Demystifying infertility

Fundamentals, tests, treatment, medications

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Demystifying infertility

This section provides an overview of infertility, including the fundamentals, medications, testing, treatment options, and additional information. Select any of the topics for more information.

- Fundamentals
- Diagnostic testing
- Treatment options
- Medications
- Additional information

Fundamentals

Select any of the topics for more information.

- Fundamental questions
- Female anatomy
- Male anatomy
- Reproductive cycle
- Causes of infertility

Fundamental questions

What is infertility?

Infertility is defined as not being able to become pregnant after regular unprotected (without contraception, like condoms or oral birth control) sexual intercourse.[1,2,3]

- 1 year if < age 34
- 6 months if > age 35

Whom does infertility affect?

Infertility can affect women or men individually or as a couple with 1 of 7 couples having trouble getting pregnant during their childbearing years.[1] About 10-15% of couples have a medical condition that interferes with conception.[2,3]

Causes:

- Female related 30-40%[2,3]
- Male related 20%[2,4,5]
- Both 30-40%[2,3,5]
- Unknown 10%[1,3]

Does age matter?

Women

Most fertile in their 20's to early 30's

- Age 30 - Healthy women have a 20% chance of becoming pregnant each month
- Age 40 - Healthy women have a 5% chance of becoming pregnant each month

The decline of female fertility happens because both the quality and the quantity of eggs gradually decline as a woman ages.[6]

Men

There is no maximum age at which a man cannot father a child. Sperm quality deteriorates as men get older but it is usually not a problem until around age 60.[6]

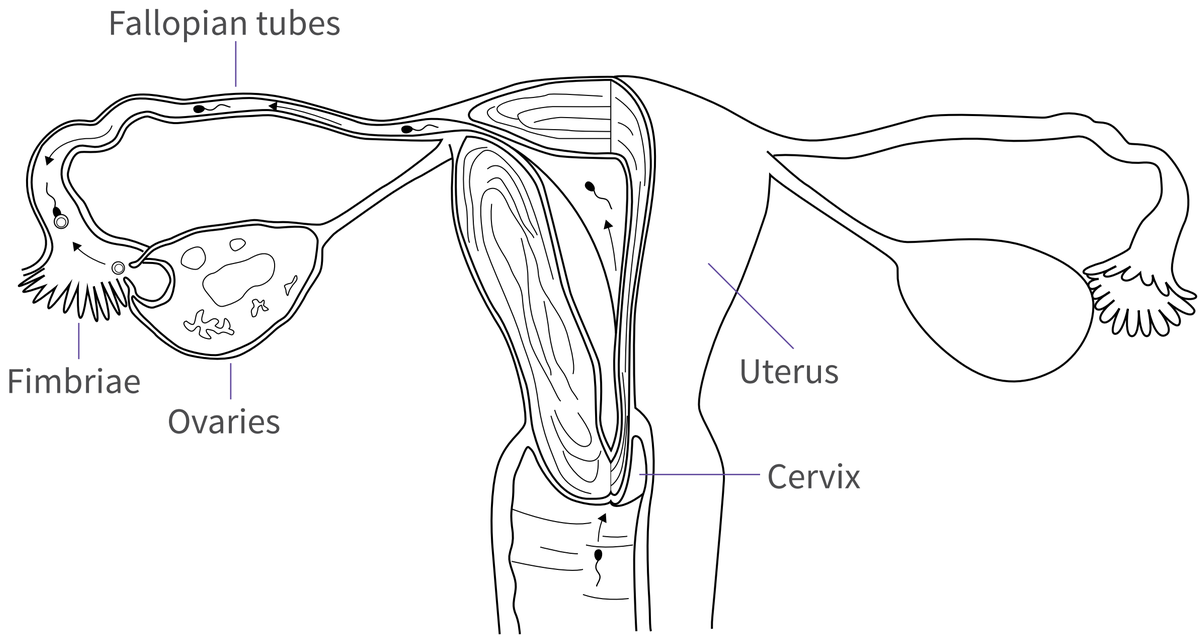
Additional resources

- Booklet: Infertility: An Overview
- Age and Fertility - A Guide for Patients

⇢ Female anatomy

Female anatomy

This diagram shows the normal shape of the vagina, uterine cavity and fallopian tubes as well as the path of the egg and sperm.



Cervix: the narrow, lower part of the uterus that opens into the vagina, where cervical mucus is secreted.[3] The sperm swim through mucus before entering the uterus and then the fallopian tubes.[1]

Fallopian tubes: pathways that connect the ovaries to the uterus. Egg and sperm normally fertilize in the fallopian tube.[1]

Fimbriae: finger-like tissues at the ends of the fallopian tubes, not directly attached to the ovaries, that help direct the oocyte/egg by sweeping it up and into the fallopian tube.[3]

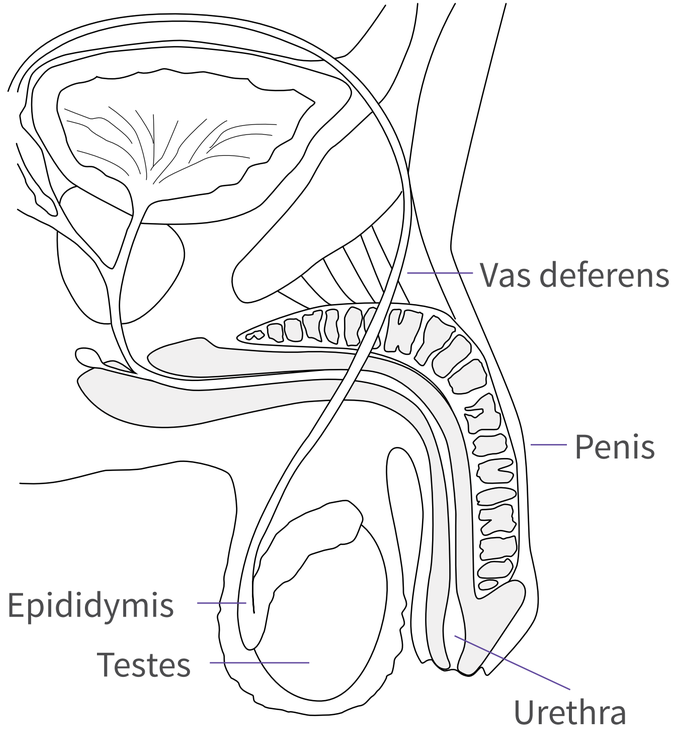
Ovaries: organs responsible for producing reproductive hormones and releasing eggs/oocytes.[7] Each follicle is a fluid-filled sac in the ovary where an egg may grow.[3]

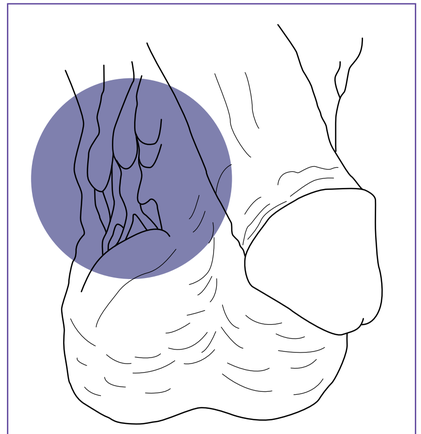
Uterus: hollow, muscular organ where a fertilized egg (embryo) can implant itself and grow during pregnancy.[1,6]

⇢ Male anatomy

Male anatomy

This diagram shows the male reproductive system. Note where a group of enlarged veins, called a varicocele, may form. Varicoceles can affect male fertility.[3,4]





Where varicoceles may form

Epididymis: location in the testicle where sperm mature and remain stored until moving into the vas deferens.[3]

Penis: is a male reproductive organ, through which semen exits during ejaculation.[9]

Testes: produce sperm and the male hormone testosterone.[3]

Urethra: a narrow, tube like structure through which urine passes on its way from the bladder to the outside of the body in both sexes. In males, it is also a passageway for sperm.[8]

Vas deferens: moves, stores and assists in the maturation of sperm.[3]

→ Reproductive cycle

Reproductive cycle

Select any of the topics for more information.

- Diagram of the reproductive cycle
- Menstruation
- Preovulation or follicular phase
- Ovulation
- Postovulation

Diagram of the reproductive cycle

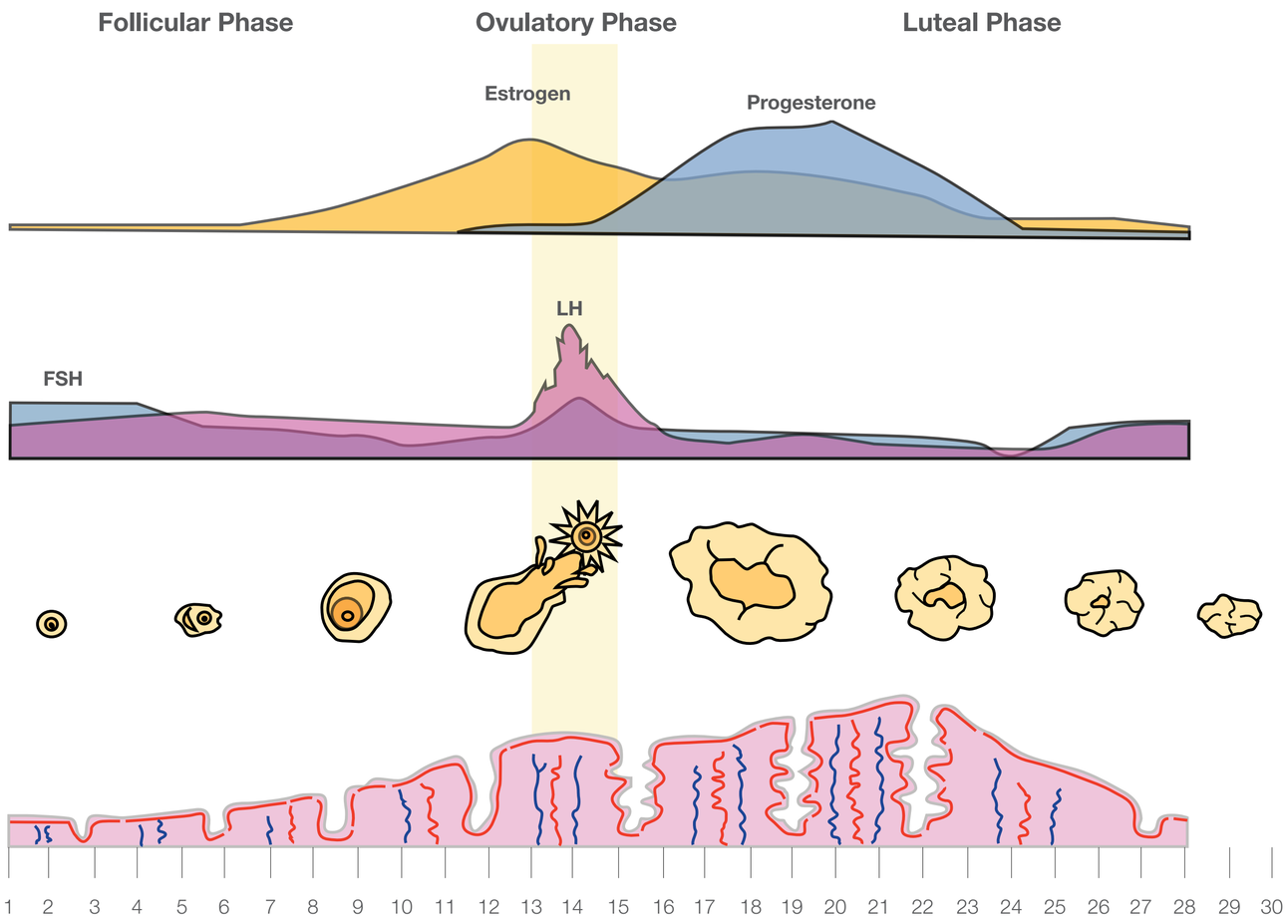


Figure 1:
Estrogen (estradiol) and Progesterone

Figure 2:
LH and FSH

Figure 3:
Ovarian Cycle

Figure 4:
Endometrial Cycle

⇢ Menstruation

Menstruation

Menstrual phase

- Menstruation is the monthly shedding of the uterine lining, also called menses.[1,3,6]

The first day of menses marks the first day of a new cycle. The menstrual phase lasts for roughly the first five days of the cycle.[3]

What happens in the ovaries

- During the menstrual phase, a small cohort, or group, of small follicles begin to grow in each ovary.
- Each follicle is a fluid-filled sac in the ovary where an egg may grow.[1,3,6]

What happens in the uterus

- Menstruation occurs because of declining levels of estrogen and progesterone.[3,6]
- Menstrual flow from the uterus consists of approximately 30 mL of blood, tissue, fluid, mucus and epithelial cells that line the uterus.[3] Volume greater than 80 mL is considered abnormal and should be evaluated. The menstrual flow passes from the uterine cavity to the cervix and through the vagina.[3]

⇢ Preovulation or follicular phase

Preovulation or follicular phase

The preovulation or follicular phase of the reproductive cycle is the time between the start of menses (shedding of the uterine lining) and ovulation (release of an egg). It is called the follicular phase because the follicles are growing during this phase.[3,6] The length of this phase of the reproductive cycle can vary more than the lengths of the ovulation and postovulation phases. When reproductive cycles are shorter or longer than 28 days, it is usually caused by variations during the follicular phase.[3]

What happens in the ovaries

- The pituitary is a gland in the brain that creates and releases hormones to control growth in the body. It releases follicle-stimulating hormone (FSH) that activates growth and estrogen production in a group of about 20 small follicles in the ovaries.[3,6]
- Around the sixth day of the reproductive cycle, one follicle in one ovary has grown larger than all the others. It becomes the dominant, or main, follicle. Increasing amounts of estrogen from the dominant follicle decreases the release of FSH. This causes the other less-developed follicles to stop growing.[3]
- The dominant follicle continues to grow and increase the amount of estrogen it makes.[3,6]

What happens in the uterus

- Growing follicles release estrogens into the blood. This stimulates the regrowth of the uterine lining.[3,6]
- The lining will continue to grow and thicken during this preovulatory/ follicular phase in anticipation of implantation.[3]

⇢ Ovulation

Ovulation

Ovulation refers to the process in which a full-grown follicle opens to release the egg (oocyte). The egg will travel through the fallopian tube to the uterus.

What occurs during ovulation[3,6]

- Ovulation usually occurs on day 14 in a 28-day cycle.
- High levels of estrogen during the last part of the preovulation phase cause the pituitary gland to produce more luteinizing hormone (LH).
- The LH surge triggers the full-grown main follicle to burst and release the egg (ovulation).
- The ovulated egg and surrounding cells are swept into the fallopian tube by the fimbriae.
- After the egg is released, the follicle collapses and a blood clot forms within it.
- The clot is absorbed by the remaining follicular cells. This forms the corpus luteum.

⇢ Postovulation

Postovulation

The postovulation or luteal phase of the reproductive cycle typically lasts for 14 days — from day 15 to day 28 — in a 28-day cycle. It represents the time between ovulation and the beginning of the next menses.[3,6]

- The *corpus luteum* will grow and release progesterone and some estrogen. Progesterone readies the uterus for a fertilized egg. It is present throughout pregnancy.
- If fertilization does not occur, the *corpus luteum* will shrink and break down within two weeks. The lack of progesterone then induces menses.[3]
- If fertilization and implantation of an embryo do occur, the *corpus luteum* will remain. It will continue to produce progesterone to support pregnancy.[3,6]
- About eight to 12 days after fertilization, an embryo will produce the hormone human chorionic gonadotropin (hCG). When hCG is found in maternal blood or urine, it is a sign of pregnancy.
- As the pregnancy progresses, the placenta begins to secrete estrogens and progesterone to support the pregnancy.[3]

What happens in the uterus

- Progesterone and estrogens produced by the *corpus luteum* support growth of the uterine lining.[3]
- These changes occur about one week after ovulation. This is about the time that a growing embryo reaches the uterus in a natural cycle.[3]

⇢ Causes of infertility

Causes of infertility

Female infertility

Female infertility can be related to age, ovulatory or hormonal problems, pelvic health issues, genetics, unexplained circumstances, lifestyle, disease or environment.[2,3,10]

- **Age** - Refers to a woman's chronological age as well as her "ovary age" or ovarian reserve. This is the ability of the ovary to produce eggs that can be fertilized. If the ovaries have aged faster than a woman's chronological age, the eggs may not be able to be fertilized. Women may have reduced ovarian reserve due to smoking, family history of premature menopause, and prior ovarian surgery. Young women may have diminished ovarian reserve even if they have no known risk factors.[6]
- **Delays in childbearing** - Women are choosing to have children later in life. In fact, 20% of women are waiting until after the age of 35 to have a child.[3,11] The combination of female fertility peaking in the mid-20s and women delaying motherhood might result in lower fertility rates for women trying to become pregnant after fertility declines more significantly around the ages of 33 to 35.[2,3,6]
- **Hormone imbalance** - Too much or not enough of the hormones involved in the normal reproductive cycle, especially during ovulation, can cause infertility. Hormones not released at the right time also affect fertility.[2,6,12]
- **Structural and functional issues** - Changes of the ovaries, fallopian tubes, uterine cavity or cervix may also be a factor in infertility.[2,3,12]
- **Genetics** - Abnormal genetic patterns, usually an inherited trait, can affect both structure and function of the reproductive system.[2,3,12]
- **Unexplained infertility** - Doesn't mean that there is no cause for the infertility. It is more likely that there is currently no technology available to understand the reason behind a specific diagnosis of infertility.[2,3]
- **Unhealthy lifestyle** - Factors such as smoking, heavy alcohol consumption, unhealthy weight such as being very thin or obese as well as use of recreational drugs can also affect fertility.[3,10,12,13]
- **Sexually transmitted disease (STD)** - Some STD's can cause pelvic inflammatory disease. This causes inflammation of reproductive organs and may result in infertility.[3,10,12]
- **Environmental and industrial toxins** - Exposure to toxins may also affect fertility.[3,10,12]

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Causes of infertility

Male infertility

Male infertility can also be related to physical issues, hormonal abnormalities, genetic causes and environmental and lifestyle factors.

- Many men are affected by physical defects that may be present at birth. Common abnormalities include[4,5,14]:
  - **Physical defects**
    - Undescended testicles: a condition where one or both of the testicles do not move down into the scrotum causing abnormalities of sperm production.[3]
    - Hypospadias: a defect present at birth where the opening of the urethra is on the underside of the penis instead of the end causing issues with ejaculation of sperm.[3]
- **Hormonal abnormalities** - Affect sperm creation as well as growth of sex organs and their cells.[4,5]
- **Lifestyle risks** - Illness, recreational drug use, smoking or work-related and environmental toxins can also affect fertility.[3,4,5]
- **Genetics** - Genetic abnormalities can cause infertility by affecting sperm production and transport.[5]

Additional resources

- Fact Sheet: Defining Infertility
- Fact Sheet: Will Toxins in the Environment Affect My Ability to Have Children?

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Diagnostic testing

Diagnostic testing

Testing helps find the cause(s) of infertility. According to the American Society for Reproductive Medicine (ASRM), the main goal is to use the “least invasive methods for detection of the most common causes of infertility.”[2,12]

- Both men and women can go through an infertility evaluation. Success can depend on knowing health histories from all people involved in the fertility work up.
- When going for testing, bring copies of any medical reports from earlier treatments, tests or surgeries to your fertility doctor.
- Gather a detailed family medical history. This includes known inherited diseases, birth defects, reproductive health problems or infertility.
- Speak with your doctor for information about the risks and benefits of available treatments.

Select any of the topics on the right for more information.

- Blood tests
- Ovulation testing
- Ultrasound screening
- Sonohysterogram or saline infusion sonohysterography (SHG)
- Hysterosalpingogram (HSG)
- Hysteroscopy
- Laparoscopy
- Endometrial biopsy
- Male fertility testing

Blood tests

Anti-Mullerian hormone (AMH) testing

A blood test for AMH can measure ovarian reserve.[2,3,14,15]

- AMH is produced directly by the ovarian follicles. The levels are related to the number of antral follicles present in the ovaries.[2,3,14,15]
- AMH levels do not change significantly throughout the menstrual cycle and generally decrease with age.[14]
- Lower AMH levels have been associated with poor responses to ovarian stimulation, poor embryo quality and poor pregnancy outcomes in IVF.[12]

Day 3 levels of FSH and estradiol hormones

Follicle-stimulating hormone (FSH) and estradiol levels in the blood on day 3 of the reproductive cycle may be used to check a woman's egg supply (ovarian reserve) or see how well the ovaries are working (ovarian function). Elevated FSH can indicate ovarian failure. Fertility centers can do this test on either day 2, day 3 or day 4 of the reproductive cycle, so you will need to check with your center for specific instructions.[2,6]

- The FSH level measurement is a simple and commonly used test of how well the ovaries can produce eggs that can be fertilized.
- Women with higher levels of FSH or estradiol levels on day 3 of the reproductive cycle may have lower pregnancy rates even with fertility treatment, including ovulation induction and assisted reproductive technologies such as in vitro fertilization (IVF).[2,6]

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Blood tests

Clomiphene citrate challenge test

This test typically evaluates ovarian reserve. It usually takes about 10 days, but each doctor may follow a different schedule. Here is a sample schedule[3,8]:

- The patient takes an initial blood test on day 3 of the reproductive cycle.[2,6]
- The patient starts taking clomiphene citrate. This stimulates ovulatory hormones and helps the doctor get a better picture of how well the ovaries are working.[2,6]
- The patient returns for additional blood tests on day 10.[2,6]
- Test results show how the ovaries are working and how they may respond to fertility medications.[2,6]
- Speak with your physician for information about the risks and benefits of available treatments.

Other hormone testing

Other hormone levels may be tested during specific times of a woman's reproductive cycle. Abnormal levels of these hormones may prevent ovulation and potential pregnancy.

- Luteinizing hormone (LH): Working together with FSH, LH stimulates production of estrogens and progesterone and the growth of eggs.[3]
- Prolactin: This hormone stimulates milk production. If it is too high, it may prevent ovulation. Treatment is usually an oral medication.[3] For more information about prolactin, click on the additional resource at right to go to the ASRM fact sheet.
- Thyroid hormones: These hormones regulate growth and development.
- Androgens: Natural steroid hormones such as testosterone and dehydroepiandrosterone (DHEA) sulfate are common examples.[3,4]

Blood tests

Additional resources

- Hyperprolactinemia (High Prolactin Levels)
- Fact Sheet: Diagnostic Testing for Female Infertility
- Fact Sheet: Ovarian reserve (predicting fertility potential in women)

Prescribing Information

- clomiphene citrate

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⇢ Ovulation testing

Ovulation testing

LH testing/Urine ovulation predictor kit

An LH kit is an over-the-counter urine test to detect ovulation.[18]

- A patient tests her urine roughly two days before ovulation is expected (usually day 14 in a 28-day cycle).[18]
- When the test finds LH in the urine, it gives a positive result. This means that ovulation should begin in the next 12 to 36 hours.[18]

Monitoring cervical mucus

Another way to detect ovulation is through cervical mucus.[3,18]

- Cervical mucus is controlled by estrogens and progesterone. It usually changes close to ovulation.[3]
- Rising levels of estrogens cause the body to make large amounts of cervical mucus. As ovulation gets closer, the mucus becomes clear and very stretchy.[2,18]
- This type of mucus indicates the time of greatest fertility.[2,18]
- Checking cervical mucus is not typically part of routine fertility testing. However, it is used for patients who may have abnormalities associated with cervical mucus production, inflammation of the cervix or possible sperm mucus interaction where these results will clearly affect certain types of treatment plans.[2,3,12]

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Ovulation testing

Ultrasound

Vaginal ultrasound monitoring is another accurate way to see if ovulation is happening.[2,12,18]

- Ultrasound will allow your doctor to see and measure a developing follicle or follicles.[2,12,18]
- Follicular ultrasound monitoring becomes more important when fertility medications are prescribed.[2,12,18]
- If your doctor starts you on fertility medications, follow-up ultrasound appointments will help monitor how the medication is working and how many follicles are growing.
- Ultrasound is also important for patient safety while taking fertility medications to make sure ovaries do not overstimulate.[2]
  [See Ultrasound screening]

Luteal phase progesterone testing

A progesterone blood test drawn several days after suspected ovulation can also confirm if ovulation has occurred.[2,3,12]

- If ovulation has occurred, the corpus luteum will produce progesterone. This will show up in a blood test.[2,3]
- If ovulation has not happened, progesterone levels will be low.[2,3]

Additional resources

- Fact Sheet: Ovulation Detection
- Fact Sheet: Diagnostic Testing for Female Infertility
- Fact Sheet: Ovarian Reserve (Predicting Fertility Potential in Women)

⇢ Ultrasound screening

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Ultrasound screening

Baseline evaluation

Before starting stimulation medications, a baseline transvaginal ultrasound may be done on day 2 or day 3 of the reproductive cycle to see if ovaries have normal-sized follicles with no cysts. Menstrual flow does not interfere with the testing.[3,18,19] Antral follicles are small follicles (about 2 mm to 8 mm in diameter). They can be seen on an ultrasound.[12,14] An Antral Follicle Count (AFC) is the sum of all antral follicles seen in both ovaries.[12,14] Antral follicle counts help the doctor measure ovarian reserve.[2,3,14,15]

Stimulation monitoring

It is important to monitor the ovaries closely during stimulation. You will need to visit the doctor's office at scheduled times for blood tests and transvaginal ultrasounds during this period of treatment. The ultrasound helps the doctor see the size and number of follicles, monitor how fast the follicles are growing and identify any signs of ovulation.[6,18,19]

- You may be required to have daily ultrasound monitoring while taking your stimulation medications.
- Specially trained sonographers, nurses and doctors typically perform follicular ultrasound monitoring.

→ Sonohysterogram or saline infusion sonohysterography (SHG)

Sonohysterogram or saline infusion sonohysterography (SHG)

This test may also be referred to as a saline infusion ultrasound. It is used to evaluate the uterus for any problems that may be causing infertility.[2,3,19]

- An SHG is a simple transvaginal ultrasound test done while saline is slowly placed into the uterus.[3,19]
- The saline allows the doctor to see the inside of the uterus to look for structural abnormalities such as fibroids or uterine polyps. It does not allow the doctor to see the fallopian tubes.[3]
- During the test, the doctor will pass a small tube through the vagina and cervix into the uterine cavity.[3]

Additional resources

- Fact Sheet: Saline Infusion Sonohysterography (SHG)

→ Hysterosalpingogram (HSG)

Hysterosalpingogram (HSG)

An HSG is an X-ray exam. It is used to see the inside of the uterus and the fallopian tubes. X-rays are taken while a dye is slowly placed into the uterus. This allows the doctor to see the pathways from the uterus to the fallopian tubes.[1,2,19,20]

- This test helps the doctor see if the fallopian tubes are open.

Additional resources

- Fact Sheet: Hysterosalpingogram (HSG)

→ Hysteroscopy

Hysteroscopy

Hysteroscopy is a test for seeing inside the uterus to find any problems.[3]

- A hysteroscope is a thin, telescope-like instrument that is placed through the vagina and cervix and into the uterus. The procedure can help a doctor find or treat a problem in the uterus. It can also help confirm results of other tests, such as HSG.[3]
- Hysteroscopy is an outpatient procedure that can be done in a doctor's office or operating room in a hospital. Local, regional or general anesthesia may be used to help reduce or prevent pain. In some cases, little or no anesthesia is needed.[3,19,20]

Hysteroscopy may be used to look for a number of conditions:

- **Infertility:** Sometimes the cause of female infertility is related to a defect in the shape or size of the uterus. One example of this is a septate uterus. This is where a thin sheet of tissue divides the inside of the uterus into two sections. These kinds of problems may not appear on earlier diagnostic tests, but may be found with hysteroscopy.[3,19,20]
- **Miscarriage:** Examining the uterus might explain the reason for miscarriages.[3]
- **Adhesions:** Bands of scar tissue, or adhesions, can sometimes form inside the uterus. These adhesions may cause infertility and changes in menstrual flow.[3,19,20]
- **Asherman syndrome:** This is a rare condition that occurs when adhesions form inside the uterus. This usually happens after uterine surgery and, in most cases, occurs in women who have had several dilation and curettage (removal of tissue) operations. Pelvic infections may also lead to Asherman syndrome.[3]
- **Abnormal uterine bleeding:** A woman might have this condition if she has heavier or longer periods than usual, bleeds between periods or has any change in previously normal monthly cycle pattern. Hysteroscopy may help determine the causes of abnormal bleeding. It may also be used to take a biopsy (a small sample of tissue).[2,20]
- **Abnormal growths:** Sometimes benign (noncancerous) growths, such as polyps and fibroids, are found using hysteroscopy. The procedure might help a doctor biopsy a suspicious growth in the uterus to find out if it might be cancerous or precancerous.[2,20]

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Hysteroscopy

Operative hysteroscopy

Hysteroscopy may also be used to correct certain conditions.[3]

- Uterine adhesions, septums or fibroids often can be removed through the hysteroscope.[3,20]
- Sometimes hysteroscopy can replace open abdominal surgery.[3]
- Operative hysteroscopy is typically done in an operating room with general anesthesia.[3,20]

Additional resources

- Fact Sheet: Managing Pelvic Pain
- Booklet: Laparoscopy and Hysteroscopy

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Laparoscopy

Laparoscopy

Laparoscopy may be used to find and treat some gynecological disorders. During a laparoscopy, doctors place a thin, lighted telescope through the navel (belly button) and into the abdomen. This provides a direct view of the uterus, ovaries and fallopian tubes. Laparoscopy is an outpatient surgical procedure involving two small incisions made under general anesthesia.[3,14,20]

- Some women with a diagnosis of infertility may need laparoscopy for a complete fertility evaluation.[2,14,20]
- Laparoscopy can be used to remove scar tissue around the ovaries and fallopian tubes, take out ovarian cysts and treat endometriosis, a condition where the lining of the uterus grows outside of the uterus.[3,14,20]

⇢ Endometrial biopsy

Endometrial biopsy

Endometrial biopsy (removing a small piece of uterine tissue) is a test to see if the lining of the uterus is at a good stage for implanting an embryo (fertilized egg). It also tests if there are enough hormones, like progesterone, to support a pregnancy. Lower hormone levels may be a sign of infertility or early miscarriage. Biopsy can also help your doctor see any abnormal bleeding, infections, hormone problems, cancer or precancer.[3,19]

- Endometrial biopsy can be done at your fertility doctor's office.[3,19]
- During a biopsy, the doctor will pass a thin plastic catheter through the vagina and cervix and into the uterus.[3,19]
- A piece of tissue will be taken from the endometrium, or lining of the uterus. This is the lining where a growing embryo must implant itself to begin pregnancy.[3,19]

This test is most often used to diagnose luteal phase defect. This is a condition in which production of the hormones needed to sustain a pregnancy, such as progesterone, is not adequate. This leaves the endometrium unable to properly nourish a beginning pregnancy. Luteal phase defects may cause infertility or early miscarriage.[3,19]

→ Male fertility testing

Male fertility testing

Other tests can determine if issues with fertility are due to male factor infertility. A trained urologist who specializes in infertility may complete these tests.

Semen analysis

A semen analysis measures several things[4,17]:

- **Volume:** Quantity of a semen sample.
- **Sperm count:** Calculation of how many sperm are in a sample.
- **Percent motility:** Percentage of sperm that have the ability to move toward an egg.
- **Presence of white blood cells:** Evidence of infection, which must be treated prior to undergoing fertility treatment.
- **Morphology/strict criteria:** Percentage of sperm with a normal shape.

Antisperm antibodies

Antisperm antibodies are proteins that attack sperm to prevent fertilization.[3,4]

- Previous infection, trauma or surgery (such as a vasectomy, even when followed by a reversal) can cause antibodies to develop. Since sperm is stored in a specific place, they may not be able to fight off these antibodies because they do not exist throughout the body.[3,4]
- Antisperm antibodies are not an issue during IVF when performing intracytoplasmic sperm injection, where sperm is directly injected into an egg.

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Male fertility testing

Endocrine evaluation

Endocrine or hormone testing involves looking at various hormone levels.[5]

- Sometimes blood tests looking for hormonal causes of male infertility are done in instances of a low sperm concentration, impaired sexual functioning or other clinical findings.[5]
- Blood tests looking at Follicle Stimulating Hormone (FSH), Testosterone (T), Luteinizing Hormone (LH) or Prolactin (PRL) may be ordered.[5]
- Speak with your physician to find out the results of these tests and how they impact your fertility.

Additional resources:

- Fact Sheet: Diagnostic Testing for Male Factor Infertility
- Fact Sheet: Sperm Shape (Morphology): Does It Affect Fertility?

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Treatment options

Treatment options

Select any of the topics for more information.

- Assisted reproductive technologies (ART)
- Intrauterine insemination (IUI)
- Ovulation induction
- Third-party reproduction

Assisted reproductive technologies (ART)

ART can involve many different kinds of procedures and treatments.[21]

Select any of the topics for more information.

- *In vitro* fertilization (IVF)
- Assisted hatching
- Cryopreservation
- Embryo transfer
- Intracytoplasmic sperm injection (ICSI)
- Sperm extraction

Additional resources

- Booklet: Assisted Reproductive Technologies (ART): A Guide for Patients

In vitro fertilization (IVF)

In IVF, a couple's eggs and sperm are fertilized in a laboratory. The embryos that grow and survive are then placed back into a woman's uterus. There are many carefully timed steps involved in IVF.[21]

1. Fertility medications help the ovaries produce multiple eggs. This is called controlled ovarian hyperstimulation. The fertility medications are the same hormones that a woman releases each month to normally produce one egg (luteinizing hormone [LH], follicle-stimulating hormone [FSH] or a combination of both). These medications are given by injection.[3,21]

2. Doctors and nurses will closely watch how your ovaries are responding while on these medications. During this time, you will need to have blood testing and transvaginal ultrasound. Your medical team will let you know how often you need to have these tests. These tests and their results allow the doctor to fine-tune your dosage as your cycle moves forward. When the ovaries have made multiple follicles (where the eggs are growing) and the doctor has decided that it is time to retrieve the eggs, you will be given an additional medication, called a trigger shot. This contains the hormone human chorionic gonadotropin (hCG). This injection helps ready your eggs for the final growth phase before retrieval.[21]

3. Egg retrieval is the removal of the eggs from the follicles. It is a same-day minor surgery done in a fertility center or hospital. You will go home to rest shortly after it is done. You will receive anesthesia, and because of this, you will not be able to drive yourself home after this procedure. The retrieval is done using a transvaginal ultrasound probe with a needle attached to it. The needle is used to draw the fluid from the fully grown follicles found in each ovary. The fluid taken from each follicle is viewed under a microscope in the IVF lab to see if there are any eggs. You will be told how many eggs have grown and have been retrieved. Some follicles do not contain eggs. These follicles are called cysts.[21] Eggs can be frozen without being fertilized (egg freezing) or on the day of egg retrieval, a sperm sample will be collected in preparation for IVF.

4. The eggs and sperm are put into incubators in the IVF laboratory to aid fertilization. The combined eggs and sperm are carefully watched for a period of one to six days, depending on the doctor's plan. The goal is to see viable (able to continue growing) embryos that can be placed into the uterus for further growth.[3,21]

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In vitro fertilization (IVF)

5. If fertilization takes place and embryos develop, you will be scheduled for transfer of an embryo or blastocyst (about a five-day-old fertilized egg) based on your doctor's recommendation. A transfer is a minor procedure in which the doctor puts the embryo or blastocyst into a thin catheter and places it into the uterus. This is also the time when any extra embryos or blastocysts may be frozen (cryopreserved) for future transfers.[21]
6. Your fertility center will send you home with additional instructions about post-transfer activities and medications. Your doctor will tell you when to come back to the office for pregnancy testing. The medications prescribed at this stage support the uterus during the implantation phase (when the embryo or blastocyst attaches to the lining of the uterus). It is important to follow the instructions given to you when you leave the center. Call your doctor or nurse if you have any questions. Do not stop any medications until told to do so by your doctor or nurse.[21]

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⇢ Assisted hatching

Assisted hatching

Assisted hatching involves creating a hole in the outer shell (zona pellucida) of the embryo prior to transfer.[3,21]

- This may increase the chances the embryo will hatch from its protective shell and attach to the lining of the uterus.[3,21]
- This may not be appropriate for all couples. It may be used for older women or couples who have had unsuccessful IVF attempts.[3,21]

→ Cryopreservation

Cryopreservation

Cryopreservation is the freezing of eggs, embryos, ovarian tissue and sperm for future use.[21,23]

• Eggs: Cryopreservation of eggs is for women who may need to preserve their fertility because of a cancer diagnosis or medical condition requiring chemotherapy and/or radiation. This procedure is also used by women who are worried about fertility as they age and want to save their eggs for the future. Talk with your doctor if you have questions about cryopreservation. Women going through this procedure take fertility medications similar to those used in IVF to produce multiple eggs for freezing.[21,23]

• Embryos: Cryopreservation allows the patient to freeze and store unused embryos. Cryopreservation of embryos may decrease the chance of multiple pregnancies because it offers the option to limit the number of embryos transferred while freezing the remaining embryos. If pregnancy does not happen after the first procedure, frozen embryos may be thawed and transferred in a future cycle. Freezing embryos may reduce the need for additional stimulation and egg retrieval.[21,23]

• Ovarian tissue: Cryopreservation of ovarian tissue is a procedure that may also be used for women who have been diagnosed with cancer. These patients often do not have time to undergo a medicated cycle with fertility medications or cannot take the fertility medications due to an illness.[23]

• Sperm: Cryopreservation of sperm has long been an option for patients. This procedure is commonly used for men who need to bank sperm because of health conditions, such as cancer, that can affect their future ability to produce healthy sperm. Sperm is also routinely frozen before any fertility treatment, such as IVF [See *in vitro* fertilization (IVF)] or intrauterine insemination (IUI) [See intrauterine insemination (IUI)], where a catheter is used to place sperm into a woman's uterus.[24]

⇢ Embryo transfer

Embryo transfer

- **Embryo transfer:** During IVF, embryo transfer means putting embryo(s) through the vagina and cervix and into the uterus. An embryo transfer most often happens on day 3 or day 5 of embryo development. Sometimes embryos are transferred on day 2 or day 6.[21]
- **Blastocyst transfer:** Under your doctor's direction, embryos may be allowed to develop in the laboratory for longer (four to six days). On day 5 or day 6 of embryo development, the blastocyst is put into the uterus through blastocyst transfer. Waiting until the embryos are more developed may allow your doctor to choose embryos that are more likely to attach to the uterine lining. This allows fewer embryos to be transferred. This also lowers the chance of multiple pregnancies.[3,21]
- **Elective single-embryo transfer (eSET):** Elective singleembryo transfer (eSET) is when a woman undergoing IVF chooses to have a single embryo transferred when multiple embryos are available. Primary goal of eSET is to decrease the risk of multiple pregnancy.[22]

Additional resources

- Fact Sheet: Why Would I Choose to Have Elective Single-Embryo Transfer (eSET)?

⇢ Intracytoplasmic sperm injection (ICSI)

Intracytoplasmic sperm injection (ICSI)

ICSI helps the sperm enter the egg, increasing the chances of fertilization.

1. The egg's outer shell and membrane are pierced with a very small needle to make a small opening through which a single sperm is injected.
2. The egg is then placed in an incubator, where fertilization may occur and the embryo may develop.
3. The resulting embryos are then placed into the uterus two to six days later.

Doctors may consider this option for couples with poor sperm quality/a history of poor egg fertilization through conventional IVF.[21,25]

Additional resources

- Fact Sheet: What is Intracytoplasmic Sperm Injection (ICSI)?

⇢ Sperm extraction

Sperm extraction

This surgical procedure is used to retrieve sperm needed for ICSI.[3,21]

- When sufficient sperm cannot be ejaculated, sperm extraction may be necessary.[3,21]
- This may require microscopic epididymal sperm aspiration, testicular sperm aspiration or percutaneous epididymal sperm aspiration.[3,21]
- These surgical procedures are performed under a local or general anesthetic during outpatient surgery.[3,21]

⇢ Intrauterine insemination (IUI)

Intrauterine insemination (IUI)

IUI is the direct placement of sperm into the uterus.[3,6,26]

- Careful timing is needed during IUI so that it is performed close to ovulation.[3,26]
- Ovulation may be detected by using an LH predictor kit. An LH predictor kit is used to test urine for LH, which shows the start of ovulation. Ultrasound and blood tests may also be used to see follicle (egg) growth before ovulation.[3,26]
- IUI may be used in a natural cycle (without fertility medication) or with fertility medications that stimulate follicle growth. Sometimes an injection of human chorionic gonadotropin (hCG) is used to trigger ovulation, then insemination is timed carefully.[3,26]
- A semen sample is collected before IUI. The sperm must be separated from the seminal fluid. Your fertility center will tell you how much time will be needed between sperm collection and insemination. IUI may also be performed with donor sperm.[3,26]
- During insemination, a small catheter is placed through the vagina and cervix and into the uterus. The sperm is then inserted through the catheter and directly into the uterus.[3,26]
- IUI may be done one or two times in your cycle depending on your doctor's plan. Additional uterine support medications may be given after the IUI procedure but before returning for a pregnancy test.[3,26]
- Always follow the instructions provided by your physician when you leave your fertility center. Call your doctor or nurse if you have any questions.

Additional resources

- Fact Sheet: Intrauterine Insemination (IUI)

⇢ Ovulation induction

Ovulation induction

This fertility treatment uses medications to induce ovulation in women who do not ovulate or those who do not ovulate regularly.[16,21]

- Your doctor may track the progress of ovulation induction by using:
  - Ultrasound to measure the size and growth of follicles.
  - Blood work to check estradiol and LH/progesterone levels.[16,21]
- Ovulation induction may be used in conjunction with timed intercourse or IUI.[16,21]

⇢ Third-party reproduction

Third-party reproduction

Third-party reproduction refers to the process in which a third party (donor) provides eggs, sperm or embryos to an infertile couple or individual (recipient) during fertility treatments. The use of a surrogate or gestational carrier is also considered third-party reproduction.[27]

Select any of the topics for more information.

- Donor egg
- Donor embryo
- Donor sperm
- Gestational carrier
- Traditional surrogacy

Donor egg

Many women may not have the option to use their own eggs. In these cases, a doctor may recommend the use of a donated egg.[21,27]

- A donor egg may be needed for many reasons, including poor egg quality, age-related infertility, premature menopause, reduced ovarian reserve or same-sex parenting. Women with certain genetic disorders, absence of ovaries or previous chemotherapy and radiation therapy may also be candidates for donor eggs.[21,27,28]
- This option uses eggs donated by a relative or friend (known or directed donor) or a woman not known to the recipient (anonymous donor).[21,27,28]
- Egg donors are carefully screened for any sexually transmitted diseases and genetic abnormalities that can be passed on to children.[21,27,28]
- Donors can be provided by your fertility center or through a professional donor agency.[27]

Donor embryo

Donor embryo

A donor embryo is another option for women who are unable to produce embryos using their own eggs.[27]

- This method may be used for infertility involving both partners, recurrent pregnancy loss or genetic disorders.[27]
- This treatment option uses cryopreserved or frozen embryos donated by couples who have gone through IVF treatment. These donor couples have more embryos than they want to use and decide to donate them to other infertility patients.[21,27]

⇢ Donor sperm

Donor sperm

The use of donor sperm is an option when the male partner has no sperm (azoospermia), low sperm count (oligospermia) or other significant sperm or seminal fluid abnormalities.[27,28]

- Problems with sperm could be caused by several factors, including previous vasectomy, radiation, chemotherapy or birth defects.[27]
- Donor insemination may be recommended if the male partner has ejaculatory dysfunction or genetic disorders.[27,28]
- Donor sperm may be recommended to single women and couples where there is no male partner.[27,28]
- This treatment option uses sperm donated by a relative or friend (known or directed donor) or a man not known to the recipient (anonymous donor).[27]
- Recipients or recipient couples often choose a donor based on certain genetic features, including physical appearance.[27]
- Sperm donors are carefully screened for any sexually transmitted diseases and genetic abnormalities that can be passed on to children.[21,27,28]
- Donor sperm can be provided by an FDA-approved sperm bank, your fertility center or a known donor.[27]

⇢ Gestational carrier

Gestational carrier

A gestational carrier (or gestational surrogate) carries a pregnancy but is not genetically related to the child. This option allows an infertile couple to have their own biological child.[21,27,29]

- Eggs are retrieved from the intended mother through IVF, then fertilized by the intended father's sperm. In some cases, donor eggs or sperm may be used.[27,28]
- The resulting embryos are transferred to the gestational carrier.[27,29]
- A gestational carrier may be used when an intended mother does not have a uterus, has problems with the function and structure of the uterus, has had recurrent pregnancy loss or a medical reason to avoid pregnancy.[27,29]
- A gestation carrier may also be used in same-sex parenting or single parenting.[27,29]

Additional resources:

- Booklet: Third-Party Reproduction: A Guide for Patients
- Fact Sheet: Gestational Carrier (Surrogate)
- Fact Sheet: Egg Donation
- Fact Sheet: Embryo Donation

⇢ Traditional surrogacy

Traditional surrogacy

A traditional surrogate carries a pregnancy for another person or couple and is also the genetic mother of the child.

- In traditional surrogacy, the female surrogate is inseminated with sperm from the male partner of the intended couple or a donor.[27,29]
- The child may be adopted by one or both of the intended parents. This is the case if donor sperm is not used.[29]
- Adoption laws may vary by state.

⇢ Medications

Medications

Select any of the topics for more information.

- Introduction
- Routes of administration
- Fertility medications
- Other medications

Introduction

During infertility treatment, it is important to know where to get your fertility medications. Most corner retail pharmacies do not have these medications readily available. Fertility medications are usually ordered through a specialty pharmacy, like AllianceRx Walgreens Pharmacy, which handles medications for more complex conditions.

The benefits in working with our specialty pharmacy include:

- A Care Team of expert pharmacists, nurses and fertility professionals who are devoted to helping patients by answering questions and providing information about medications, delivery options and insurance coverage.
- Research and confirmation of insurance coverage for fertility medications.
- Easy ordering and medication delivery based on the medication schedule set by your doctor.

We realize this can be a very stressful time. Our goal is to make it easier in any way we can. We are here to help. Please feel free to contact us at 800-424-9002 or visit our website to learn more about our 24/7 support services.

Additional resources

- Website: Walgreens.com/Fertility

⇢ Routes of administration

Routes of administration

The various medications used in fertility treatment require different routes of administration (how they enter the body).

Ovarian stimulation medications may be administered by these methods:

- **Oral:** Medication taken by mouth.
- **Subcutaneous injection:** Injecting medication into the fatty tissue just below the surface of the skin using a small, fine needle.
  - **Injection sites:** Lower abdomen, at least two inches to the side of or below the belly button, upper outer arm or upper outer thigh.
- **Intramuscular injection:** Injecting medication into the muscle at a 90-degree angle using a longer needle.
  - **Injection sites:** Upper outer quadrant or area of the buttock or the front outer thigh.

Other medications may be administered by the following methods:

- **Transdermal:** Applied to the skin in the form of a patch.
- **Vaginal:** Inserted and absorbed in the vagina.
- **Intranasal:** Absorbed through the nasal passages, usually in the form of a nasal spray.
- **Intravenous:** Injected into the vein. This method is commonly used to deliver medications during the egg retrieval in an in vitro fertilization (IVF) cycle.

Additional resources

- Injection training guides

⇢ Fertility medications

Fertility medications

Your doctor may prescribe medication therapy to treat infertility. Different types of fertility medications control hormone levels that can help or cause ovulation. These medications may be administered orally, vaginally or by injection.

Some fertility medications need to be prepared and self-injected at home. Your doctor will give you instructions on how to do this. Always follow the instructions provided by your physician. It is very important that you are confident in your ability to inject yourself with medication or that you can have someone give you the injections. If you are not comfortable giving or receiving your injectable medication, talk to your doctor, nurse or pharmacist. They might also be able to tell you how to correctly prepare your medication and how to follow correct injection techniques.

NOTE: It is important for you to tell your doctors, nurses and pharmacists of any allergies, including an allergy to latex since some latex may be in medication packaging.

Additional resources

- Injection training guides
- Booklet: Medications for Inducing Ovulation

Select any of the topics for more information.

- Medications for ovarian stimulation
- Medications for ovarian control
- Medications for ovulation
- Medications for uterine support

Medications for ovarian stimulation

Oral

Certain oral medications may be used to start and improve ovulation in women. These are commonly used as the first treatment for female infertility.[3,15]

- These medications are typically taken on days 3 to 7 or days 5 to 9 of the reproductive cycle.[3,15]
- Clomiphene citrate is the most prescribed fertility medication to stimulate ovulation.[15] Clomid (clomiphene citrate) is a brand name for this medication.[3,15]

Injected

Other medications can stimulate growth of follicles and eggs. Gonadotropins are medications that contain follicle-stimulating hormone (FSH) or a combination of FSH and luteinizing hormone (LH). They may be referred to as “stimulation” medications.[3,15]

- After an ultrasound and blood tests have confirmed the ovaries are suppressed, these medications are typically started on day 2 or day 3 of the reproductive cycle.[15,21]
- These medications stimulate growth of multiple follicles and the eggs within them.[3,15]
- This treatment requires frequent monitoring (ultrasound and blood work).[3]
- These medications are taken at the same time each day.[15]
- These medications are taken for seven to 12 days or more if ovaries are slow to respond. Your doctor will provide instructions.[3,15]
- Take these medications by subcutaneous injection or intramuscular injection, as directed by your doctor.[15]
- Follistim AQ, Gonal-f Multi-Dose, Gonal-f RFF 75, Gonal-f RFF Redi-Ject, and Menopur are the most frequently prescribed gonadotropins.[15]

Medications for ovarian stimulation

Additional resources

- Fact Sheet: Side Effects of Injectable Fertility Drugs (gonadotropins)
- Booklet: Medications for Inducing Ovulation: A Guide for Patients
- Fact Sheet: Oral Medicines for Inducing Ovulation

Prescribing information

- clomiphene citrate

Medication information

- Clomid (clomiphene citrate)

⇢ Medications for ovarian control

Medications for ovarian control

Other medications are prescribed to control the timing of ovulation or prevent early ovulation.

Gonadotropin-releasing hormone (GnRH) agonist

- Has the same actions as GnRH, which is produced by the hypothalamus.
- Used with ovarian stimulation medication to prevent early ovulation.[14,15]
- Taken for 10 to 28 days, depending on your doctor's instructions.[14]
- Taken by subcutaneous injection or as an intranasal spray.[15]
- Commonly given as Leuprolide acetate.[14,15]

GnRH antagonist

- Opposes the action of GnRH hormone.
- Used with ovarian stimulation medication to prevent early ovulation.[3,15]
- Taken for four to five days in conjunction with stimulation medication, depending on your doctor's instructions.[14]
- Taken by subcutaneous injection.[15]
- Commonly given as Ganirelix acetate for injection, Fyremadel or Cetrotide.[15]

Medications for ovulation

Medications for ovulation

Human chorionic gonadotropin (hCG) – ovulation stimulation medication

- This medication is used as an LH substitute to trigger ovulation and help with the final growth of the egg(s).[3,15]
- The timing of the “trigger shot” is extremely important because it will determine the timing of the egg retrieval.[15]
- Stimulation medications are stopped when this injection is given.[15]
- This medication is given by subcutaneous or intramuscular injection, depending on the brand.[15]
- Common medications include hCG, Novarel, Pregnyl and Ovidrel PreFilled Syringe.[15]

⇢ Medications for uterine support

Medications for uterine support

Progesterone – pregnancy support medication

- A hormone produced by the ovaries.[30]
- May be given after ovulation to support the growth of the uterine lining (endometrium) to help it receive the embryo.[15,30]
- Frequently started after egg retrieval or intrauterine insemination (IUI).[30]
- May be taken until the results of a pregnancy test two weeks after hCG injection; if the patient is pregnant, through the first 12 weeks of pregnancy.[30]
- Can be taken as an intramuscular injection or vaginal suppositories, gel or tablets.[30]
- Examples include Progesterone Injection USP, CRINONE (progesterone) gel and ENDOMETRIN (progesterone) insert.[30]

Additional resources

- Fact Sheet: Progesterone Supplementation During In Vitro Fertilization (IVF) Cycles

Prescribing information

- Crinone
- Endometrin

Medication information

- Crinone
- Endometrin

⇢ Other medications

Other medications

- **Birth control pills/oral contraceptive pills (OCPs)** are a man-made (synthetic) mixture of estrogen and progesterone.[31] In fertility treatment, OCPs may be used to control the menstrual cycle.
- **Steroids** may be used to reduce inflammatory response by the body to medication stimulation in women undergoing IVF, as well as the IVF procedure itself.
- **Antibiotics** may be prescribed to prevent or treat infections before undergoing IVF or IUI.
- **Prenatal vitamins** may be taken before and during pregnancy to ensure adequate amounts of folic acid. Folic acid has been shown to protect against birth defects of the spine and brain.[32]
- **Insulin-sensitizing medications** may reduce insulin, a hormone controlling blood glucose, by helping the body to better use insulin and increase the movement of glucose into the cells. They are often prescribed to women diagnosed with polycystic ovary syndrome (PCOS).[3,15]

Additional resources

- Fact Sheet: Polycystic ovary syndrome (PCOS)

⇢ Additional information

Additional information

Select any of the topics for more information.

- Acupuncture and infertility
- Age and infertility
- Cancer and fertility preservation
- Coping with stress
- Preconception care
- Genetic testing
- Recurrent pregnancy loss/miscarriage
- Weight and infertility

Acupuncture and infertility

Acupuncture is the therapeutic application of fine metallic needles into defined points on the body. It has been increasingly used as a natural and complementary therapy for infertility. It is performed by specially trained practitioners.[33,34,35,36]

- Acupuncture professionals believe that acupuncture can be used to treat a variety of illnesses, including pain, nausea, fatigue and infertility.
- Modern science is trying to better understand and measure how acupuncture works and how well it works.
- A 1996 World Health Organization report identified conditions, including female infertility, for which acupuncture may have therapeutic effects.[33]

Acupuncture and infertility treatment

Acupuncture is used to help both men and women with infertility.[35,36,37,38]

- In men, it can serve to increase fertility. Research has shown that acupuncture can increase sperm count and motility, or the percentage of sperm with the ability to move toward an egg.[3,35,36,38]
- Some preliminary research has shown that acupuncture may increase blood flow to the uterus. In theory, this may enhance the opportunity for embryo implantation. However, there is a need to see more conclusive evidence to support this theory.[3,35,36,38]
- In women, a link has been found between acupuncture and the production of endorphins. These are hormones produced in the brain that play a part in the reproductive cycle.[3,35,37,38]
- Acupuncture treatment can reduce stress in both men and women.[3,35,37,38]
- Talk to your doctor before scheduling any acupuncture treatment.

Additional resources

- Fact Sheet: Acupuncture and infertility treatment

⇢ Age and infertility

Age and infertility

Because men and women are living longer, many are delaying childbearing.[6,39]

- The average age of a woman having her first child has increased significantly over the past 30 years as more women have pursued higher education and careers and postponed marriage.[3,6,39]
- Twenty percent of women are waiting until after age 35 to have a child.[6] According to the Centers for Disease Control and Prevention's (CDC) National Center for Health Statistics, the number of first births to women age 35 and older increased nearly eight times between 1970 and 2006.[3,11]

Age and female fertility

The age-related decline in female fertility is well documented.

- Fertility decreases in women with age, especially after age 35.[2,12] Although the ability to achieve a pregnancy decreases in all women as they age, the precise age when a woman can no longer conceive varies between individuals.[3,39]
- Success rates for assisted reproductive technologies (ART) also decline as women age, as the number of retrieved eggs and embryos decreases.[3,39]
- Roughly one-third of couples in which the female partner is age 35 or older will have problems with fertility.[40,41]

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Age and infertility

Ovarian reserve

Although chronological age is an important factor of fertility, it alone does not predict the chances for pregnancy. Your doctor may recommend tests that can predict ovarian reserve. This can show how well the ovaries are able to make eggs that can be fertilized.[2,6]

- Tests can determine the number of ovarian follicles. This shows how well the ovaries are working.[2,6]
- These tests can also help predict egg quality.[2,6]

Age and male fertility

Age can also play a role in a man's fertility. However, issues usually do not begin as early as they might in women. Sperm quality deteriorates somewhat as men get older, but it generally does not become a problem before a man is in his 60s.[6] Your doctor can recommend tests to check for decreased male fertility.

Additional resources

- Fact Sheet: Ovarian Reserve (Predicting Fertility Potential in Women)
- Fact Sheet: Reproductive Aging in Women
- Website: www.reproductivefacts.org
- Fact Sheet: Diagnostic Testing for Male Factor Fertility

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Cancer and fertility preservation

Cancer and fertility preservation

Annually, about 140,000 men and women under the age of 45 will be diagnosed with cancer.[42] In the United States, there are approximately 800,000 reproductive-aged men and women who have cancer. Many have concerns about their fertility due to the likelihood there could be damage to eggs and sperm from lifesaving cancer treatments.[42,43]

Fertility preservation (FP) is a growing field that helps women, men and children overcome the complications of infertility associated with cancer treatment such as chemotherapy and radiation therapy.[44]

Additional resources

- Fact Sheet: Female Cancers, Cyropreservation, and Fertility
- Fact Sheet: Male Cancer, Cryopreservation, and Fertility

You can find more information about fertility preservation from these organizations:

Website: Oncofertility Consortium for Patients
The Oncofertility Consortium also offers iSaveFertility, which contains information for patients and families about fertility after cancer treatment.

Nationwide Referral FERTLINE Patient Navigator:
Call 866-708-FERT(3378)

Website: SaveMyFertility.org
Patient and Provider Pocket Guides (Women, Men and Children Diagnosed with Cancer)

Website: Alliance for Fertility Preservation

Website: RESOLVE: The National Infertility Association

Website: Stupid Cancer

⇢ Coping with stress

Coping with stress

What is stress?

Stress refers to the potential wear and tear on the mind and body that occurs while adjusting to daily changes and challenges in life. During a health crisis, many people can experience traumatic stress. This is usually triggered by a specific event that threatens a person's life or general well-being. Negative stress can overwhelm coping and problem-solving abilities.[45]

Stress is also defined as any event that a person views as threatening or harmful. Stress can result in the heightened activity of many body functions. Acute stress does not last for very long, but can result in increased heart rate, blood pressure and respiration, as well as sweaty palms and cool, clammy skin. Chronic stress can persist over time and may lead to depression and changes in the immune system and sleep patterns.[46]

Why is infertility stressful?

Research has shown that women undergoing infertility treatment have the same level of stress, anxiety and depression as women with cancer, heart disease or HIV/AIDS. Each month an infertile couple tries to conceive, they are faced with this stress.[46,47]

Most couples are accustomed to planning their lives. However, when diagnosed with infertility, many couples may no longer feel in control of their bodies or their life plan. Infertility can be a major crisis because their important life goal of parenthood is threatened. Experience has likely shown them that if they work hard at something, they can achieve it. With infertility, this may not be the case.[46]

- Infertility testing and treatments can be physically, emotionally and financially stressful.
- A couple's intimacy may often be affected by the infertility experience. This can further increase stress levels.
- Trying to coordinate medical appointments with career responsibilities can also increase pressures on couples with infertility.

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Coping with stress

To reduce stress, it may be helpful to see a mental health professional, ideally one who specializes in or is familiar with issues for those dealing with infertility prior to/during infertility treatment. Group support can also be valuable.[48]

- Many mental health professionals have special training in the medical and psychological aspects of infertility.
- Group counseling allows you to share your experiences, feelings and information with others who are undergoing a similar experience. Support groups are also a good setting to listen and learn from others and explore thoughts about future options such as new technologies, adoption or child-free living.
- Many fertility centers have access to these professionals and can refer you to them for consultation.
- Below are links to national support groups that can provide information, support and additional resources:

Resolve: The National Infertility Association

This is a nonprofit organization with an established nationwide network to promote reproductive health and provide support to women and men living with infertility. Resolve has extensive online information and local chapters in many areas. For more information, visit the Resolve website.

Family Equality

Family Equality's mission is to advance legal and lived equality for LGBTQ families, and for those who wish to form them, through building community, changing hearts and minds, and driving policy change.

Coping with stress

Tips for reducing stress during infertility treatment

- Keep the lines of communication open with your partner.[45]
- Get emotional support so you do not feel isolated. Individual or couples counseling, support groups and books on infertility can help validate your feelings and help you cope.
- Learn stress-reduction techniques such as meditation or yoga.[45]
- Avoid excessive intake of caffeine and other stimulants. These can worsen symptoms of stress.[45]
- Exercise regularly to release physical and emotional tension.[45]
- Follow a medical treatment plan that is comfortable for both you and your partner.[45]
- Learn as much as you can about the cause of your infertility and the treatment options available. Visit your local library or book stores or contact the American Society for Reproductive Medicine (ASRM) for additional information on infertility.[45]

Additional resources:

- Fact Sheet: Stress and Infertility
- Infosheet: Infertility - 20 Things You Can Do Now to Foster Emotional Wellness

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⇢ Preconception care

Preconception care

The goal of preconception care is to identify and reduce reproductive health risks prior to conception.[49,50] Lifestyle choices and environmental factors can affect fertility and pregnancy outcomes. Many of these risks can be avoided.

A comprehensive assessment of patients trying to conceive includes a review of the following health risks:

Reproductive conditions

Be sure to tell your doctor about your reproductive health history. This includes miscarriages, abortions, infections and surgeries.

Environmental hazards

Exposure to environmental health hazards, such as toxic chemicals, can also affect fertility.[3,4]

- Toxic chemicals can be in the home, workplace and neighborhood.
- Environmental exposure to herbicides and pesticides have been associated with decreased fertility in women.

Medical conditions

- Review your medical history with your doctor and fertility center.
- Give your doctor and fertility center a complete list of your diseases and conditions.
- Work with your doctor to manage any health conditions before starting fertility treatment.
- Make a list of any medications you are currently taking. Give it to your doctor and nurse.
- Ask your doctor if your medications are safe to use during fertility treatment, conception and pregnancy.

Alcohol

- Consuming alcohol can impair male and female fertility and cause damage to a developing fetus during pregnancy.[5,10,53]
- In men, alcohol consumption has been associated with decreased semen quality and impotence.[3,10]

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Preconception care

- In both men and women, even modest amounts of alcohol consumption have been associated with lower pregnancy rates through ART.[3]
- Women should avoid alcohol while pregnant or trying to conceive because damage can occur in the earliest weeks of pregnancy, even before a woman knows that she is pregnant.[54]

Recreational drugs

- Recreational drug use can also affect fertility and normal reproductive function in both men and women.[3,41,55]
- Marijuana use can interfere with normal ovulation because it inhibits the secretion of gonadotropin-releasing hormone.[3,55]
- The use of recreational drugs, including anabolic steroids and marijuana, may decrease sperm concentration and testosterone production. This can impair a man's ability to fertilize an egg.[3,55]
- Cocaine use can impair spermatogenesis (formation of sperm) in men. It can increase the risk of tubal disease in women.[3,54]
- Recreational drugs can also harm a developing fetus during pregnancy.

Smoking

- Smoking increases the risk of heart disease, cancer and chronic lung disease. Recent studies have also demonstrated that men and women who smoke also have decreased fertility.[3,49] The longer someone smokes and the more a person smokes, the greater the effect it will have on overall health, including fertility.
- The negative effects of secondhand smoke are only slightly less damaging than active smoking by either partner.[3]
- Nearly twice as many in vitro fertilization (IVF) attempts are required to achieve conception in smokers than in nonsmokers.[51]
- In males, smoking negatively affects sperm production and increases abnormalities in sperm shape and function.[17]
- Smoking or exposure to secondhand smoke appears to accelerate the loss of eggs and reproductive function in women.[51]

Preconception care

- Stopping smoking can improve ART outcomes. One study showed that stopping smoking for at least two months before attempting IVF significantly improved chances for conception.[51]
- Smoking during pregnancy increases the risk for premature labor, fetal growth restriction, mental retardation and other birth defects and complications.[51]
- There are many additional resources for quitting smoking. The toll-free national hotline, 800-QUIT-NOW, is one resource for stopping smoking.

Zika virus

Zika is a virus spread primarily by the bite of an infected Aedes species mosquito.[52] It can be spread through intimate sexual contact, blood transfusion, and from mother to fetus during pregnancy.[52]

- Infection during pregnancy can cause birth defects such as microcephaly.
  - Microcephaly is a medical disorder where the head is smaller than normal and is associated with brain shrinkage and cell death, causing serious developmental problems in the child.[53]
- Symptoms can be mild or absent, making it difficult to know if you have it. While most people will have no symptoms, symptoms can include fever, rash, joint pain, conjunctivitis (red eyes), muscle pain, and headache.[53] If you or your partner live, have visited or plan to travel to an area were the infected Aedes mosquitos have been found, talk with your physician before attempting to get pregnant.[52]

Additional resources

- Website: www.cdc.gov
- Website: www.reproductivefacts.org

Preconception care

- Fact Sheet: Smoking and Infertility
- Website: CDC Resources – Smoking Cessation
- Website: www.smokefree.gov
- Website: CDC Resources – Alcohol and Public Health
- Website: CDC Resources – Fetal Alcohol Spectrum Disorders
- Website: National Institute on Alcohol Abuse and Alcoholism
- Website: March of Dimes: Alcohol during pregnancy
- Website: www.drugabuse.gov
- Website: The Effects of Workplace Hazards on Male Reproductive Health
- Website: The Effects of Workplace Hazards on Female Reproductive Health
- Fact Sheet: Optimizing Natural Fertility
- Fact Sheet: Optimizing Male Fertility
- Fact Sheet: What do I need to know about Zika virus and trying to have a baby?

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⇢ Genetic testing

Genetic testing

Preimplantation genetic diagnosis (PGD)

PGD is the genetic testing of embryos created through IVF. This procedure allows a couple to learn genetic information about the embryos before they are transferred into the uterus. This testing process can also be used when there is a known risk of inherited chromosomal abnormalities. PGD is especially helpful for patients who have a family history of a genetic disease, such as cystic fibrosis, sickle cell anemia, Duchenne muscular dystrophy, Fragile X syndrome or Tay-Sachs disease. Ask your fertility center for a complete list of which diseases are included in PGD.[55,56]

Preimplantation Genetic Screening (PGS)

PGS is a technique used in conjunction with in vitro fertilization (IVF) to screen embryos for any genetic issues that may lead to a disease, disorder or birth defect. PGS involves testing an embryo for chromosomal abnormalities. Many embryos with chromosomal abnormalities will not lead to a pregnancy, or will result in a miscarriage. All women will have some eggs that are chromosomally abnormal and all men will have some sperm that are chromosomally abnormal. The percentage of embryos that are abnormal can be affected by many factors, including the age and health history of the parents. PGS may be recommended for someone with recurrent miscarriage, someone who is older or whose ovaries do not work as well as expected, or someone with multiple failed fertility treatments. Anyone interested in PGS should consult with a fertility specialist so that the procedure and any alternatives can be discussed.[57]

PGD/PGS process

- The genetic material for testing can be obtained from one or two cells removed from an early embryo (blastomeres).
- The cells are then biopsied for genetic abnormalities.
- The cells can be analyzed to assess the number of chromosomes or detect specific gene mutations.
- After the biopsy and genetic analysis, a selection of normal genetic embryos can then be transferred into the uterus or cryopreserved (frozen) for future use.

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Genetic testing

Carrier screening

Carrier screening is done on potential parents using a blood or a tissue (swabbed from inside the cheek) sample. These screening tests are used to find out whether a person carries a gene for certain inherited disorders. A carrier is defined as a person who shows no sign of a particular disorder but, could pass the gene on to their children.[58,59] Carrier screening can be done on potential parents before or during a pregnancy. Depending on your family background or family history carrier screening for other diseases may be recommended by your doctor.[58,59]

Additional resources

- Fact Sheet: Preimplantation Genetic Testing
- Fact Sheet: Genetic Screening for Birth Defects

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Recurrent pregnancy loss/miscarriage

Recurrent pregnancy loss/miscarriage

Miscarriages are common.[50,56]

- Roughly 25% of pregnancies end in miscarriage, usually in the first 12 weeks.
- Two or more failed pregnancies or miscarriages is considered recurrent pregnancy loss.
- Less than 5% of women will experience two consecutive, or back-to-back, miscarriages. Only 1% will experience three or more consecutive miscarriages.
- Women who have three or more miscarriages should have further diagnostic testing, especially if the miscarriages have been consecutive.
- Even after having three miscarriages, a woman has a 60-80% chance of conceiving and carrying a full-term pregnancy.

There may be several reasons for miscarriage or recurrent pregnancy loss:

Chromosomal abnormalities

More than half of all miscarriages during the first 13 weeks of pregnancy are caused by problems in the fetal chromosomes.[3,50]

- Chromosomes are tiny structures inside the body cells that carry the basic identity of heredity.
- Each chromosome contains genes that determine a person's appearance, sex and blood type.
- Problems in the number or structure of the chromosomes or genes can lead to miscarriage.
- Frequently, miscarriage is the body's way of ending a pregnancy in which the fetus was not developing normally.
- Most chromosomal problems occur by chance. They are not likely to recur in later pregnancies.
- In a small number of cases, chromosomal problems may cause repeated miscarriage. To help find out why this is happening, your doctor may order a karyotype. This is a special blood test to analyze chromosome structure.

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Recurrent pregnancy loss/miscarriage

Age

Miscarriages become more common as a woman ages.[3,50]

- More than one-third of all pregnancies in women over the age of 40 end in miscarriage.
- Most of the embryos in these miscarriages have an abnormal number of chromosomes.

Uterine abnormalities

Many abnormalities of the uterus are linked to miscarriage.[3,50]

- A hysterosalpingogram, sonohysterogram, ultrasound or hysteroscopy can spot abnormalities of the uterus.
- These abnormalities may be congenital defects, growths, scarring or adhesions.
- Some of these abnormalities can be successfully treated with surgery.

Disorders and illnesses

Disorders of the immune system can lead to miscarriage.[3,50]

- The immune system defends the body against disease by recognizing and attacking foreign substances.
- The mother's body normally protects the fetus from an attack by her own antibodies. In some cases, this protection may be absent in a woman's blood.

In some cases, a mother's illness has been linked to miscarriage.[3,50]

- Autoimmune disorders, congenital heart disease, severe kidney disease with high blood pressure, uncontrolled diabetes, thyroid disease or an intrauterine infection may interfere with conception and pregnancy.
- When these illnesses are treated, the chances for a successful pregnancy improve.

Recurrent pregnancy loss/miscarriage

Thrombophilias

Thrombophilias are disorders that increase a woman's risk of blood clots. These clots can increase the risk of fetal death, especially in the second half of pregnancy.[3,50]

Hormone imbalance

Hormone imbalance may also lead to repeated miscarriage.[3,50]

- The hormone progesterone prepares the lining of the uterus for the fertilized egg during the second half of the menstrual cycle.
- When an egg is fertilized, progesterone continues to prepare the uterine lining for the embryo.
- The right amount of progesterone must be produced to maintain the pregnancy, otherwise miscarriage may occur.
- If tests indicate that a woman's body is not producing enough progesterone, supplements can be prescribed to correct the problem.

Environmental and lifestyle factors

In some cases, environmental and lifestyle factors may lead to greater risk of miscarriage.[3,50]

- Women, who smoke, drink excessive alcohol or use recreational drugs, especially cocaine, increase their risk of miscarriage.
- Exposure to high levels of radiation or toxic substances may also be a factor in repeated miscarriage.

Unexplained causes

In 50% to 70% of failed pregnancies, no explanation for miscarriage or recurrent pregnancy loss is ever definitively determined.[3,50]

Additional resources:

- Fact Sheet: Genetic Screening for Birth Defects
- Fact Sheet: What is Recurrent Pregnancy Loss (RPL)?

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⇢ Weight and infertility

Weight and infertility

According to the ASRM, 12% of all infertility cases are the result of a woman either weighing too little or too much.[60]

- The reproductive hormone estrogen is produced in fat cells.[60]
- If a woman has too much body fat, the body produces too much estrogen and begins to act as if it is on birth control. This limits her odds of getting pregnant.[60]
- A woman with too little body fat can't produce enough estrogen.[60] Her reproductive cycle will begin to shut down. She may not have a menstrual period nor be able to ovulate.[13,60]
- Both underweight and overweight women can have irregular cycles in which ovulation does not occur.[13]

Obesity in men has also been associated with changes in testosterone levels and other hormones important for reproduction.[13]

To determine if you are at a healthy weight, you will need to know your body mass index (BMI). There are many websites you can use to calculate your BMI as long as you know your height and weight. A BMI between 19 and 24 is considered normal.[13,61]

Additional resources

- Fact Sheet: Weight and Fertility

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Medication information

Clomid (clomiphene citrate) tablet

This drug is usually given to women who want to get pregnant but have infrequent or absent periods. These women have healthy ovaries but have trouble producing eggs on their own. This drug helps boost hormones that can produce eggs.

Common Side Effects

Common side effects of this drug include the following:

- ovaries that are too large
- hot flashes
- abdominal and pelvic discomfort
- bloating
- nausea
- vomiting
- breast discomfort
- vision changes and problems
- headache
- unusual uterine bleeding

Less common side effects include the following:

- irritated lining of the abdomen
- increased appetite
- constipation
- rash
- depression
- diarrhea
- fatigue
- hair loss/dry hair
- increased urine or need to urinate
- trouble sleeping
- lightheadedness

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Medication information

- nervousness
- vaginal dryness
- dizziness
- weight changes

Some patients have reported other side effects. The manufacturer states it is not clear how often these occur or if this drug is the cause of these conditions. These additional side effects include the following:

- fever
- ringing in the ears
- weakness
- irregular heartbeat
- chest pain
- swelling
- high blood pressure
- feeling of a fast heartbeat
- swollen blood vessels
- blood clot in the lung
- shortness of breath
- rapid heartbeat
- blood clots
- migraine
- prickly or numb feeling in the body
- seizure
- stroke
- fainting
- acne
- allergic reaction
- red skin or rash
- red bumps under the skin

Medication information

- itching or hives
- excess body hair
- inflamed pancreas
- endometriosis
- ovarian cysts
- painful twisting of the ovaries
- bleeding in the ovaries
- pregnancy outside of the uterus
- uterine bleeding
- thin uterine lining
- liver problems or liver disease
- high triglycerides
- joint pain
- back pain
- muscle pain
- tumors and cancer
- anxiety
- irritability
- mood changes
- loss of sense of reality
- eye problems
- vision changes
- high white blood cell count
- thyroid problems

Some have also reported birth defects in children born after taking this drug.

Medication information

Serious Side Effects

This drug can cause blurred vision or visual spots and flashes. This can make it unsafe to drive a car or use a machine. Tell your doctor right away if you have any of these symptoms.

This drug can also excite the ovaries too much. It can make them too large. It can also cause ovarian hyperstimulation syndrome (OHSS). This can fill the abdomen or lungs with fluid. These problems can become fatal. Call your doctor right away if you have abdominal pain or bloating, nausea, vomiting, diarrhea or weight gain.

This drug can cause high levels of a type of fat in your blood called triglycerides. This is more likely for those with a family history of high triglycerides.

This drug might also cause a pregnancy with more than one baby. It might also cause pregnancy outside of the uterus.

Using this drug for a long time can raise the risk for ovarian cancer. **Speak with your doctor for information about the risks and benefits of available treatments.**

Other Information

Only doctors with experience treating infertility should prescribe this drug. Ask your doctor if this drug is right for you. Some patients should not take this drug.

Do not take this drug if you have any of the following conditions:

- allergy to clomiphene citrate or any other ingredients in Clomid or similar drugs
- known or suspected pregnancy
- liver disease
- unusual uterine bleeding
- ovarian cysts
- thyroid or adrenal gland problems
- pituitary tumor or other brain tumor

Medication information

Tell your doctor if you are breastfeeding. It is not known if this drug passes into breastmilk. This drug might also slow breastmilk production.

The usual starting dose of this drug is 50 mg a day for five days. The timing of this dose will depend on an individual patient's treatment plan.

If a patient does not ovulate with the first course of this drug, the usual dose for a second course is 100 mg a day for five days. This is the highest recommended dose for this drug.

This drug is a tablet taken by mouth. Your doctor will tell you how and when to take it.

Always follow the instructions provided by your doctor.

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=be399623-6400-475d-93d3-1dedd4d43017
Accessed 04/20/22

Medication information

Crinone (progesterone) gel

This drug is typically given to women who do not make enough progesterone. Progesterone helps strengthen the uterine lining to support a pregnancy. This drug is used as part of fertility treatment. It is also used to bring back periods for women whose periods stopped after previously normal cycles.

Common Side Effects

For those taking this drug during a donor egg transfer, the most common side effects of this drug include the following:

- cramps
- headache
- breast pain
- pain
- bloating
- nausea
- vaginal discharge
- dizziness
- yeast infection
- vaginal itching

For those taking this drug during in vitro fertilization, the most common side effects of this drug include the following:

- enlarged breasts
- constipation
- sleepiness
- nausea
- perineal pain
- headache
- nervousness
- waking often at night to urinate
- abdominal pain

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Medication information

- depression
- loss of interest in sex
- diarrhea
- joint pain
- pain during sex
- vomiting

For those taking this drug with estrogen to bring back a stopped period, the most common side effects of this drug include the following:

- cramps
- mood changes
- fatigue
- sleep problems
- headache
- depression
- bloating
- abdominal pain
- nausea
- increased appetite
- back pain
- upper respiratory tract infection
- muscle pain
- vaginal itching

This drug is a gel. It can cause some white discharge from the vagina. This is normal, even many days after using this drug.

Medication information

Serious Side Effects

This drug can raise the risk for blood clots and blood vessel problems. It can raise the risk for stroke and heart attack. These problems can become fatal. Call your doctor right away if you have any of the following symptoms:

- pain in your calves or chest
- sudden shortness of breath
- coughing up blood
- severe headache
- vomiting
- dizziness
- faintness
- changes in sight or speech
- weakness or numbness in an arm or leg

Some women who have taken this drug have had miscarriages. Others have reported birth defects. **Speak with your doctor for information about the risks and benefits of available treatments.**

Other Information

Ask your doctor if this drug is right for you. Some patients should not take this drug.

Do not take this drug if you have any of the following conditions:

- allergy to progesterone or any other ingredients in Crinone or similar drugs
- unusual vaginal bleeding
- liver disease
- known or suspected cancer in the breast or sex organs
- miscarriage where tissue is still in the uterus
- history of blood clots

Tell your doctor if you are breastfeeding. This drug passes into breastmilk. It is not known how this might affect a nursing baby.

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Medication information

For increasing progesterone during fertility treatment, the usual dose is Crinone 8% (90 mg) once a day. For replacing progesterone in women who have trouble making eggs or are not able to make eggs, the usual dose is Crinone 8% (90 mg) two times a day.

For treating a stopped period, the usual dose is Crinone 4% (45 mg) every other day for up to six doses. If this does not work, the next usual dose is Crinone 8% (90 mg) every other day for up to six doses.

This drug is inserted into the vagina. Your doctor will teach you how to prepare and insert the drug. Do not use this drug at the same time as any other products placed into the vagina. Use Crinone six hours before or six hours after any other product that is placed into the vagina.

Always follow the instructions provided by your doctor.

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=75e97aa1-daa4-45f9-b2e2-1a371302914e
Accessed 04/20/22

Medication information

Endometrin (progesterone) insert

This drug is typically given to women who do not make enough progesterone. Progesterone helps strengthen the uterine lining to support a pregnancy. It is used as part of fertility treatment.

Common Side Effects

The most common side effects of this drug include pain after egg retrieval, stomach pain, nausea and ovarian hyperstimulation syndrome.

Other common side effects include the following:

- bloating
- headache
- uterine cramps
- vaginal bleeding
- vomiting
- constipation
- fatigue
- urinary tract infection

Less common side effects include vaginal irritation, hives and swelling.

This drug might also cause tender breasts, mood changes, irritability and drowsiness.

Serious Side Effects

This drug can raise the risk for blood clots and blood vessel problems. It can raise the risk for stroke and heart attack. These problems can become fatal. Call your doctor right away if you have any of the following symptoms:

- pain in your calves or chest
- sudden shortness of breath
- coughing up blood
- severe headache

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Medication information

- vomiting
- dizziness
- faintness
- changes in sight or speech
- weakness or numbness in an arm or leg

Tell your doctor right away if your skin or eyes turn yellow or if you have unusual vaginal bleeding.

This drug can make depression worse. Tell your doctor if you have a history of depression.

Some women who have taken this drug have had miscarriage and pregnancy outside of the uterus. Others have reported birth defects.

Speak with your doctor for information about the risks and benefits of available treatments.

Other Information

Ask your doctor if this drug is right for you. Some patients should not take this drug.

Do not take this drug if you have any of the following conditions:

- allergy to progesterone or any other ingredients in Endometrin or similar drugs
- miscarriage where tissue is still in the uterus
- pregnancy outside of the uterus
- unusual vaginal bleeding
- liver problems
- known or suspected pregnancy
- blood clots or history of blood clots

Tell your doctor if you are breastfeeding. This drug passes into breastmilk. It is not known how this might affect a nursing baby.

Medication information

In women under age 35, the usual dose of this drug is 100 mg two or three times a day, starting the day after an egg is retrieved. This can continue for up to 10 weeks.

This drug is a tablet inserted into the vagina. Your doctor will teach you how to prepare and insert the drug. Do not use this drug at the same time as any other products placed into the vagina.

Always follow the instructions provided by your doctor.

http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=2ba50fa9-b349-40cb-9a4b-1af8faa4ec09
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