

FERTILITY 101



EMD
SERONO



REPRODUCTION & INFERTILITY

FEMALE INFERTILITY

MALE INFERTILITY

ADVANCED TREATMENTS

RESOURCES

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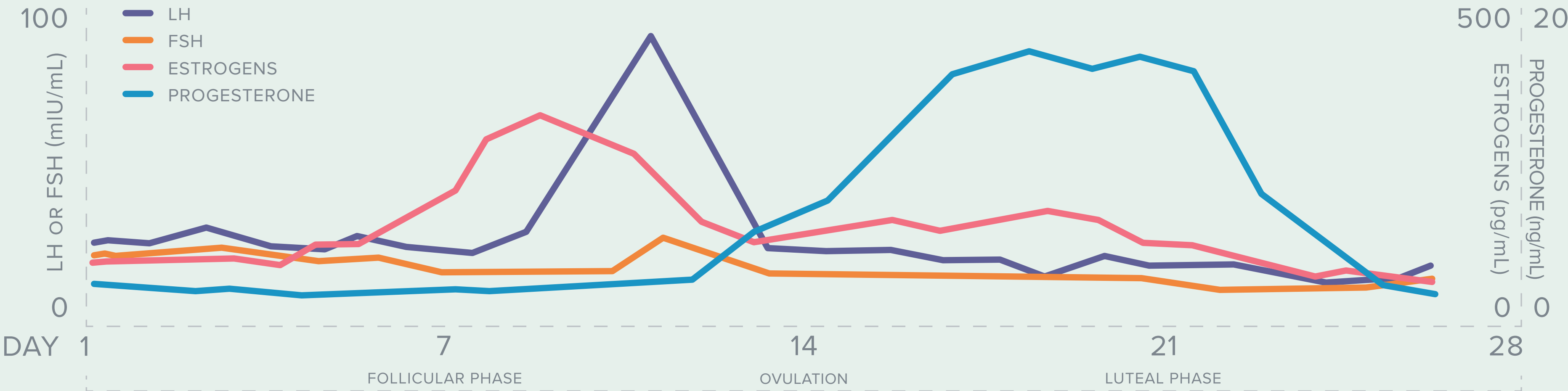


UNDERSTANDING FEMALE REPRODUCTION

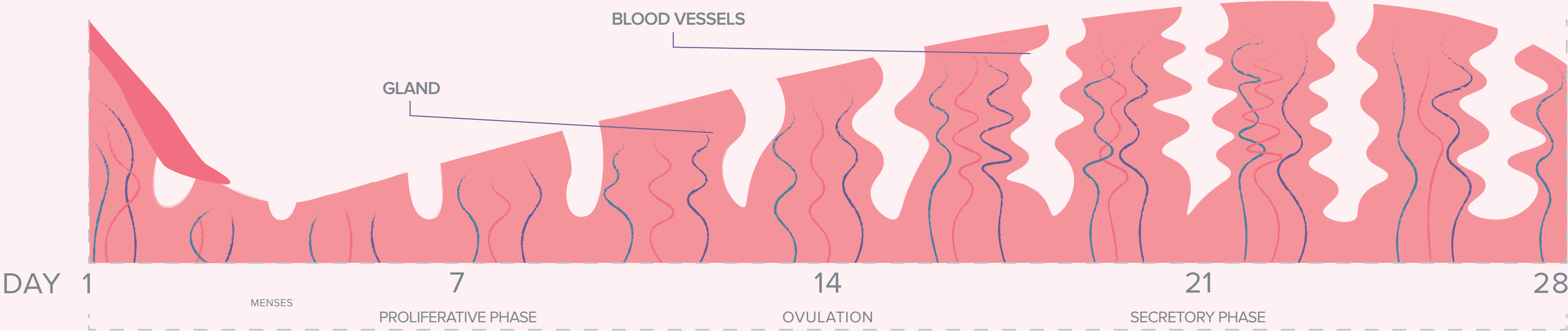
FOLLICULAR CYCLE



HORMONAL CYCLE

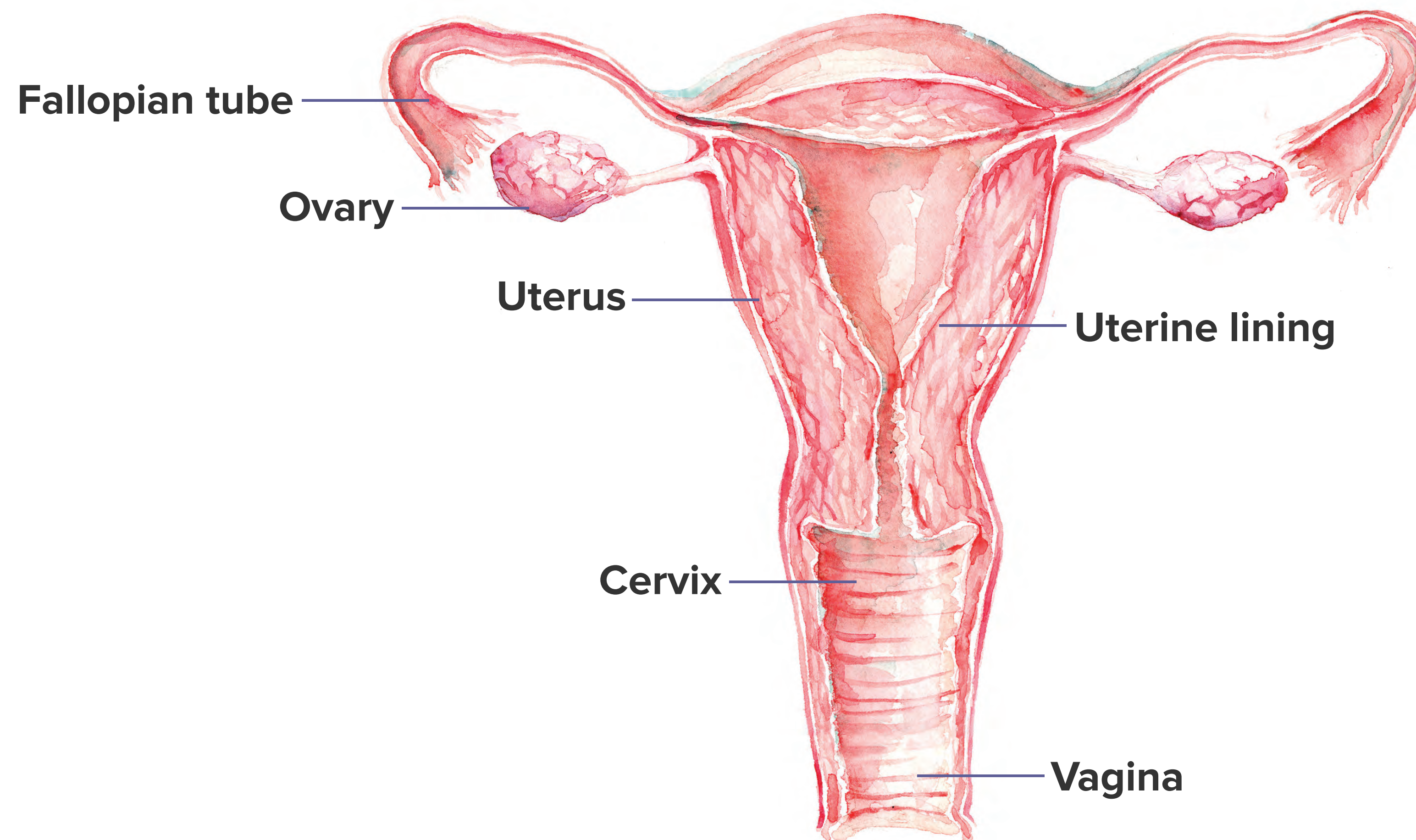


UTERINE CYCLE



UNDERSTANDING FEMALE REPRODUCTION

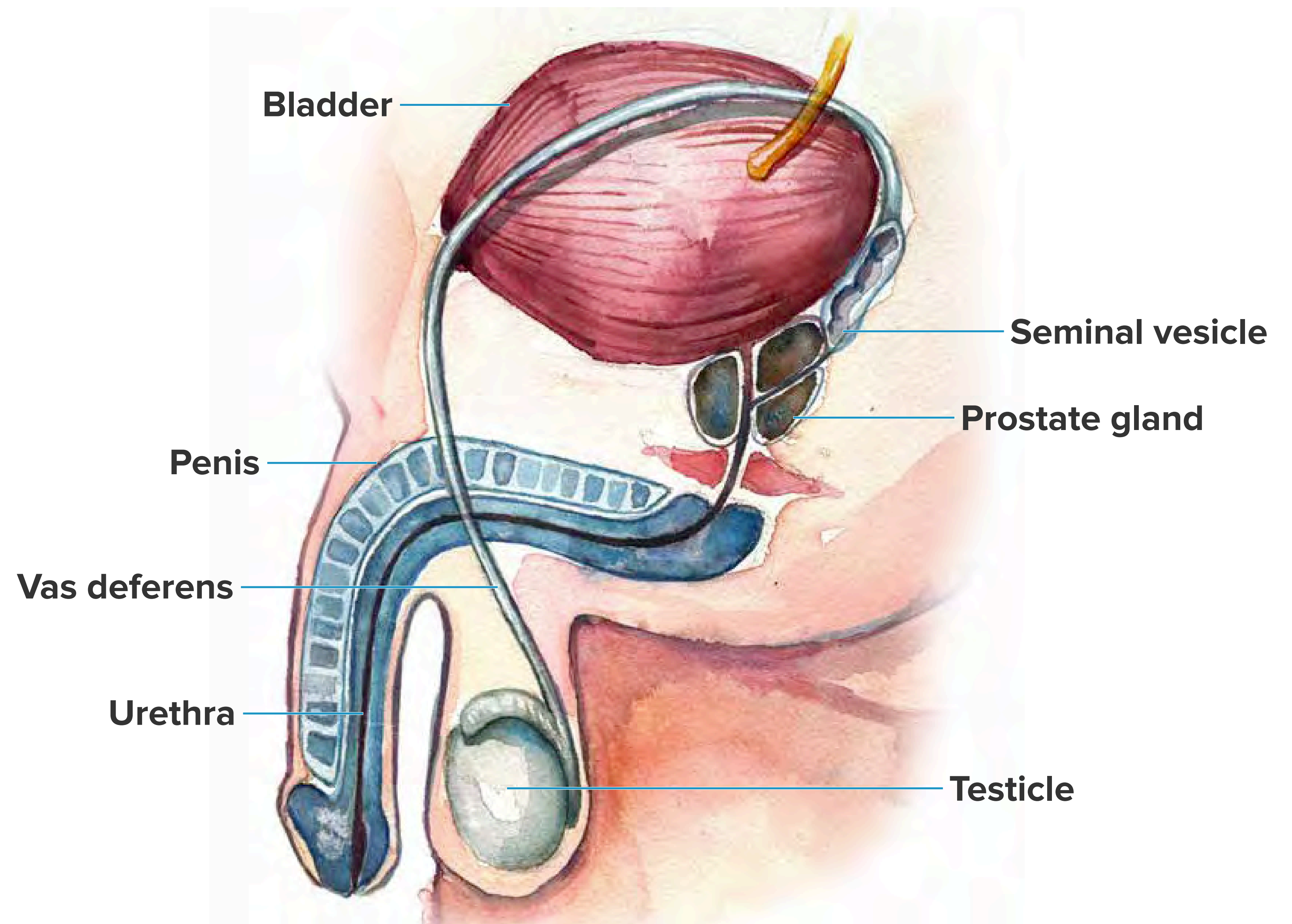
The ovaries contain a woman's lifetime supply of immature eggs—approximately 2 million eggs at birth.¹ They also produce the hormones estrogen and progesterone. The sperm and egg meet for fertilization in the fallopian tubes. A fertilized egg then attaches itself to the lining of the uterus and begins to develop. The vagina is the passage that leads from the outside of the body to the cervix—the opening to the uterus.²



UNDERSTANDING MALE REPRODUCTION

SEVERAL FACTORS PLAY A ROLE IN DETERMINING FERTILITY SUCCESS

-  **SPERM COUNT**
(number of sperm)
-  **SPERM MOTILITY**
(ability to move)
-  **FORWARD PROGRESSION**
(quality of movement)
-  **SPERM MORPHOLOGY**
(size and shape)
-  **SEMEN VOLUME**
(amount of fluid released)



WHAT IS INFERTILITY?

Infertility is defined as the inability to get pregnant³:



**AFTER 1 YEAR OF
REGULAR, UNPROTECTED
INTERCOURSE**



**AFTER 6 MONTHS OF
REGULAR, UNPROTECTED
INTERCOURSE**

Infertility is more common than you think^{3,4}



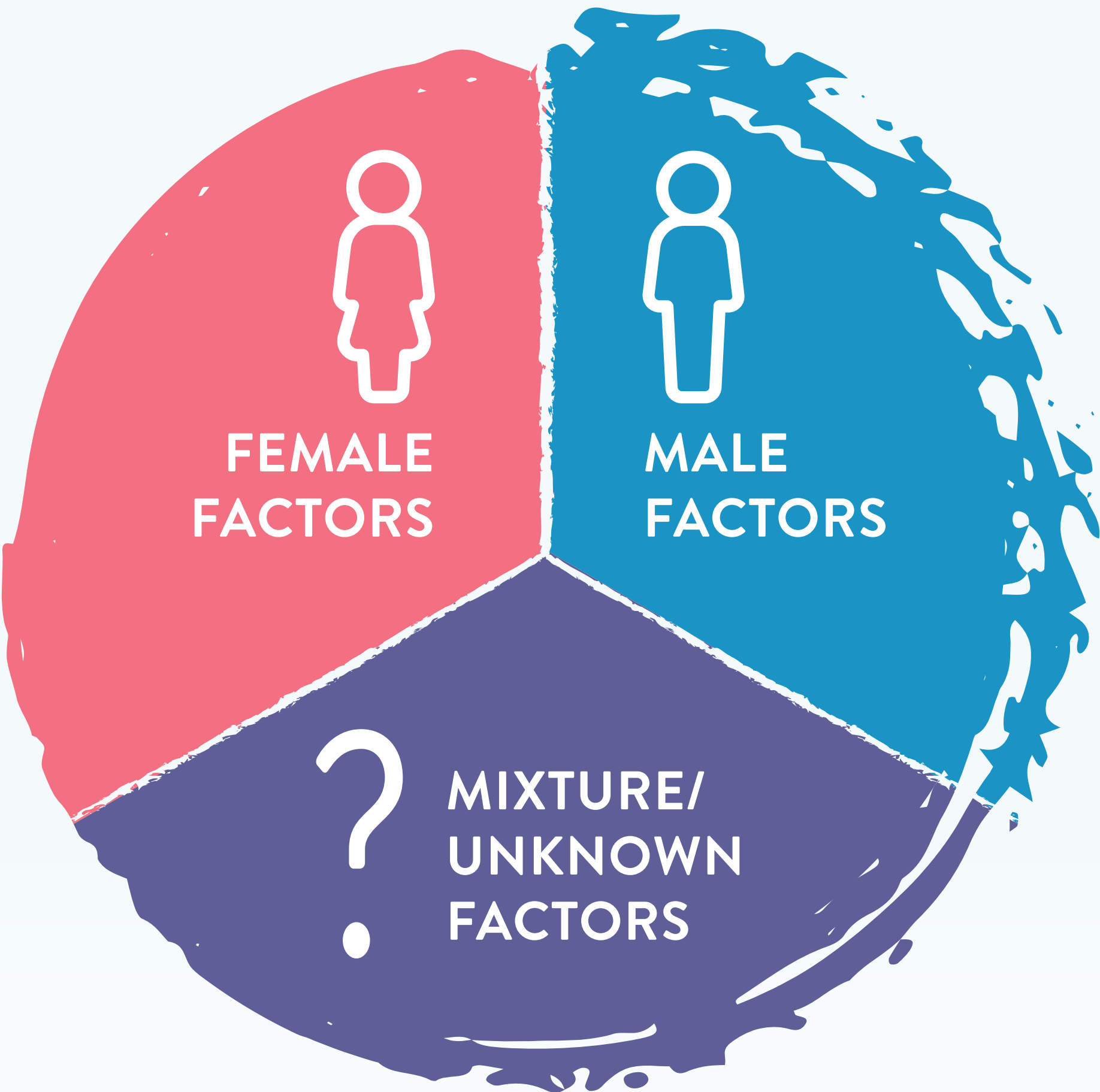
**1 IN 8 COUPLES IN THE US
EXPERIENCE DIFFICULTY CONCEIVING**
(or about 7.3 million American women)

According to the CDC, 11% of women of childbearing age struggle with infertility

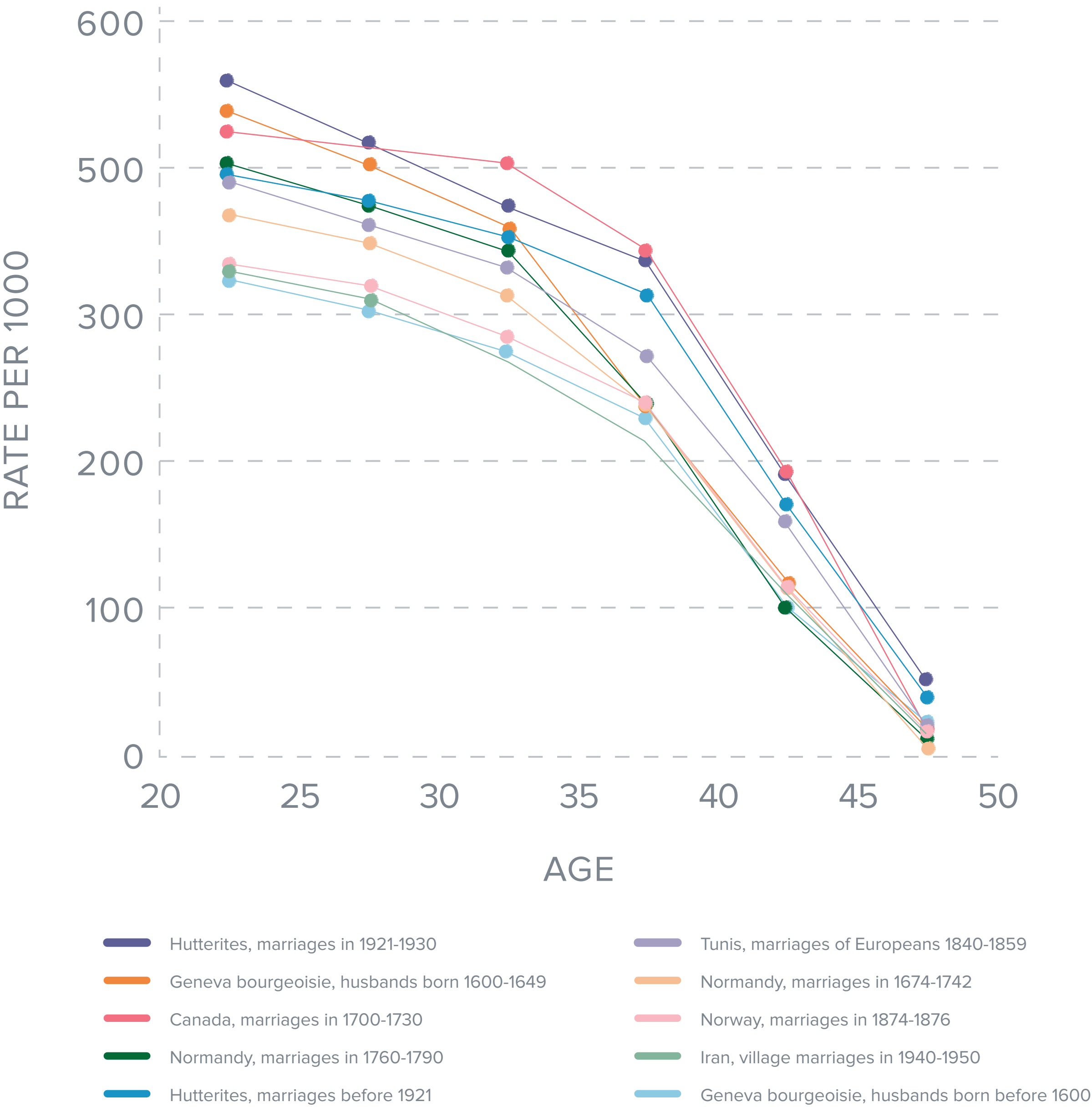


WHAT CAUSES INFERTILITY?

The US Office on Women’s Health estimates that infertility cases are equally caused by⁴:



NATURAL FERTILITY DECREASES WITH AGE⁵



FEMALE FACTORS

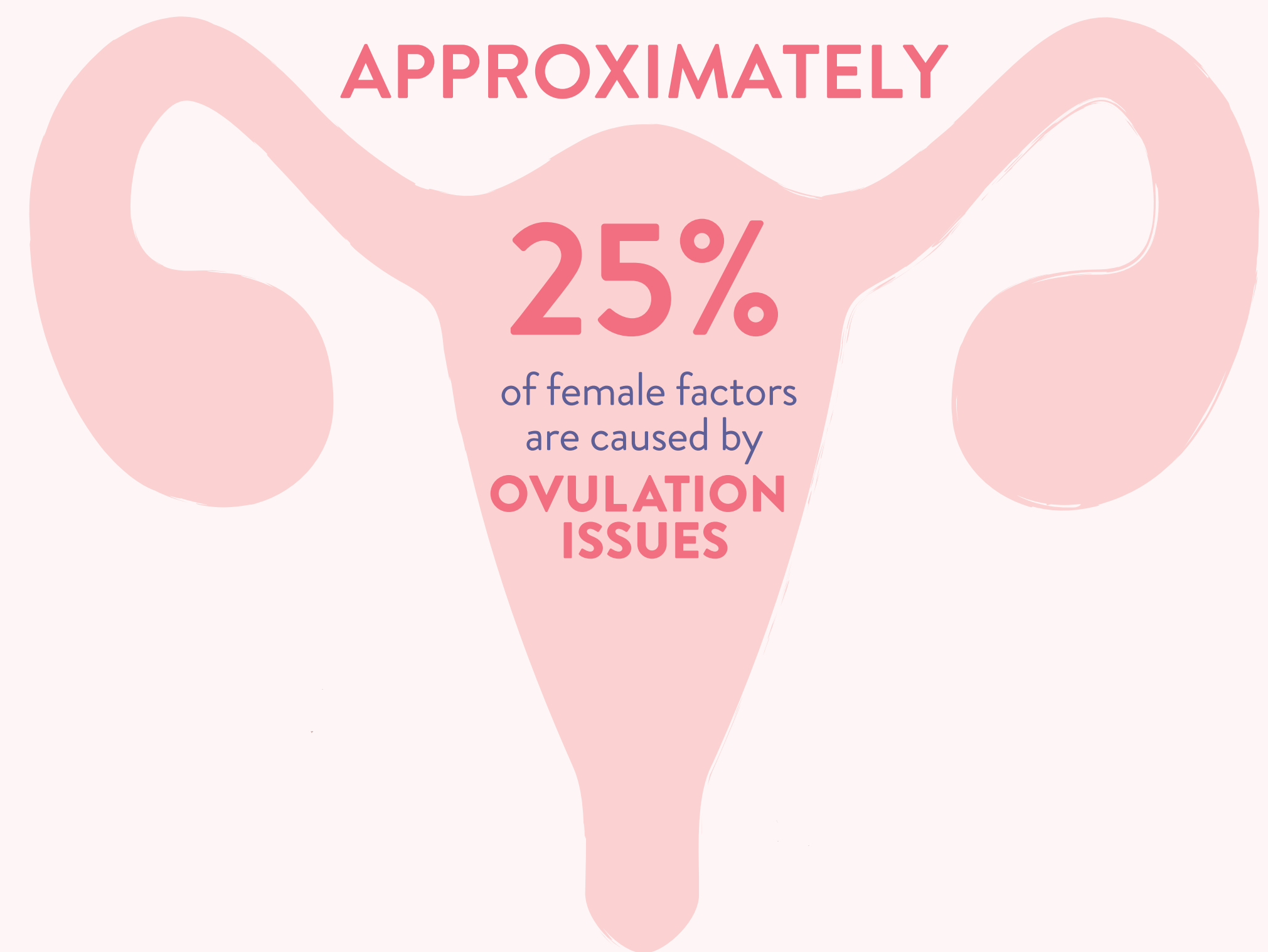
There are a number of biological issues that can cause infertility in women.

Age



Women over 35 years old should be evaluated and treated after 6 months of failed conception attempts, or sooner if clinically indicated. In women over 40, immediate evaluation and treatment are warranted.⁶

Ovulatory issues^{7,8}



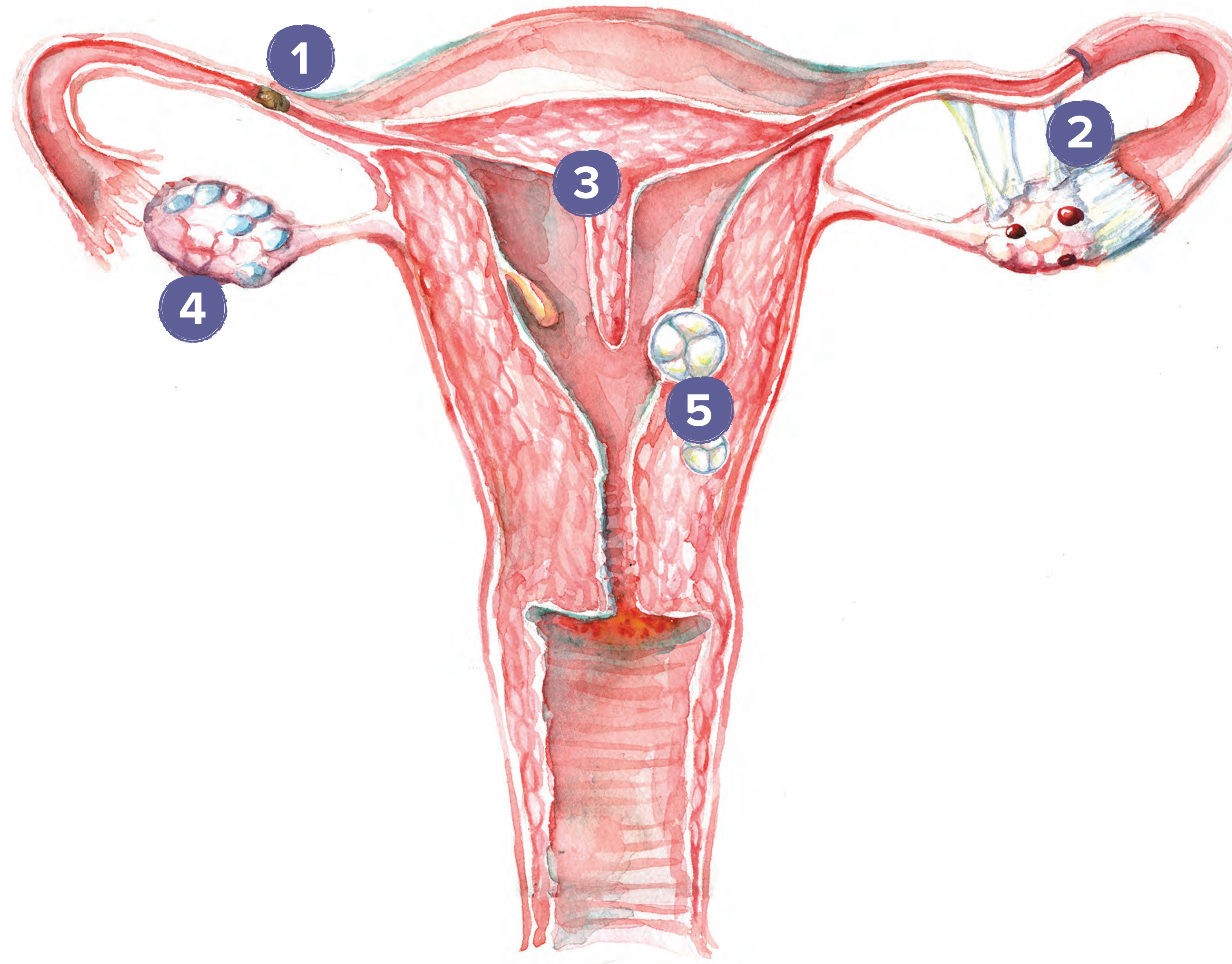
Most of the time, it's due to hormonal imbalances, caused by faulty communication between the brain and the glands responsible for releasing hormones. Abnormal ovulation may also be associated with significant changes in weight, including extremely low body weight or being overweight.



FEMALE FACTORS

Physical issues⁷

- 1 **Blocked fallopian tubes** can prevent sperm and eggs from uniting or an embryo from implanting. Causes include past infections or sexually transmitted diseases
- 2 **Adhesions**, or areas of scarred tissue, are caused by surgery, endometriosis, or pelvic inflammatory disease
- 3 **Uterine septum** is a congenital malformation in which the uterine cavity is partitioned
- 4 **Polycystic ovary syndrome (PCOS)** causes ovarian cysts due to abnormal hormone levels, sometimes enlarging the ovaries. It's a leading cause of female infertility
- 5 **Fibroids** are generally noncancerous growths in the uterus
- 6 **Endometriosis** (not pictured) causes cells that normally line the uterine cavity to implant on the ovaries or other pelvic organs. It affects about 40% of women who have no other diagnosable infertility problem⁹



EVALUATION: AFC AND DIAGNOSTIC BLOODWORK

Types of testing

A number of tests can be performed at specific points in the hormonal cycle to confirm the physiologic changes characteristic of a healthy reproductive cycle. These tests include:

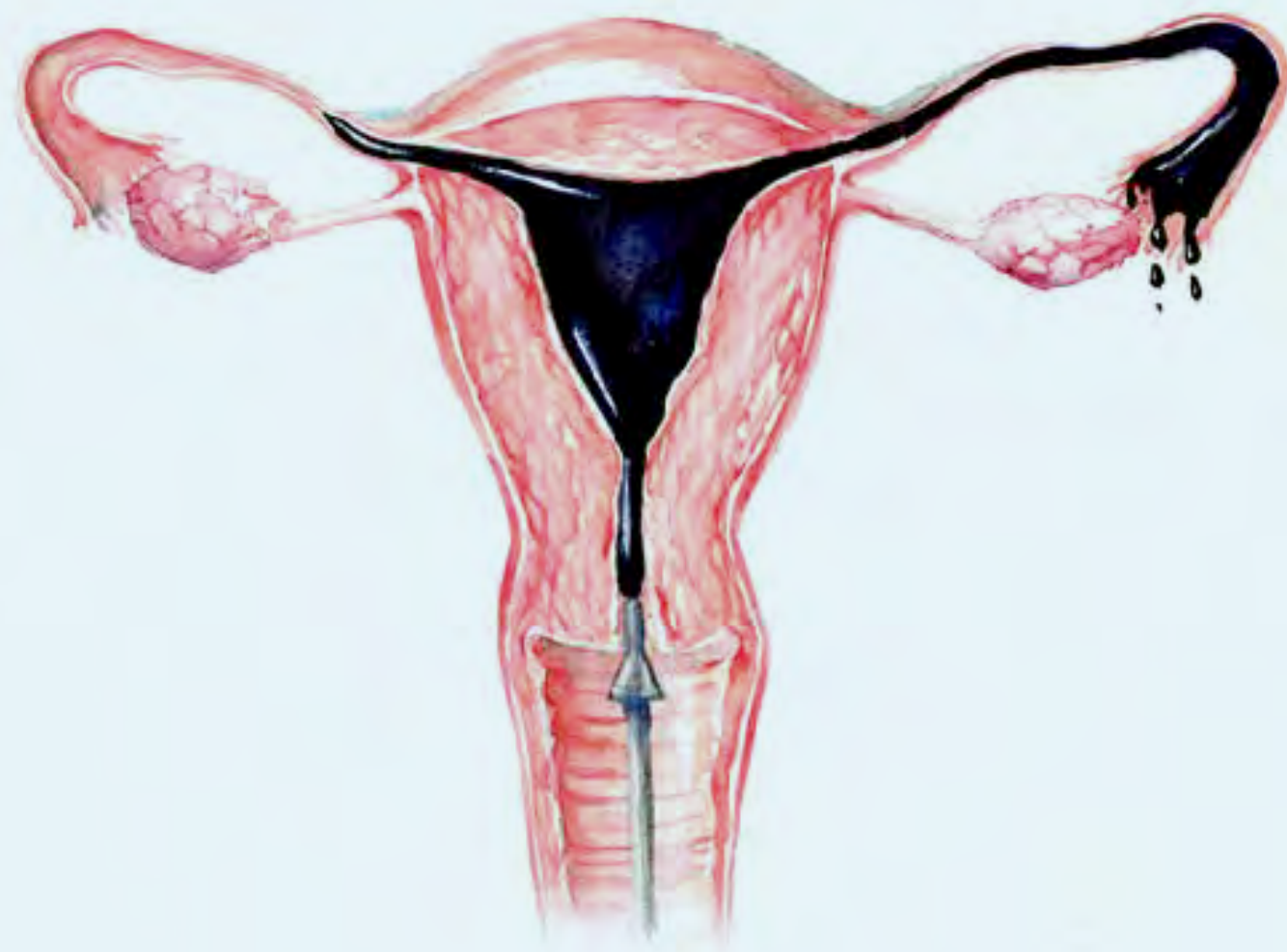
- **Antral follicle count (AFC):** Measures ovarian reserve by visually counting the number of egg-containing follicles developing on both ovaries using a transvaginal ultrasound
- **Anti-mullerian hormone (AMH) levels:** This hormone is produced by the follicles early in their development. Lower AMH indicates decreased ovarian reserve. Low AMH or high FSH indicate that chances of conception may be lower²
- **LH levels in urine:** LH levels rise in the days prior to ovulation; testing can reveal the LH surge
- **Measuring progesterone levels:** Testing progesterone 1 week after ovulation should reveal high levels characteristic of the luteal phase
- **Other tests:** FSH and E2 ordered together on cycle day 2 or 3, TSH, and prolactin

LH = LUTEINIZING HORMONE. FSH = FOLLICLE-STIMULATING HORMONE. E2 = ESTRADIOL. P4 = SERUM PROGESTERONE. HCG = HUMAN CHORIONIC GONADOTROPIN. TSH = THYROID-STIMULATING HORMONE.



EVALUATION: REPRODUCTIVE SYSTEM¹⁰

Imaging tests can be used to examine the reproductive system to find the cause of infertility. Some of these tests allow indirect viewing of structures.



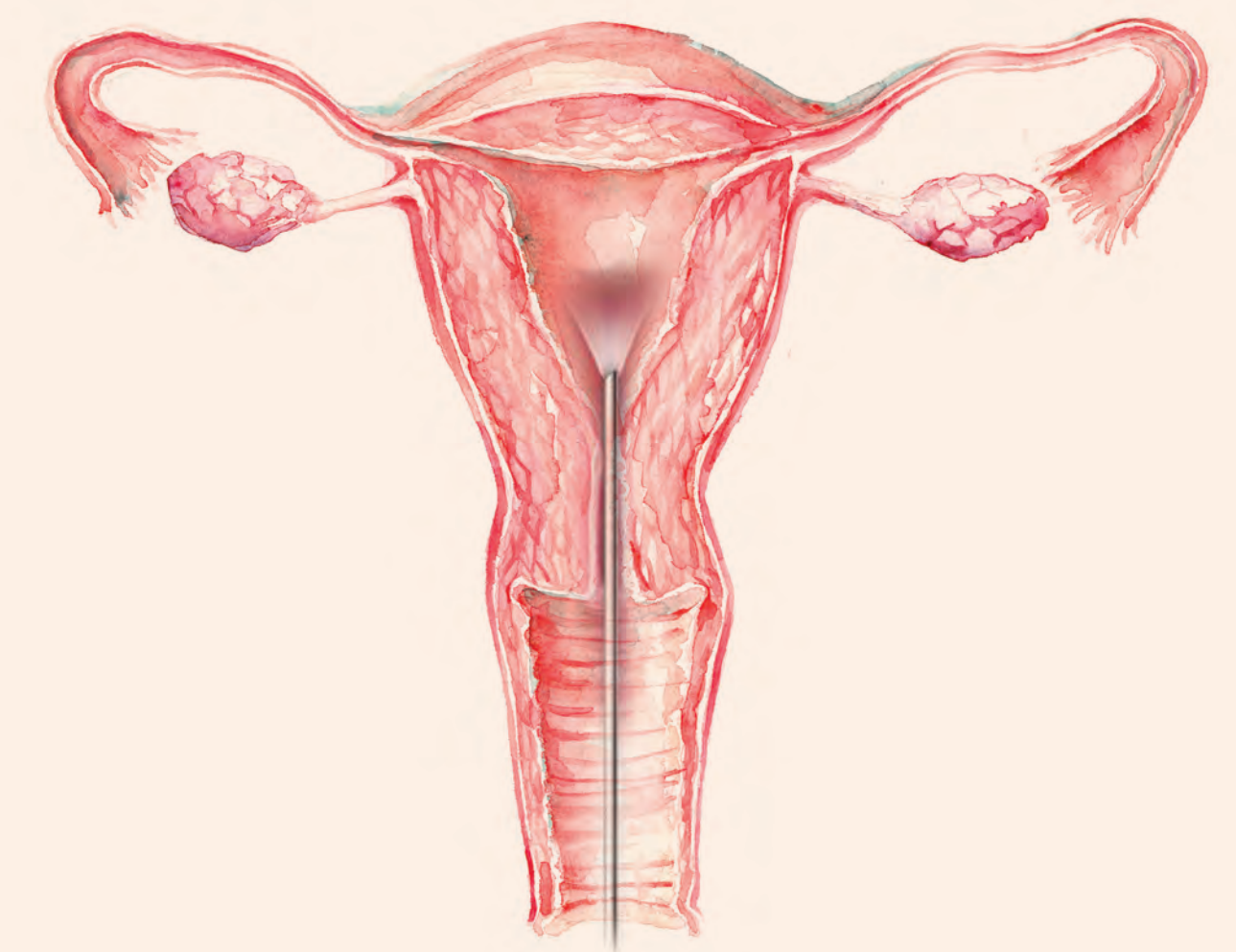
Hysterosalpingography (HSG)

Visualizes the openness of the uterine cavity and fallopian tubes



Saline infusion sonohysterogram (SIS)

An ultrasound test to evaluate the uterus



Hysteroscopy (HSC)

Involves inserting a small fiber-optic camera through the cervix and into the uterine cavity

DIAGNOSIS: OVULATION DISORDERS

The most important factor in female infertility is the woman's age.

Diminished ovarian reserve

- Women are born with a finite number of oocytes (1 to 2 million at birth)
- The ovarian reserve decreases through reproductive years
- Fertility in women peaks between the ages of 20 and 24
- Fertility can decrease as much as 95% in women aged 40 to 45 years

Less common factors

Primary ovarian insufficiency (POI)

POI is the dysfunction of ovaries before age 40

- Amenorrhea (the absence of menstruation)
- Hypoestrogenism (lack of estrogen)
- Elevated serum gonadotropin levels in women younger than 40 years

Most women with POI have intermittent ovarian function, and pregnancy may occur

Functional hypothalamic amenorrhea (FHA)

FHA is a form of chronic anovulation (when the ovaries don't release an oocyte during the menstrual cycle) due to impairment of gonadotropin-releasing hormone (GnRH)

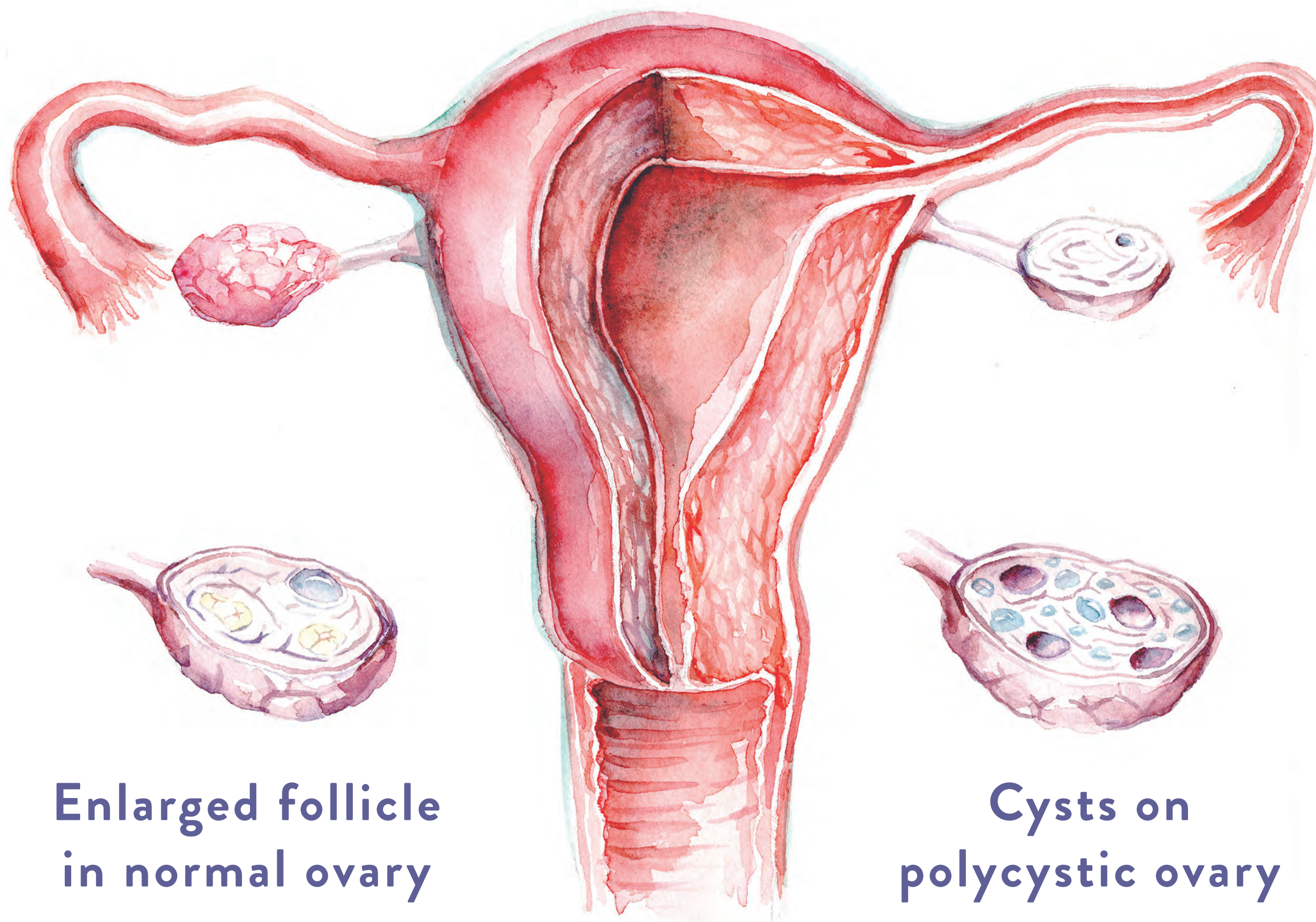
- Often associated with stress, weight loss, excessive exercise, or a combination of these
- May be reversed with a multidisciplinary approach, including dietary, medical, and mental health support



DIAGNOSIS: OVULATION DISORDERS

Polycystic ovary syndrome (PCOS)¹¹

PCOS causes the ovaries to secrete abnormally high amounts of androgens (male hormones) that often cause problems with ovulation. Women with PCOS have enlarged ovaries that contain small cysts.



Enlarged follicle
in normal ovary

Cysts on
polycystic ovary

SYMPTOMS

PCOS can be completely asymptomatic. More often, the following symptoms are present:

- Weight gain or obesity
- Excessive hair and/or abnormal hair growth patterns
- Irregular periods or a complete absence of menstruation (amenorrhea)
- Acne
- Oily skin
- Enlarged ovaries or multiple ovarian cysts on the outermost edge of the ovary, as seen by ultrasound

CRITERIA

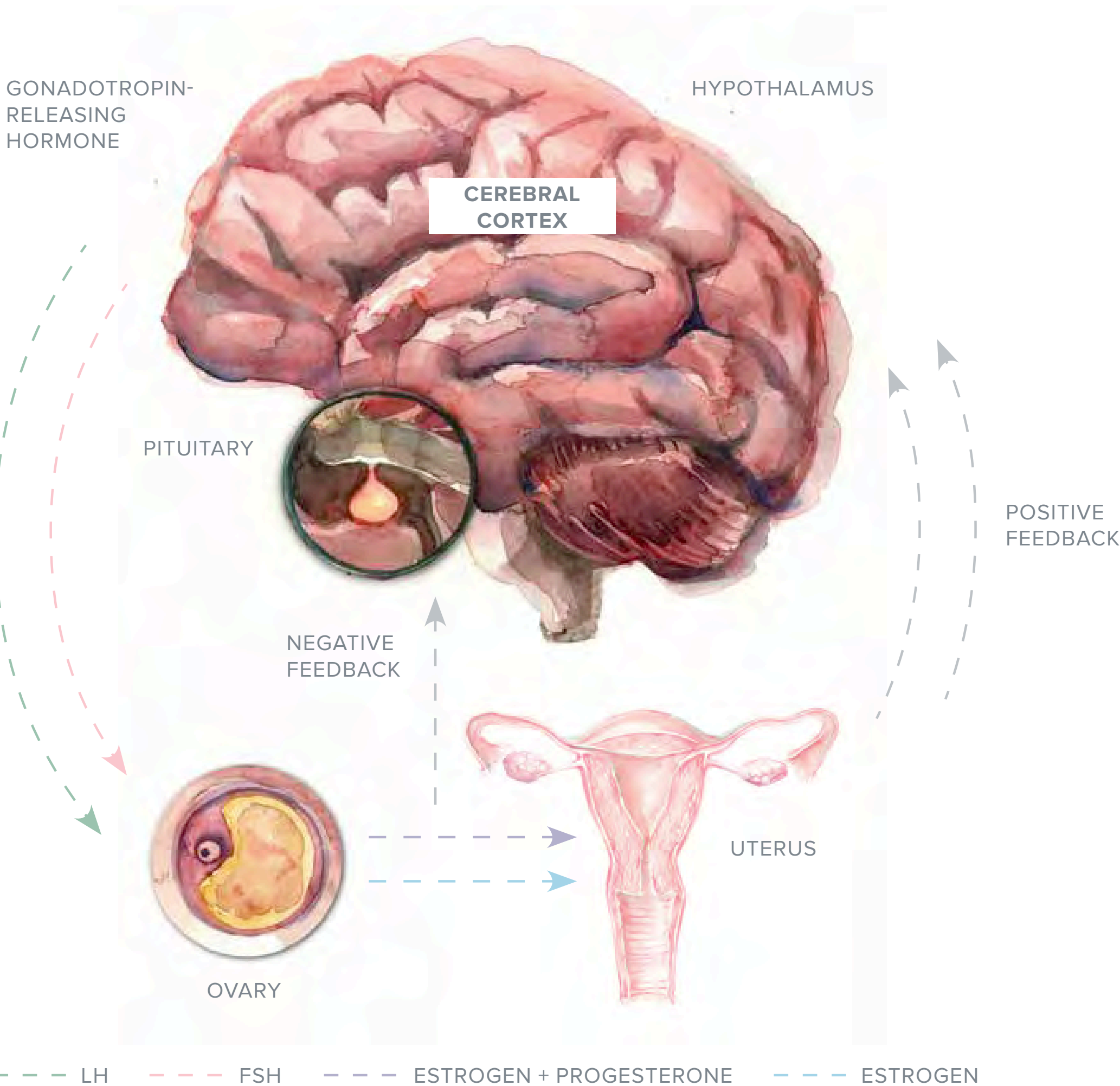
According to the widely accepted Rotterdam Criteria, two of the following are required for PCOS diagnosis¹²:

- Polycystic ovaries
- Hyperandrogenism
- Menstrual irregularity

DIAGNOSIS: OVULATION DISORDERS

Hypothalamic/pituitary disorders¹¹

Hyperprolactinemia is the excessive production of the hormone prolactin (responsible for milk production). An excess of prolactin can suppress ovulation and be symptomatic of hypothyroidism (when the body lacks thyroid hormone) or luteal phase defects.



CAUSES

- Tumors on the pituitary gland (known as prolactinomas)
- Anorexia
- Thyroid gland disorder
- Surgical scars on the chest wall, and other chest wall irritations (such as shingles)
- Medications including some tranquilizers, blood pressure medications, and anti-nausea drugs
- Oral contraceptives and recreational drugs

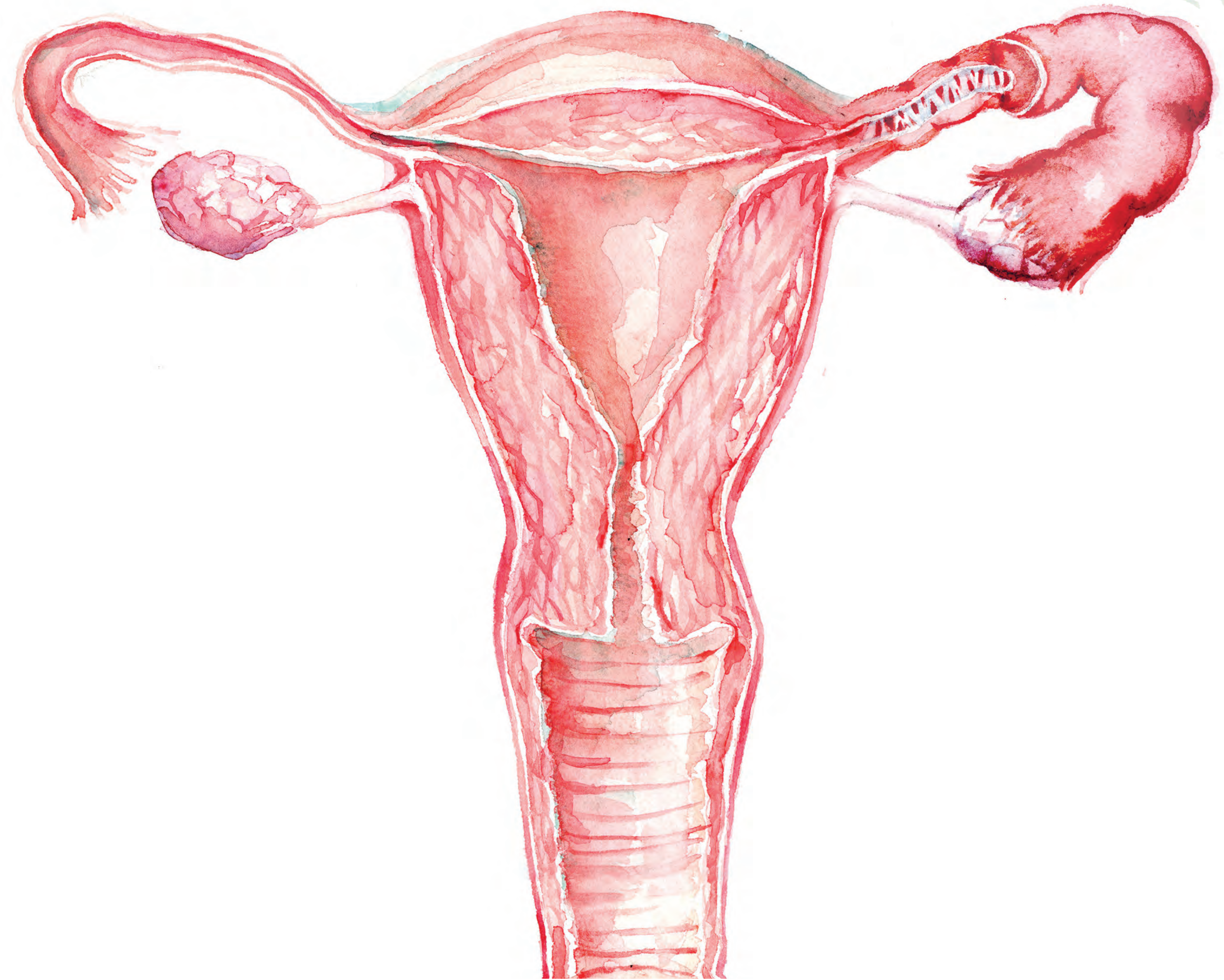
SYMPTOMS

Symptoms include production of breast milk by non-nursing women and anovulation, or lack of ovulation.



DIAGNOSIS: TUBAL, PELVIC, AND UTERINE FACTORS

- **Pelvic inflammatory disease (PID)**, a condition in which the upper reproductive organs in a woman become infected. The disease can affect the lining of the uterus, ovaries, and fallopian tubes¹¹
- **Sexually transmitted diseases** and scarring, which may also cause infertility even if PID is not present
- **Uterine factors** such as fibroids, Asherman syndrome, and Mullerian abnormalities, including septum



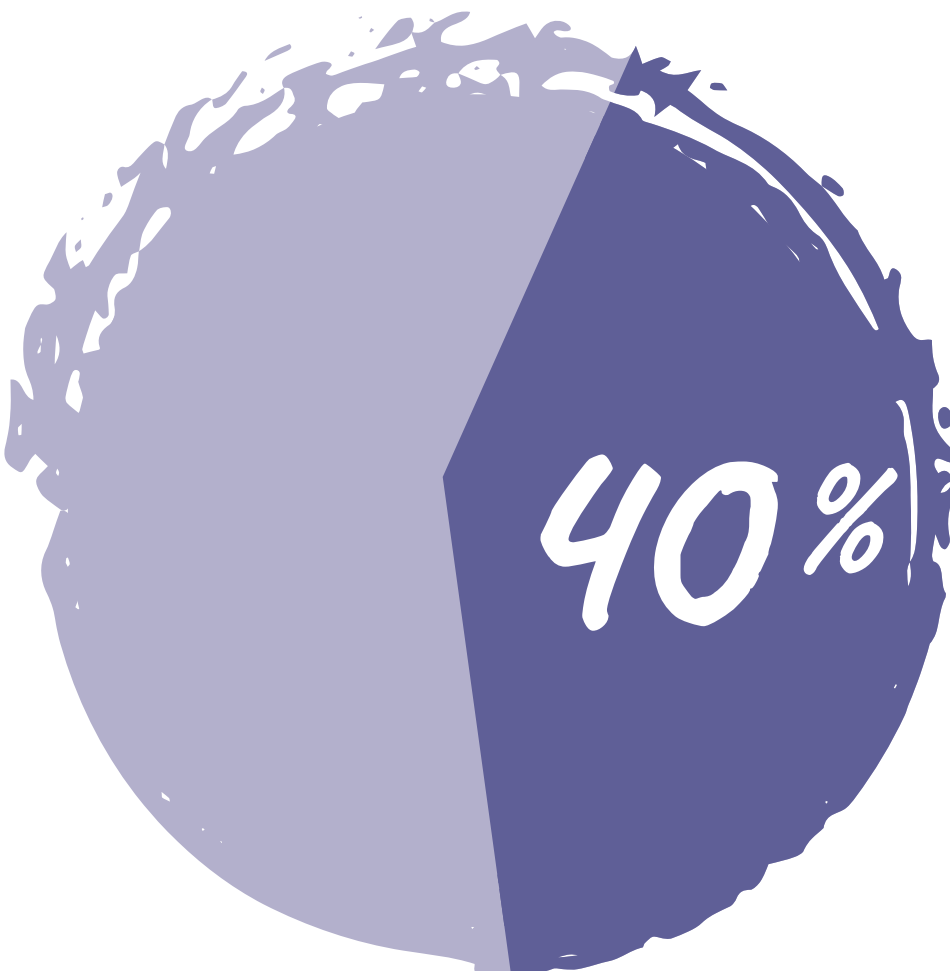
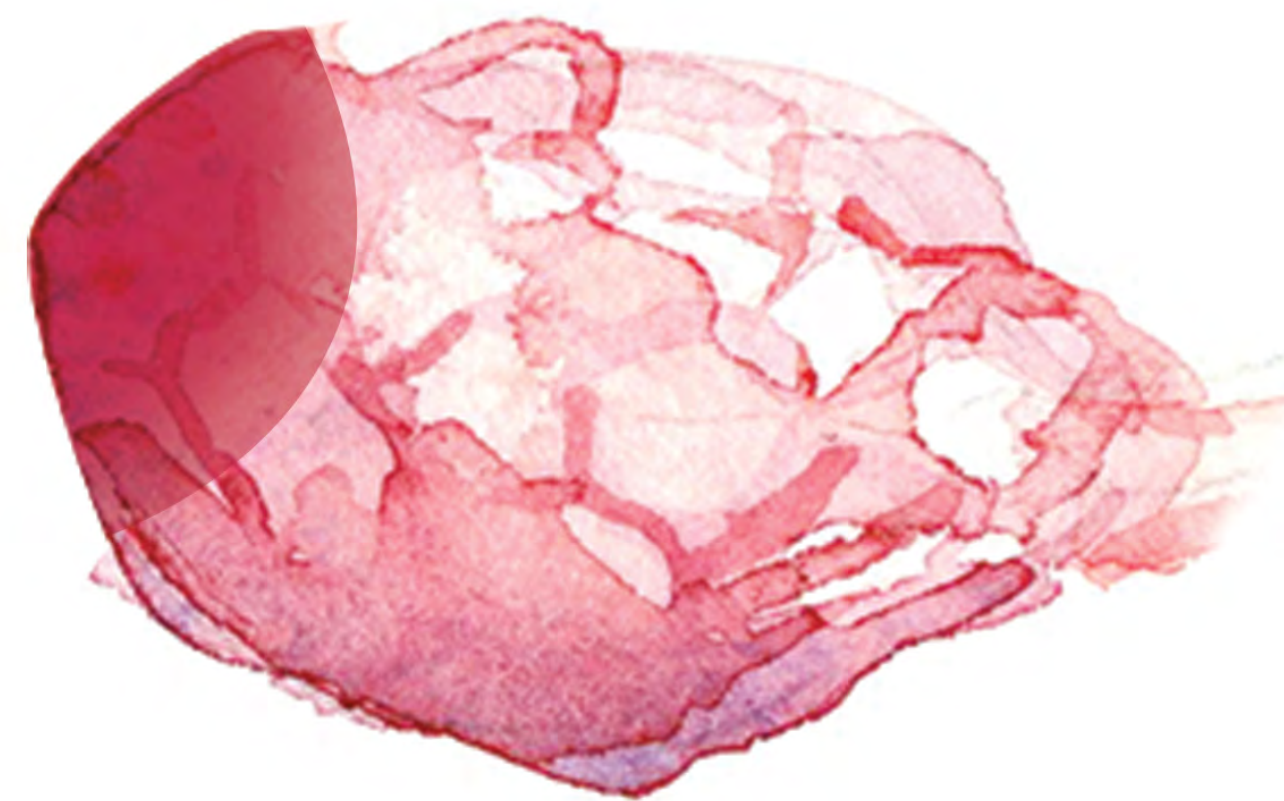
PELVIC INFLAMMATORY DISEASE



DIAGNOSIS: TUBAL, PELVIC, AND UTERINE FACTORS

Endometriosis

Endometriosis occurs when tissue that lines the uterus (endometrium tissue) grows outside the uterus.¹³ It results when menstrual bleeding flows backward through the fallopian tubes.¹¹ It can block the fallopian tubes and prevent the sperm from reaching and fertilizing the egg.¹¹



ALMOST 40% OF
WOMEN WITH
INFERTILITY HAVE
ENDOMETRIOSIS⁹

CAUSES

The cause is not clear, but a leading theory is retrograde menstruation. Researchers also think that it could be genetic, since female family members sometimes share the condition.

SYMPTOMS

- Soreness during intercourse
- Painful, heavy menstrual periods

Some women may not exhibit any symptoms at all.

TREATMENT: SURGERY & OVULATION INDUCTION¹⁴

Surgery

Surgery may be necessary to:

- Remove uterine fibroids, polyps, or scarring
- Remove a uterine septum
- Repair or remove fallopian tubes (may necessitate the use of IVF)
- Debulk endometriosis

Ovulation induction (OI)

OI is the process of administering drugs to help induce ovulation. There are 3 phases¹¹:



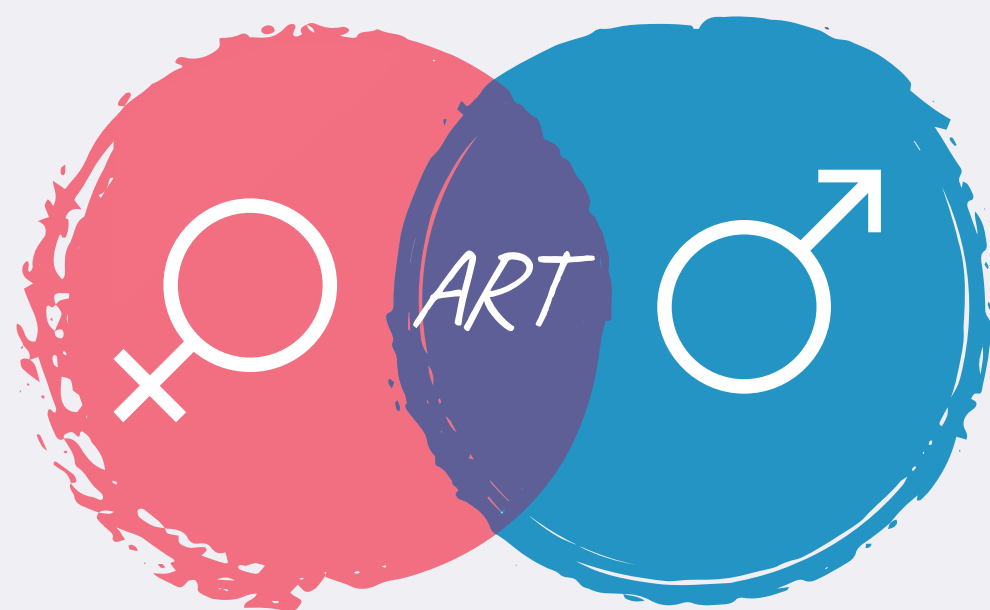
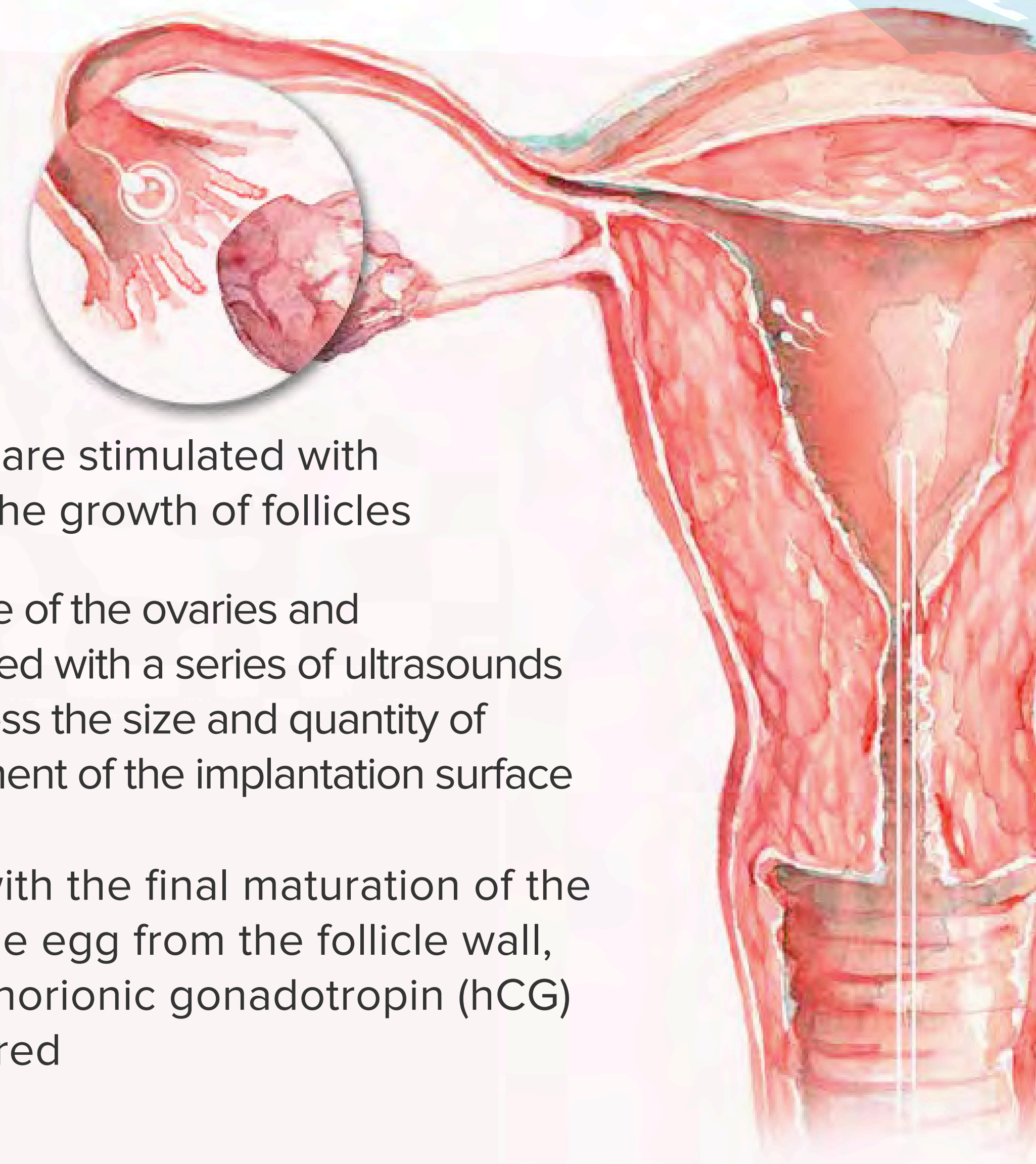
Stimulation: The ovaries are stimulated with medication to promote the growth of follicles



Monitoring: The response of the ovaries and endometrium are monitored with a series of ultrasounds and/or blood tests to assess the size and quantity of follicles and the development of the implantation surface



Egg release: To assist with the final maturation of the egg and loosening of the egg from the follicle wall, an injection of human chorionic gonadotropin (hCG) is sometimes administered



Assisted reproductive technologies (ART) treat both female and male infertility issues, including:

- In vitro fertilization (IVF)
- Third-party-assisted ART

LEARN MORE
ABOUT ART
PROCEDURES



TREATMENT: INTRAUTERINE INSEMINATION (IUI)

IUI is a medical procedure in which sperm is placed into the woman's uterus to facilitate fertilization.

Insemination can happen in 2 ways:



**FRESH
SPERM**



**FROZEN
SPERM**

Sperm collection¹¹

If your partner's sperm is used:

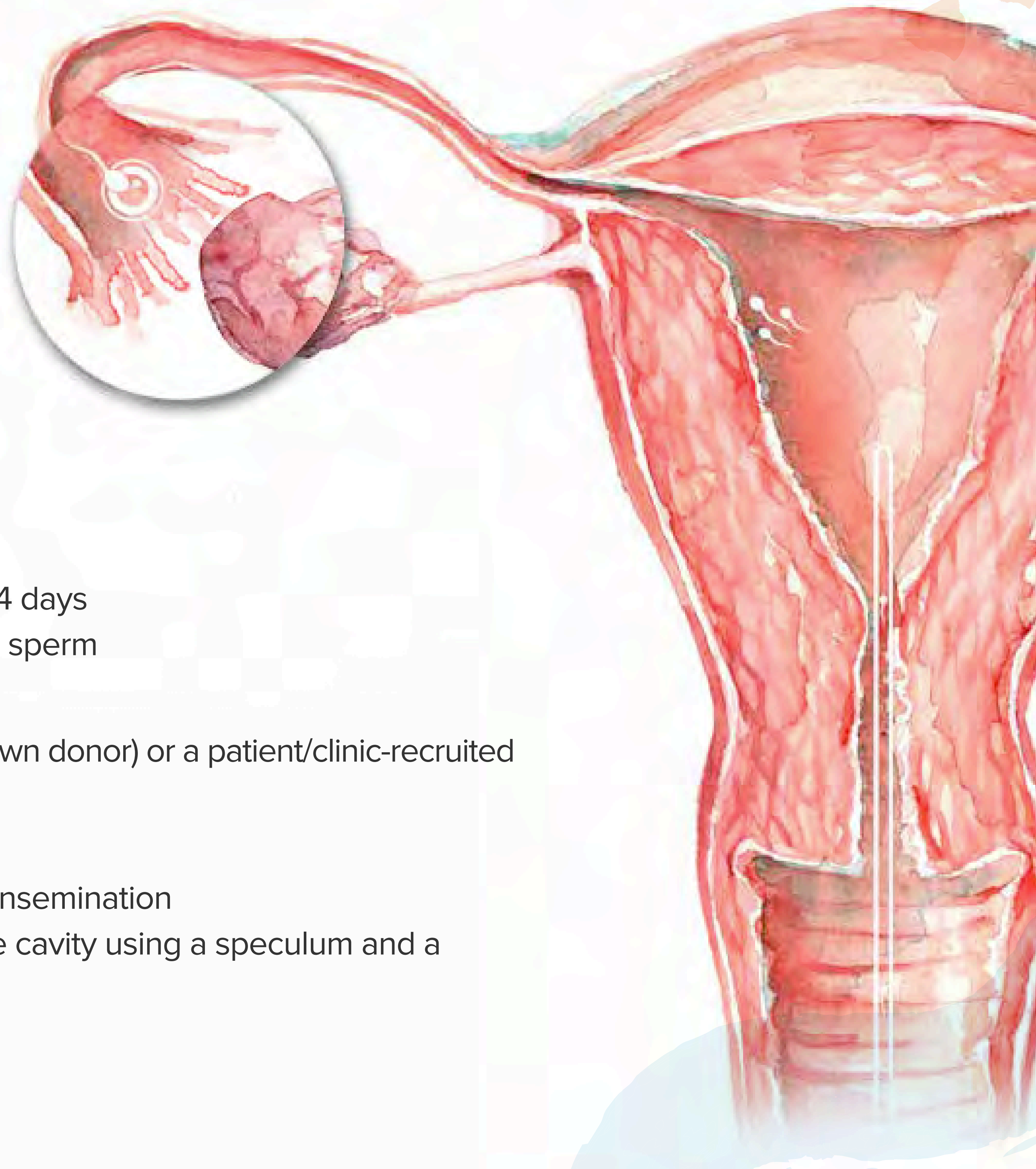
- An optimal sample can be collected after abstaining for 2 to 4 days
- Sample is analyzed and processed to concentrate the motile sperm

If banked sperm is used:

- Sperm is obtained from either a recipient-recruited donor (known donor) or a patient/clinic-recruited donor (anonymous donor)

Once sperm is collected:

- A concentrated, washed sample of motile sperm is used for insemination
- The final sperm preparation is gently inserted into the uterine cavity using a speculum and a disposable catheter to bypass the cervix



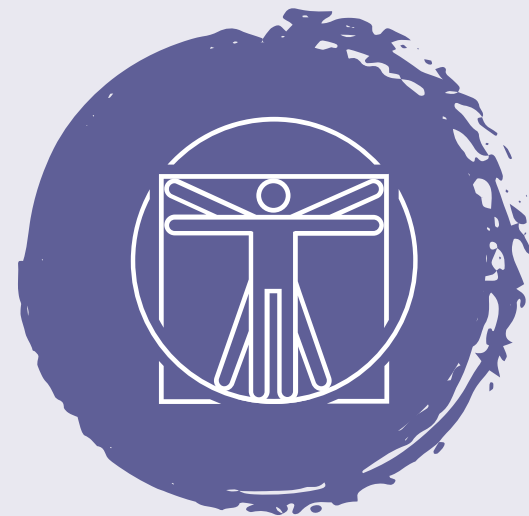
MALE FACTORS

There are a number of biological issues that can cause infertility in men.



SPERM ISSUES

- **Sperm count** (number of sperm)
- **Motility** (ability to move, quality of movement, forward progression)
- **Morphology** (size and shape)



PHYSICAL ISSUES

- **Erectile dysfunction:** inability to get or sustain an erection
- **Undescended testis:** testis has not reached its normal position in the scrotum, causing it to function abnormally and potentially not produce sperm
- **Retrograde ejaculation:** ejaculate containing the sperm flows backward into the bladder instead of leaving the penis
- **Scrotal varicocele:** similar to varicose veins in the leg, this common testicular condition may hinder sperm production and lower sperm quality



OTHER FACTORS⁶

- **Environmental factors** (such as heat, radiation, or chemicals)
- **Medications**



EVALUATION: SEMEN ANALYSIS

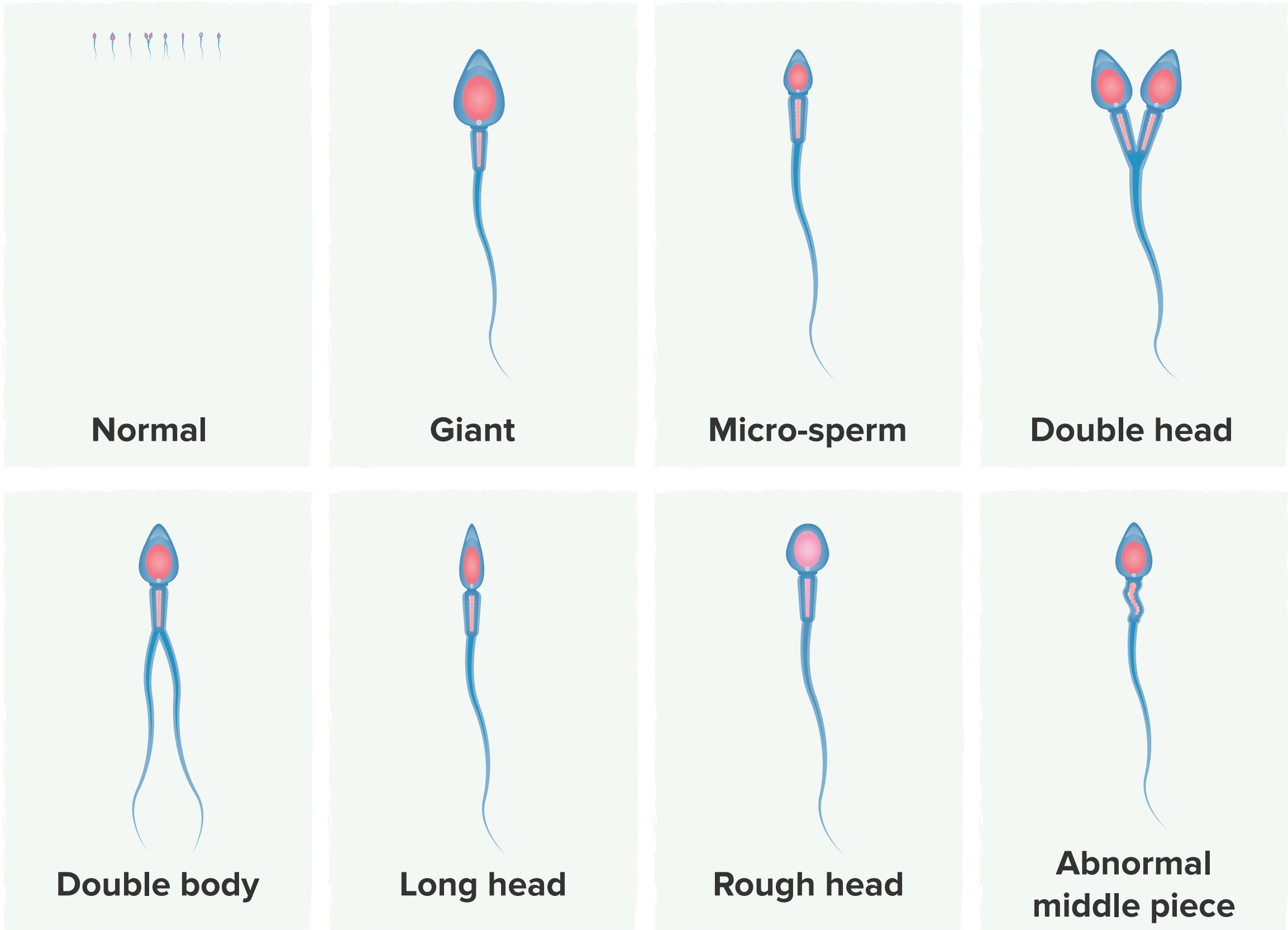
The cornerstone of male evaluation is semen analysis.¹⁵ A semen analysis includes an evaluation of the volume, concentration, number, motility, and morphology.

WHO lower reference limits (95% CI)

Semen volume (amount):	>1.5 mL
Sperm concentration:	>15 million/mL
Total sperm number:	>39 million sperm/ejaculate
Total motility (rapid, slow, or nonprogressive movement):	>40%
Progressive motility (purposeful forward movement):	>32%
Normal morphology (structure):	>4%

WHO = WORLD HEALTH ORGANIZATION.

Sperm morphology



ADDITIONAL SEMEN TESTS THAT MALES MIGHT UNDERGO¹⁵

- Testing for antibodies that bind to sperm
- Semen culture to check for infections
- Biochemical tests of sperm function
- Sperm deoxyribonucleic acid (DNA) fragmentation assay to determine the percentage of DNA fragmentation

TREATMENT¹⁶

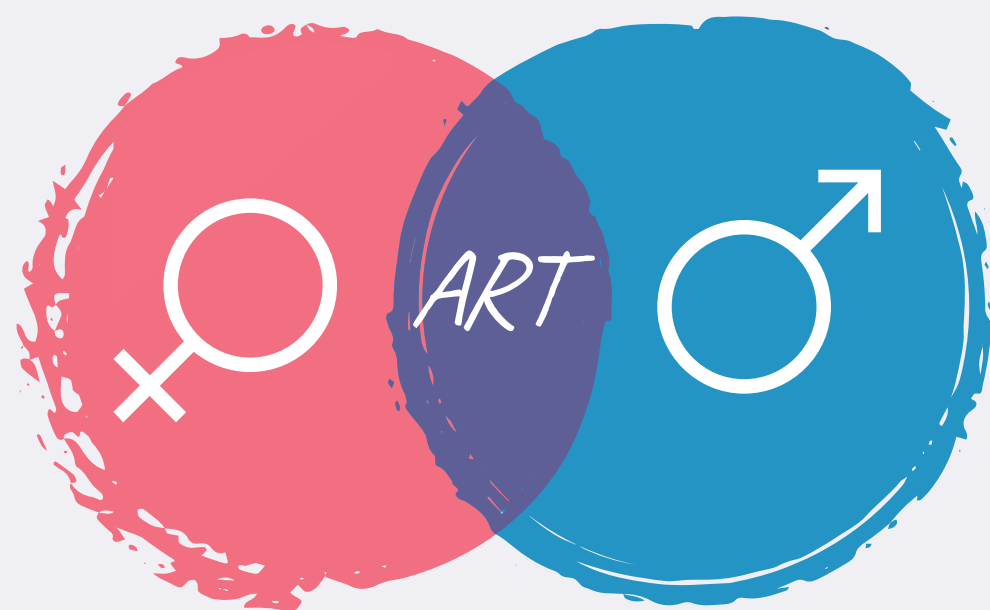
Surgery

Surgery may be necessary to:

- Repair blockages of male reproductive tract
- Repair a varicocele
- Percutaneous epididymal sperm aspiration (PESA), testicular sperm aspiration (TESA), testicular sperm extraction (TESE), or microepididymal sperm aspiration (MESA)

Medications

Medications are used to help with hormone imbalances and erectile dysfunction. Hormone injections may also be used to increase testosterone and sperm.



Assisted reproductive technologies (ART) treat both female and male infertility issues, including:

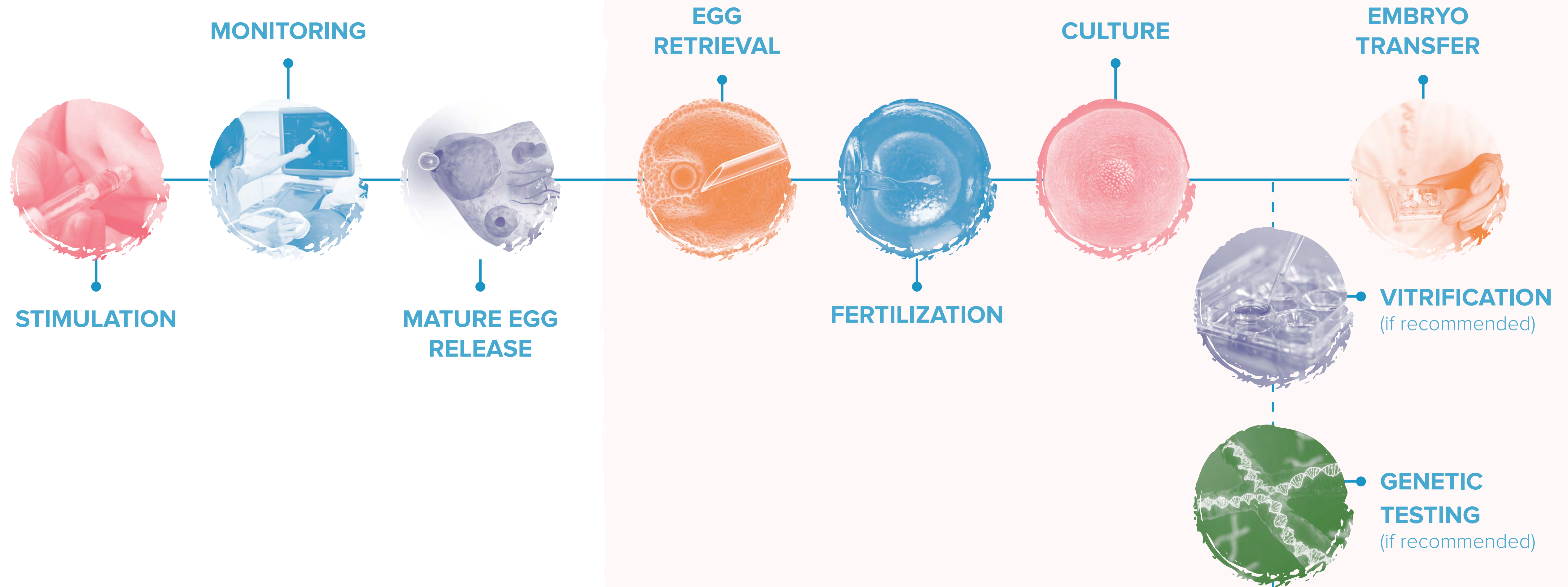
- In vitro fertilization (IVF)
- Third-party-assisted ART

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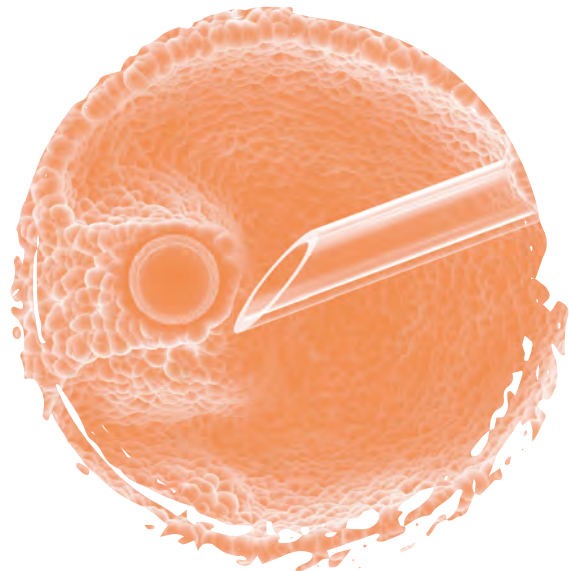
IN VITRO FERTILIZATION (IVF)

Another treatment option is IVF, which occurs after the 3 phases of ovulation induction:

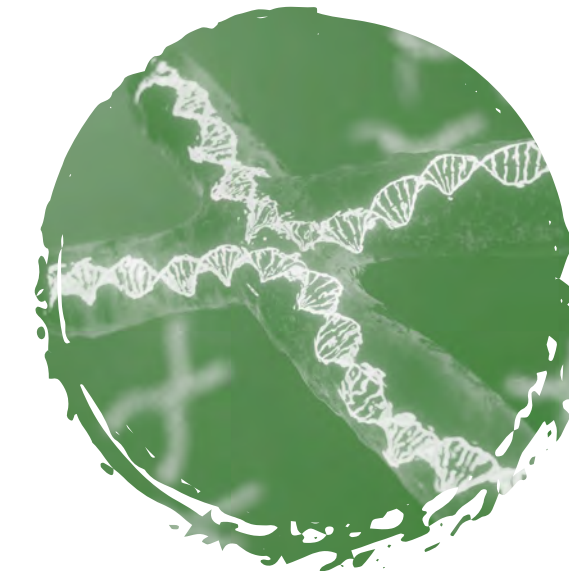


IN VITRO FERTILIZATION (IVF)

Another treatment option is IVF. Fertilization through IVF involves¹⁷:



Egg retrieval: Upon inducing ovulation, eggs are retrieved from the ovaries. This is performed roughly a day and a half after hCG is administered under ultrasound guidance



Genetic testing: Preimplantation genetic testing for aneuploidies (PGT-A) or preimplantation genetic testing for monogenic disorders (PGT-M) may be done to identify genetic defects within embryos prior to implantation. You may be referred to a genetic counselor if the testing is recommended

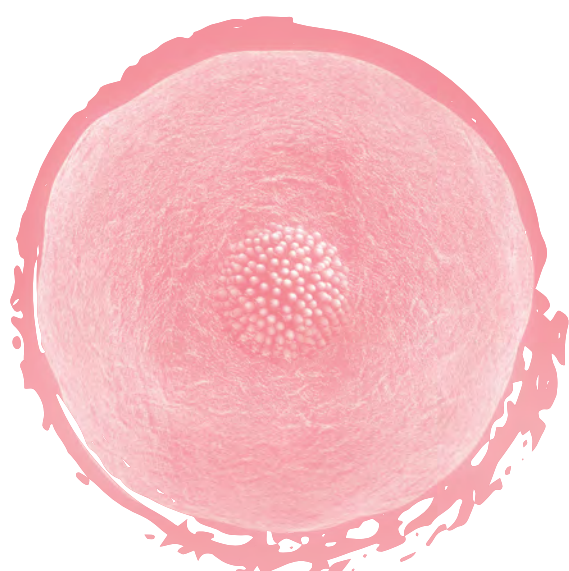


Fertilization:

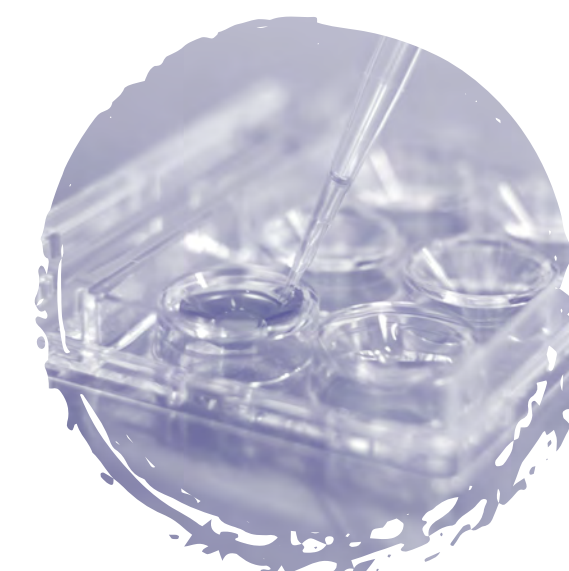
- **Insemination:** The sperm sample is washed and concentrated, then added to the eggs
- **Intracytoplasmic sperm injection (ICSI):** A single sperm is injected directly into each egg



Embryo transfer: The embryo chosen for transfer is loaded into a transfer catheter which is passed through the cervix into the uterus, and gently released. Generally, only 1 embryo is transferred; in exceptional cases 2 are transferred



Culture: Embryos are grown in a lab for about 3 to 6 days, but can vary depending on the lab



Vitrification: Vitrification is used to freeze and store embryos until they are ready to use. This is the same technology used to freeze eggs

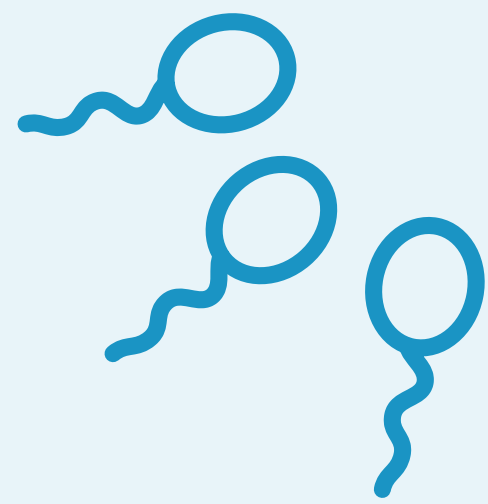
THIRD-PARTY REPRODUCTION

Third-party reproduction refers to the use of eggs, sperm, or embryos donated by a third person (donor) to enable an individual or couple to become parents.¹⁸ These include:



DONOR EGG (fresh or frozen)

Donor eggs, either obtained from an egg bank or a fresh donor cycle, can provide options for same-sex male couples or when a woman's own eggs have not resulted in a successful pregnancy.



DONOR SPERM

Donor sperm provides options for single women, same-sex female couples, and couples with severe male-factor infertility.



DONOR EMBRYO

Excess embryos can be made available for donation to help others become parents.



GESTATIONAL CARRIER

A gestational carrier is an arrangement where a woman carries and delivers a child for another couple or person (intended parent).¹⁸



THE TWO-WEEK WAIT

Regardless of the ART treatment option chosen, after transfer comes a waiting period before a pregnancy test can be taken, known as the “two-week wait.”¹⁹ This can be a difficult time, filled with hope but also anxiety.



PROGESTERONE

Progesterone may be prescribed during the two-week wait to help thicken the uterine lining and help the embryo attach and grow. This may be given as an injection, a capsule, or a gel inserted into the vagina.²⁰



PREGNANCY TESTING AND CARE¹⁹

A pregnancy test will be conducted 9 to 12 days after transfer. If the result is positive, the pregnancy will be closely monitored with scans and bloodwork at the fertility clinic. Care is typically transferred to an obstetrician around 8 to 10 weeks into pregnancy.



EMD SERONO SAVINGS PROGRAMS

FertilitySavings.com provides financial support services to help make medications more affordable, including:



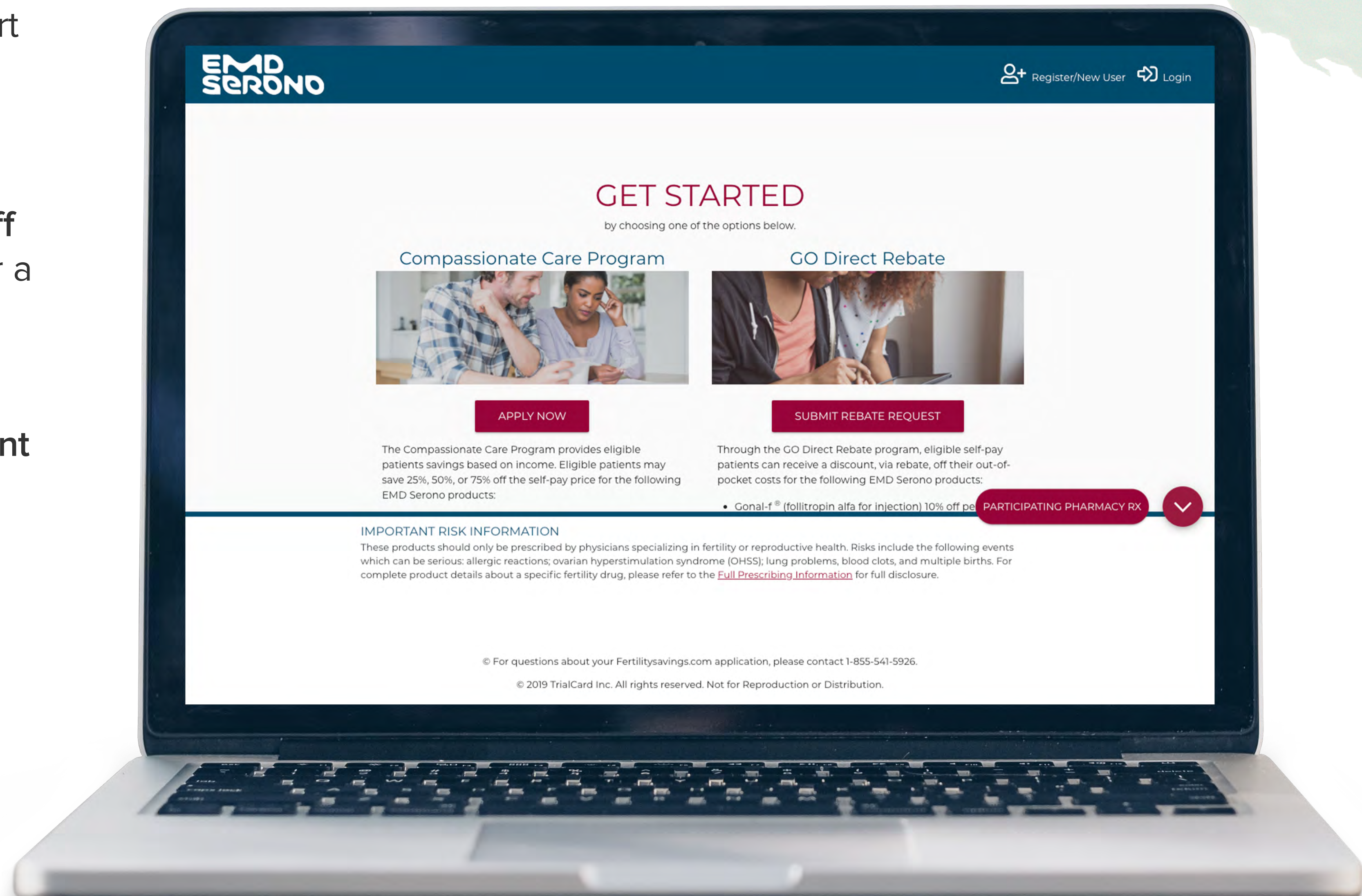
Savings of 25%, 50%, or 75% off the self-pay medication price, or a 10% rebate, for eligible patients



Out-of-pocket cost reimbursement for qualifying medications



Special programs for eligible veterans and qualifying oncology patients



More information is available at **FertilitySavings.com**



FERTILITY.COM PATIENT SUPPORT WEBSITE

Fertility.com is a customizable web experience that provides emotional support, treatment information, and financial considerations for every stage of the fertility journey.



Videos of real patients sharing real experiences



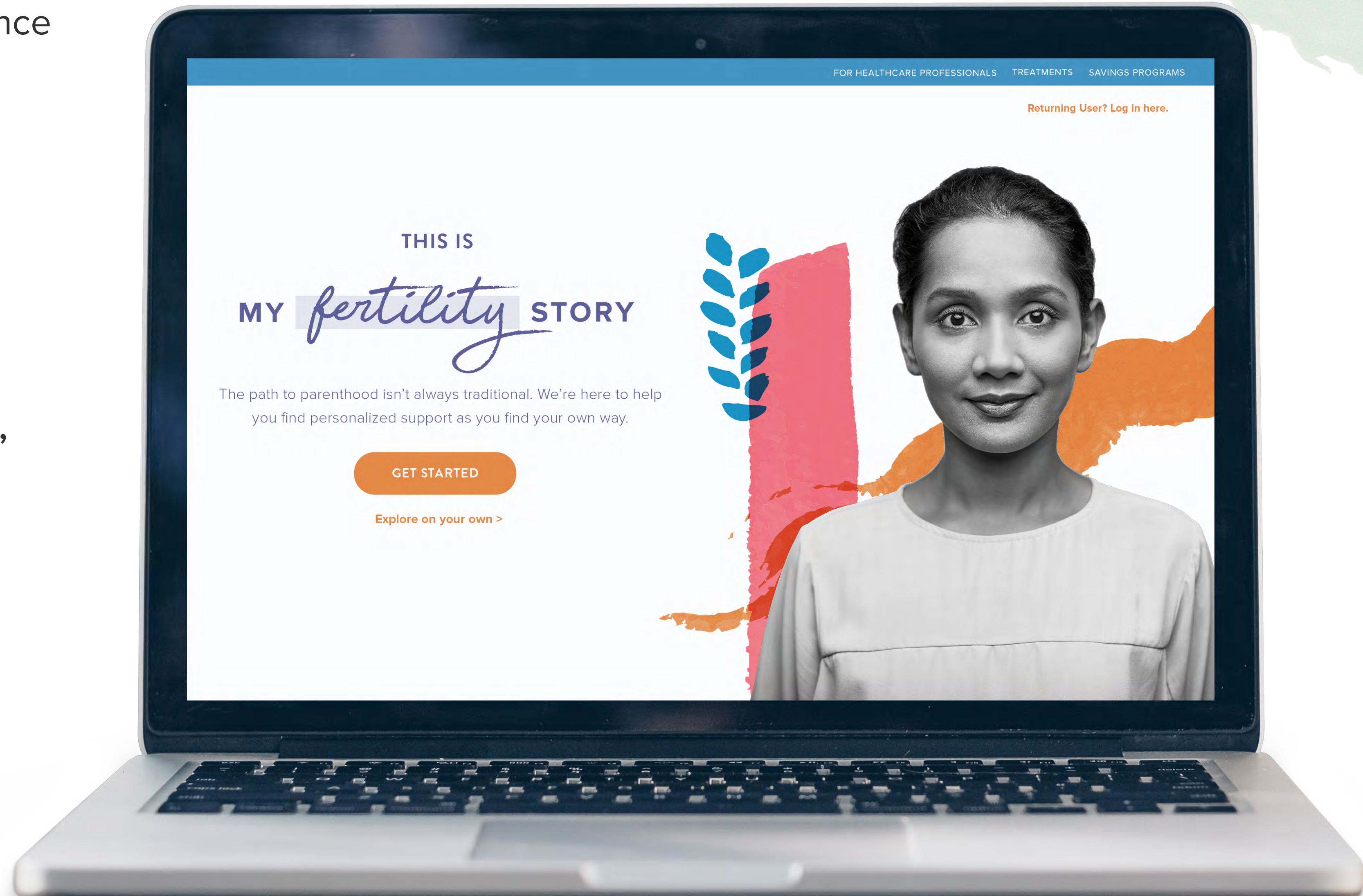
What to expect during treatment, including cycle definitions, timelines, and medications used



Financial information and tips to help treatment costs



Where to find support during treatment



More information is available at **Fertility.com**



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THANK YOU

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serono**

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