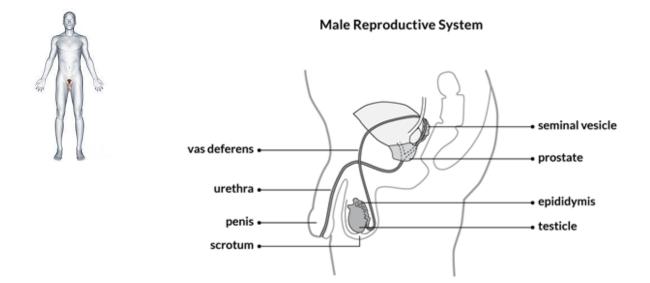


Preserving Fertility for the Future

Basics of the Male Reproductive System



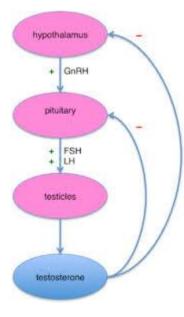
The male reproductive system includes:

- **testicles**: makes and stores sperm and makes the hormone testosterone (at puberty). The testicles are contained in the scrotal sac, which hangs beneath the penis.
- **duct system** (epididymis, vas deferens): transports sperm (seminal fluid) that allows the seminal fluid/sperm to travel.
- **glands** (seminal vesicles, prostate gland): provide the fluids that lubricates the duct system and carries the sperm. These fluids and sperm combine and travel through the urethra and out through the penis. The urethra is also how urine leaves the body, so it is also part of the urinary system.
- **penis:** The urethra runs through the penis. There is a small opening at the end of the penis. During sex, the seminal fluid (containing sperm) exit the penis through this opening.

When a boy reaches puberty, usually between ages 9 and 15, the pituitary gland releases hormones (luteinizing hormone/LH and follicle stimulating hormone/FSH) that 'tell' the testicles to begin making testosterone, the primary male sex hormone. The spike in testosterone starts the changes of puberty – the testicles and scrotum get larger; hair starts to grow in the pubic area, face, and armpits; the voice deepens; muscles get bigger; and there is usually a growth spurt. Puberty is also when the testicles start making sperm. They will make millions of sperm cells every day. The head of each sperm contains genetic material (DNA). Each sperm and egg cell has only half of the DNA found in other cells. If the sperm fertilizes an egg, the DNA of the sperm and the DNA in the female's egg will combine. This new

single cell (zygote) now contains all of the genetic material needed to start to form a human—half from the mother and half from the father. The zygote will continue to divide. Each cell created during this division will contain an exact copy of the DNA in the original zygote. After about the 4th week, the zygote becomes a blastocyst, and implants in the nutrient rich lining (endometrium) of the uterus.

The male reproductive system depends on hormones such as LH, FSH, and testosterone. Testosterone is an androgen hormone, along with DHEA (made in adrenal glands – precursor to testosterone and estrogen) and DHT (made in skin and liver from testosterone). Both females and males have androgens but males have far more.



Here is how hormones control male reproduction:

- The hypothalamus (part of the brain) releases GnRH*
- GnRH triggers the pituitary gland to release FSH and LH.
- FSH and LH stimulate sperm production and release.
- The testicles need testosterone is needed to make sperm.

*GnRH (gonadotropin-releasing hormone) is also called LHRH (luteinizing hormone-releasing hormone)

In addition to the characteristics that testosterone causes during puberty, during adult life, it also affects a man's libido (sexual desire) and sexual function.

How cancer treatments may affect your fertility

Cancer treatments can affect fertility. Your doctor may talk with you about whether or not cancer treatment may lower your fertility or cause infertility. If your doctor doesn't discuss fertility with you before treatment begins, you may need to start the conversation. It is important to learn how your cancer treatment(s) may affect your fertility before you start treatment, if possible.

Whether your fertility will be affected by cancer treatment may depend on multiple factors such as:

- ✓ your age
- ✓ your current and past medical history
- ✓ your current fertility (before treatment)
- ✓ the type of cancer you have and the treatment(s) you will receive
- ✓ the amount (dose) of your treatment and how long you are in treatment
- ✓ if you've completed treatment, the amount of time since your cancer treatment

Cancer treatments are important for your future health, but they may harm reproductive organs and glands that control fertility. Changes to your fertility may be temporary or permanent. Talk with your health care team to learn what to expect, based on your treatment(s).

Treatment	Effect in Males
Chemotherapy (especially alkylating agents- such as cisplatin, cytoxan, and dacarbazine) Hormone (endocrine) therapy leuprolide (Lupron®), goserelin (Zoladex®), triptorelin (Trelstar®), histrelin (Vantas®), degarelix (Firmagon®), relugolix (Orgovyx®), flutamide, bicalutamide (Casodex®), nilutamide (Nilandron®), enzalutamide (Xtandi®), apalutamide (Erleada®), darolutamide (Nubeqa®), abiraterone (Yonsa, Zytiga), aminoglutethimide (Cytadren®)	Can damage sperm in men and sperm- forming cells (germ cells) in young boys. Can decrease the production of sperm. Side effects may include hot flashes, night sweats, and erectile dysfunction.
Radiation therapy to or near the abdomen, pelvis, reproductive organs, or spine. Radiation dose and body part radiated can play a role in whether fertility is affected.	May lower sperm counts and testosterone levels, causing infertility. May destroy sperm cells and the stem cells that make sperm. For some cancers, the testicles can be protected from radiation with testicular shielding. Radiation therapy to the brain can damage the pituitary gland and decrease the production of testosterone and sperm.
Surgery	Surgery for cancers of the reproductive system and for cancers in the pelvis region can damage organs or nearby nerves and lymph nodes, and /or cause scarring, which can affect fertility. The size and location of the tumor are important factors in whether or not fertility is affected.
Bone marrow transplants, stem cell transplants	Involves receiving high doses of chemotherapy and/or radiation. These treatments can damage sperm and sperm- forming cells.
Other treatments	Talk with your doctor to learn whether or not other types of treatment such as immunotherapy and targeted cancer therapy may affect your fertility.

Questions for your doctor

- Could treatment cause or increase my risk of infertility?
- Could treatment make it difficult to become pregnant or carry a pregnancy in the future?
- Are there other recommended treatments that might not cause fertility problems?
- Which fertility option(s) would you advise for me?
- What fertility preservation options are available here? At a fertility clinic?
- Is birth control recommended? Is condom use advised?
- After treatment, what are the chances my fertility will return? How long might it take?

Coping and Support

For some people, infertility can be one of the most difficult aspects of their cancer treatment, but it may not affect you right away. The diagnosis and fear about treatments and the outcome may be more concerning. If you may want children at some point in the future, **it is important to discuss it with your doctor before you start treatment because you may need to act before treatment begins.** Talking about it and learning about your options may help you feel better. If you want support or even just discuss fertility with others facing the same challenges, Roswell Park has multiple options:

- professionally-led support groups such as the Young Adult Workshops, for those aged 18 to 39 who have cancer. For more information call <u>716-845-1664</u> or email <u>Ashley.King@RoswellPark.org</u>.
- online community <u>https://community.roswellpark.org</u>
- cancer coach program: <u>https://www.roswellpark.org/cancer-care/support/resource-center/cancer-coach</u>
- survivorship program: <u>https://www.roswellpark.org/survivorship</u>
- AYA fertility preservation program (collaborative with Buffalo IVF Associates): <u>https://www.roswellpark.org/young-adult-cancer/fertility-preservation</u>

What are the options to preserve fertility for males?

If you decide to try and preserve your fertility, there are options available. Talk with your doctor about the best option(s) for you. When possible, your doctor will work with a fertility specialist to develop a treatment plan for you that includes preserving your fertility. Discuss success rates, cost, and availability of the procedures listed below. The details can vary widely.

- Sperm banking (semen cryopreservation) is the most common and easy option for young men of reproductive age who may want children in the future. Semen is collected, checked over, frozen, and stored. Sperm call be frozen indefinitely.
- Testicular shielding (gonadal shielding) is a procedure in which a protective shield (cover) is placed on the outside of your body to protect the testicles from radiation.
- Testicular sperm extraction (TESE) is a medical procedure used to collect sperm when a male can't produce a semen sample. The semen is frozen for future use.
- Testicular tissue freezing (testicular tissue cryopreservation) is still considered an experimental procedure. It may be used for boys who have not gone through puberty yet and are at high risk of infertility.

Resources and additional information

- American Society for Reproductive Medicine: <u>https://www.reproductivefacts.org</u> Reproductive medical information as well as educational videos
- Buffalo Infertility & IVF Associates: <u>https://www.buffaloivf.com</u>
- LIVESTRONG Fertility: Understand your fertility risks and options, and get access to fertility preservation discounts. https://www.livestrong.org/what-we-do/program/fertility
- **Oncofertility Consortium:** Learn more about fertility preservation options, connect with a patient navigator and search a database of providers. https://oncofertility.msu.edu
- Resolve: The National Infertility Association: <u>https://resolve.org</u>
- Society for Assisted Reproductive Technology: <u>https://www.sart.org</u>
- Sam Fund: Support for young adult cancer survivors: <u>http://www.thesamfund.org</u>
- ReproTech Limited: Cryostorage: <u>https://www.reprotech.com</u>

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Terms

acrosome: a small cavity located at the head of the sperm that contains an enzyme that can penetrate the protective coating of an oocyte (female egg) so the sperm can fertilize the egg.

Assisted Reproductive Technology (ART): All interventions that include the in vitro handling of both human oocytes and sperm or of embryos for the purpose of reproduction. This includes, but is not limited to, IVF and embryo transfer ET, intracytoplasmic sperm injection ICSI, embryo biopsy, preimplantation genetic testing PGT, assisted hatching, gamete intrafallopian transfer GIFT, zygote intrafallopian transfer, gamete and embryo cryopreservation, semen, oocyte and embryo donation, and gestational carrier cycles. Thus, ART does not, and ART-only registries do not, include assisted insemination using sperm from either a woman's partner or a sperm donor.

blastocyst: The stage of preimplantation embryo development that occurs around day 5–6 after insemination or ICSI. The blastocyst contains a fluid filled central cavity (blastocoele), an outer layer of cells (trophectoderm) and an inner group of cells.

cryopreservation: Using very low temperatures to preserve biological material such as. gametes, zygotes, cleavage-stage embryos, blastocysts, or gonadal tissue.

diminished ovarian reserve: A term generally used to indicate a reduced number and/or reduced quality of oocytes, such that the ability to reproduce is decreased.

donor insemination: The process of placing laboratory processed sperm or semen from a man into the reproductive tract of a woman who is not his intimate sexual partner, for the purpose of initiating a pregnancy.

ectopic pregnancy (tubal pregnancy): A pregnancy outside the uterus, often in the fallopian tubes. A fertilized egg cannot survive outside the uterus and there is no procedure that can transfer the embryo into the uterus. If this type of pregnancy is allowed to continue, the embryo's growth will burst the fallopian tube and put the mother's life at risk.

embryo: The biological organism resulting from the development of the zygote, until eight completed weeks after fertilization, equivalent to 10 weeks of gestational age.

epididymis: A convoluted, highly coiled duct in males where sperm matures and are stored. The mature sperm travels from the testicles (where sperm is made) through the vas deferens, gets mixed with seminal fluid from the seminal vesicle, and goes into the urethra. Semen is ejaculated from the penis through the urethra.

erectile dysfunction: Inability to have and/or sustain an erection sufficient for intercourse fetus: The stages of development of an organism from eight completed weeks of fertilization (about 10 weeks of pregnancy) until the end of pregnancy

fertility: The ability to produce children.

fertility preservation: A type of procedure used to help keep a person's ability to have children. A fertility preservation procedure is done before a medical treatment that may cause infertility, such as radiation therapy or chemotherapy.

gonads: Organs that produce gametes (reproductive cells) such as a testicle or an ovary.

hypo: Prefix meaning low/under

hyper: Prefix meaning high/excess

infertility: The inability to produce children.

implantation: The attachment and subsequent penetration by a fertilized egg into the endometrium of the uterus. This process starts 5 to 7 days after fertilization of the egg.

In Vitro Fertilization (IVF): A sequence of procedures that involves extracorporeal fertilization of gametes. It includes conventional in vitro insemination and ICSI.

In Vitro Maturation (IVM): A sequence of laboratory procedures that enable extracorporeal maturation of immature oocytes into fully mature oocytes that are capable of being fertilized with potential to develop into embryos.

IntraCytoplasmic Sperm Injection (ICSI): A procedure in which a single spermatozoon is injected into the oocyte cytoplasm.

luteal phase defect: A poorly defined abnormality of the endometrium presumably due to abnormally low progesterone secretion or action on the endometrium.

Medically assisted reproduction (MAR): Reproduction brought about through various interventions, procedures, surgeries and technologies to treat different forms of fertility impairment and infertility. These include ovulation induction, ovarian stimulation, ovulation triggering, all ART procedures, uterine transplantation and intra-uterine, intracervical and intravaginal insemination with semen of husband/partner or donor.

pre-implantation embryo: An embryo at a stage of development beginning with division of the zygote into two cells and ending just prior to implantation into a uterus.

salpingectomy: The surgical removal of an entire Fallopian tube.

oocyte: The female egg

semen analysis: A description of the ejaculate to assess function of the male reproductive tract. Characteristic parameters include volume, pH, concentration, motility, vitality, morphology of spermatozoa and presence of other cells.

sperm: The male reproductive cell.

sperm motility: The percentage of moving spermatozoa relative to the total number of spermatozoa. **spontaneous abortion:** The spontaneous loss of an intra-uterine pregnancy prior to 22 completed weeks of gestational age. (May be called a miscarriage)

testicular sperm aspiration/extraction (TESA/TESE): A surgical procedure involving one or more testicular biopsies or needle aspirations to obtain sperm for use in IVF and/or ICSI.

total sperm count: The calculated total number of sperm in the ejaculate (semen volume multiplied by the sperm concentration determined from an aliquot of semen).

zygote: A single cell resulting from fertilization of a mature oocyte by a spermatozoon and before completion of the first mitotic division.