increasing her chance of experiencing anemia, depending on the amount and length of her period.³³

Variations in hormone levels after menopause may also influence cognition and mood.³⁴ In a study of 643 healthy postmenopausal women, researchers found that while estrogen had little effect on tests of executive function or global cognition, progesterone concentrations were associated with verbal memory. The researchers suggest this positive association merits additional study.

Bioidentical progesterone, also known as micronized progesterone in the oral form, has been successful in helping relieve hot flashes and night sweats during menopause. Dr. Jerilynn Prior from the University of British Columbia Vancouver presented her study at an endocrine society meeting during which she compared the use of progesterone to placebo.³⁵

The study assigned 114 postmenopausal women into one of two groups, a placebo group and another who took 300 mg of micronized oral progesterone daily. To be eligible for the study, the women had to be off hormone therapy for at least six months.³⁶

At the end of the 12-week study, researchers found that the group taking micronized progesterone demonstrated a 56% decrease in a score reflecting the number and intensity of symptoms, while the women taking the placebo reported a 28% decrease.³⁷

Age Does Affect Hormone Balance

As is borne out by the number of women struggling with hormonal imbalances as they age and those requiring fertility assistance to become pregnant after 40,³⁸ Beckley is vocal about the difficulty women may have supporting a pregnancy after she turns 40.³⁹

Beckley says,⁴⁰ “The closer a woman gets to menopause, the least likely her body is going to be able to support a pregnancy.” Much of this is related to the imbalance of hormones required to successfully support a pregnancy that occurs as women age.

Her research in designing the progesterone urine test led Beckley to believe 30% to 40% of women who undergo IVF treatment to become pregnant ultimately do not need IVF.⁴¹ Instead, they may require progesterone to develop a healthy endometrial lining and support early pregnancy.

Overall Fertility Is on the Decline

Couples experience infertility for a number of reasons. In a study⁴² released in 2017, researchers evaluated 38 years of information and found sperm counts declined

significantly between 1973 and 2011. The sperm counts declined 52% to 59% in men located in North America, Europe and Australia.

The Australian Department of Health reports 1 in every 6 Australian couples suffers from fertility problems, which they attribute to the decision to have children later in life as well as declining sperm count. Quality and lifestyle factors such as smoking, not eating healthfully, consuming excessive amounts of alcohol and not having a healthy BMI also affect fertility.⁴³

In May 2019, the Pew Research Center reported that for the fourth year in a row, key fertility indicators for U.S. couples declined, reaching a record low.⁴⁴ Two of the three indicators used to determine fertility reflected a decline in numbers.

The total fertility rate, or the estimation of the number of children a woman would have in her lifetime, was 1.73 children in 2018. This was lower than the estimate of 1.74 from the mid-1970s.⁴⁵ Research suggests men's fertility is affected by environmental toxins and chemicals you may find in your own home.

Additionally, statistics from the CDC show the number of new births was down 2% in 2018 as compared to 2017, but the number of premature births was rising. Infertility and pregnancy are complex conditions that likely need a comprehensive approach to experience a successful outcome.

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