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Hello and welcome to another episode of The APAOG Podcast. I'm the show's hosting creator Morgan Bechtel, and today we'll be discussing infertility.

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Fertility, or the ability of a person to procreate or create an offspring, has been a subject of great importance throughout time for a long time, a woman's worth and value in society was measured by her ability to bare children. Monarchies relied on the ability of the royal line to continue, and societal expectations aside, infertility.

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Can be a devastating diagnosis to a person, but until diagnosis, many people don't know what fertility truly means or how it can occur. Today, we'll review the pathophysiology, common symptoms, diagnosis, and available treatment options.

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So listen close as we dive into the details of infertility. Infertility is defined as the failure to achieve pregnancy within 12 months of unprotected inner.

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Course or insemination in a patient less than 35 years old, or the failure to achieve pregnancy within six months in a patient 35 years or older. For many years, women were considered to be the sole responsibility for the fertility of a couple, but we now know that it takes 2 to tango, IE we need an egg and a sperm to make baby.

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When talking about the causes of infertility, I'm going to break them down into two main groups, biological female factors and biological male factors. We'll start with the biological female factors for.

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Infertility is found in up to 19% of heterosexual women with no prior births and consists of the inability to produce healthy eggs and impaired fecundity, which is the difficulty carrying pregnancy to term. There are several known causes of female infertility, and this includes ovulatory dysfunction, PCOS.

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Thyroid disorders. Hypogonadotropic. Hypogonadism.

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Gum prolactinomas, fallopian tube abnormalities and endometriosis. Now let's dive into each one in a little bit more detail. Ovulatory dysfunction is associated with approximately 40% of female infertility cases and is defined as the failure of the ovaries to consistently and reliably progress through the ovarian cycle.



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Regulate one oocyte per cycle. For more details on the menstrual cycle, take a listen to our menstrual cycle episode from Season 1. But how do we assess ovulation? We assess ovulation by measuring the LH surge, meaning luteinizing hormone.

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Via urine test, we also can use an ultrasound to monitor follicular development and measure luteal phase serum progesterone, typically around day 21 of the cycle.

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And also by graphing basal body temperature. Now next we'll talk about primary ovarian insufficiency, which was previously known as premature ovarian failure. Primary ovarian insufficiency is defined as the permanent cessation of menses prior to age 40 and there's many known causes including autoimmune diseases.

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A fragile X mutation and toxic medication.

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Ends chromosomal abnormalities and surgical destruction of ovarian tissue. Symptoms of primary ovarian insufficiency include things like oligomenorrhea, which is irregular, or inconsistencies, or amenorrhea, which is again that loss of menses.

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Symptoms also include hot flashes, night sweats, vaginal dryness and irritability.

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Make this diagnosis by measuring a day three FSH. If it's greater than 25 and is occurring with low or normal E2 on two separate occasions, we can diagnose primary ovarian insufficiency. We can also diagnose primary ovarian insufficiency if a patient has amenorrhea for greater than four months and there's no known pregnancy or other.

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Endocrine disorders like Addison's autoimmune.

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On that FMR1 mutation etcetera. As a cause the treatment for primary ovarian insufficiency mainly is treating the comorbidities. So we put patients on hormone replacement for menopausal symptoms and for bone health and for more episode on the symptomatic treatment of menopausal symptoms see the menopause episode from earlier in the season.

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For patients with primary ovarian insufficiency who desire.



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Pregnancy often the use of donor eggs called donated oocytes, are used. Now, one thing to note is that some individuals experience intermittent returns of ovulation, and there's about a 5 to 10% chance of pregnancy in this population. Next, we'll talk about PCOS, or Polycystic Ovarian syndrome now. This is the most common cause of ovulatory.

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Dysfunction and it occurs in approximately 4 to 6% of reproductive age women to make a diagnosis of PCOS, a patient must meet two of the three criteria, known as the Rotterdam criteria, and that includes oligo or anovulation, which is marked by a regular or absent menses. Clinical and biochemical signs of hyperandrogenism.

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Which is the hirsutism cystic acne elevated total testosterone, things like that. And of course, polycystic ovaries. On ultrasound, the first line treatment of infertility secondary to PCOS.

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Is the use of oral ovulation induction agents like Letrozole AKA Femara or clomiphene citrate, which is also called clomid HCG trigger shots like ovidrel and novarel are also used, and we'll talk a little bit more about these medications later. The second line treatment for infertility in PCOS patients includes injectable.

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Medications with IVF patients with PCOS have pretty good outcomes with IVF because they have many follicles.

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Meaning they have many.

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Eggs there is a higher risk of ovarian hyperstimulation syndrome in PCOS, patients and ovarian hyperstimulation syndrome.

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OHSS is when the ovaries swell and fluid leaks into the body. Now symptoms of mild OHSS include abdominal pain, bloating, weight gain and nausea. Next, we'll talk about Hypogonadotropic hypogonadism. This is when the hypothalamus, or the pituitary gland does not produce the hormones that signal to the testes in males.

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Or ovaries in females to produce sex hormones as a quick reminder, the hypothalamus makes GnRH Gonadotropin-releasing hormone, which triggers the pituitary gland to produce FSH, follicle-stimulating hormone, and.



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LH luteinizing hormone, which in biological females stimulates the ovaries to make estradiol and progesterone and biological males, triggers the testes to make testosterone and stimulates spermatogenesis.

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Causes of hypogonadotropic hypogonadism include disordered eating, extreme exercise, extreme stress, elevated prolactin from prolactinomas.

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Hyperthyroidism intracranial lesions, high doses or long term use of opioids or steroids and genetic conditions like Calaman syndrome, which is a genetic condition that causes delayed or absent puberty and little to no sense of smell. Symptoms of hypogonadotropic hypogonadism depends on the age of the patient.

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Mainly, if they've gone through puberty yet in children, symptoms may present as a lack of growth or sexual development.

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Meaning very late puberty or incomplete puberty in females. This includes lack of breast development and menstrual periods, and the males. This is a lack of testes and penis enlargement and retainment of higher pitched voice and lack of facial hair. Symptoms in adults may present as low libido amenorrhea increased fatigue, weight gain, mood changes.

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And of course, infertility diagnosis can be made by measuring serum FSH.

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LH estradiol, or testosterone levels treatment involves treating the underlying cause of the hypogonadotropic hypogonadism. But if symptoms persist after treatment, then gonadotropins can be used to induce ovulation. Next, we're going to talk about thyroid dysfunction and its role in infertility. Both Hypo and hyperthyroidism can cause menstrual irregularities.

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And ovulatory dysfunction. Hypothyroidism is treated with supplemental thyroid hormones, like levothyroxine. Hyperthyroidism is treated with thyroid suppressing medications like methimazole and propylthiouracil or PTU.

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It's important to remember that should pregnancy occur, PTU is preferred in the first trimester because methimazole is associated with birth defects, including aplasia, acutis, and esophageal atresia. However, it's recommended that physicians consider switching to methimazole after the first trimester because the risk of liver failure associated with PTU use is greater than the risk of congenital abnormalities.



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Next, we'll talk about Prolactinomas. Prolactinomas are the most common pituitary adenoma, meaning benign tumor that causes excessive production of prolactin.

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Higher prolactin levels results in a decrease in G&RH, which in course in turn decreases LH FSH, E2 and testosterone.

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Symptoms of a prolactinoma include galactorrhea, which is a milky discharge from the breast vision changes.

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Is which occurs when the tumor is pressing on the optic nerve, and symptoms of hypogonadism, as mentioned previously. We diagnose Prolactinomas first with the serum prolactin level, and then with a confirmatory brain CT or MRI. There are two main treatment options for prolactinomas and the treatment option depends on the size of the tumor. For smaller tumors, dopamine.

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Magnus, like Capicola line, bromocriptine and pergolide are used to decrease the production of prolactin for macroadenomas surgical removal of the tumor is indicated.

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Next, we'll talk about tube fact.

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Years, so two factors of infertility account for approximately 14 to 30% of couples with infertility, inflammation and scarring from prior public infections like PID, gonorrhea, and chlamydia, peritonitis, endometriosis and prior pelvic surgeries can impact the patency of the fallopian tubes and result in infertility.

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There are several ways to describe fallopian tube occlusions. 1 is by its location, either distal or proximal to the uterus.

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And by the amount of blockage, either partial or complete, distal occlusions include things like when the fibre or the finger like projections at the end of the fallopian tubes are stuck together. The fibre responsible for sweeping the newly released egg from the ovary into the fallopian tube.

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So of course, if those fibre stuck together, it kind of impedes this sweeping motion that allows it to travel into the fallopian tube.



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And subsequently, to the uterus, fibre adhesions can also cause a condition called a hydrocele, pinks, which is when the blockage of a woman's fallopian tube causes a fluid buildup and dilation of the tube at its end. When the fallopian tube is blocked, the cells inside the tube secrete a fluid that can escape. Therefore dilating the tube.

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It's important to note that partial occlusions can result in ectopic pregnancies.

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Since the sperm still has a chance, I mean, however small, of fertilizing the egg diagnosis of tubal abnormalities is made via a hysterosalpingogram, which is when contrast dye is inserted through the cervix to fill the uterus and show the patency of the uterus and fallopian tubes on X-ray imaging. Another method for diagnosing tubal.

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Abnormalities include something called a fend view, which is when water and air is injected into the uterus, and tubes and then ultrasound is used to visualize any abnormalities. The most invasive, but most definitive way to evaluate the patency of the fallopian tube.

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Is of course, with a surgical laparoscopy. There are two main treatment options for fallopian abnormalities. There are surgical options, like a neosalpingostomy, where a new opening is created in the fallopian tube to allow the egg to travel into the uterus, and the other option is IVF or in vitro fertilization, and this is an option because it really bypasses the fallopian tubes.

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A salpingectomy or surgical removal of the fallopian tubes is done prior to IVF. If there is a hydrocele.

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Links as that excessive fluid is thought to have a direct embryo toxic effect and thought that the tubal fluid may mechanically flush the embryo from the uterus. These complications of hydrocele pings are thought to reduce IVF pregnancy rates by as much as 50%. The next cause of infertility and biological females will talk about is endometriosis.

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And quick reminder that endometriosis is when endometrial tissue exists outside the uterus about 25 to 50% of infertile women have endometriosis and about 30 to 50% of women with endometriosis have info.

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Ability endometriosis causes infertility by distorting pelvic anatomy, reducing equality, and reducing implantation rates. Symptoms of endometriosis include things like dysmenorrhea, dyspareunia, dysphasia, dysuria, but up to 20% of patients are asymptomatic, and it's important to note that severity of symptoms do not correlate with the severity of disease.



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The initial diagnosis of endometriosis is clinical and is made by assessing symptoms and exam findings and some exam findings and endometriosis include things like.

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A fixed uterus, or ovaries on palpation and exam tenderness.

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On ultrasound, there may be endometriomas fixed ovaries, retrofixed uterus, and uterosacral thickening. close Laparoscopy is the only definitive diagnosis at the moment. The treatment of endometriosis-related infertility involves things like debulking surgery, the use of Lupron to suppress further endometrial growth, and IVF to learn more about endometriosis in a bit more.

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Quote.

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Detail. Check out our episode from earlier this.

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Reason.

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Lastly, there are cases of unexplained infertility where there is no cause identified after evaluation, and this occurs in up to 30% of couples with infertility.

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Empiric often starting with oral medications to aid in ovulation in combination with intrauterine insemination.

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However, if a patient prefers to just start IVF off the bat, of course that can happen. Now let's talk about infertility and biological males. Male infertility is the sole factor in 20 to 30% of infertile.

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Roles and it plays some contributing role or factor to overall infertility and approximately 50% of couples experiencing infertility.

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The most common cause of male infertility is testicular defects in spermatogenesis, which accounts for approximately 70 to 80% of cases. This includes a low sperm count called oligospermia or absence of sperm, azoospermia.



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And it's diagnosed via semen sample. Unfortunately, the most common cause of these abnormalities is idiopathic, meaning there's no identifiable cause, but other causes include things like chromosomal abnormalities like Klinefelter's. Congenital abnormalities can also affect sperm production, things like cryptorchidism or the undescended testicles.

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Myotonic dystrophy and androgen receptor disorders acquired abnormalities in sperm production includes things like varicoceles infection like viral orchitis from the mumps virus, which include alternating agents and anti androgens.

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Environmental toxins, tobacco use and even excessive heat anti-sperm antibodies can also result in oligo or azoospermia. The second most common cause of male infertility is idiopathic, which accounts for approximately 10 to 20% of cases. This means that the patient has had multiple normal semen analysis and they can achieve pregnancy with a partner.

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With no known fertility issues, the third most common cause of male infertility is endocrine and systemic disorders, which accounts for roughly 5 to 15% of male infertility. This includes any disorder affecting the hypothalamus or pituitary gland.

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That results in the reduction of gonadotropin releasing hormone and subsequent hypogonadotropic hypogonadism, the least common cause of male infertility is sperm transport disorders, which accounts for roughly 2 to 5% of cases. As a refresher on the male anatomy, immature sperm is made in the testes and it travels through a coiled.

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Cord like structure called the epididymis, which stores the sperm and helps mature when prepping for ejaculation. The sperm is then carried through a tube called the vas deferens to the seminal vesicle and prostate, which adds important nutrients and lubrication to help protect the sperm from the hostile environment of the female vagina and U.

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Lastly, the sperm travels to the ejaculatory duct into the urethra and eventually expelled, so abnormalities in sperm transport can occur with a absent or dysfunctional epididymis obstruction or congenital absence of the vas deferens. Sometimes there is a ejaculatory duct obstruction, which can cause low volume.

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Sperm, low sperm count and low motility. And of course, sexual dysfunction, like the inability to obtain or maintain an erection can cause infertility.





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Now that we've reviewed the causes of infertility, let's discuss the treatments approximately 2.3% of all infants born in the United States every year are conceived using assisted reproductive technology through several treatments for infertility, which include ovulation, induction, timed intercourse, intrauterine insemination.

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Vitro fertilization and embryo transplantation.

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We'll start with timed intercourse, intrauterine insemination, and intracervical insemination.

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As the title suggests, time intercourse insemination involves the strategic timing of intercourse and insemination to the window of time when the female partner is most for.

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Intracervical insemination is when the donor or partner sperm is inserted into the cervix and intrigued in. In insemination is when the donor or partners firm is inserted into the uterus. Now these methods are typically paired with ovulation induction agents, and we'll talk more about this in a moment. For this process, patients will either have ultrasound.

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Monitoring starting on day eight to 10 of their cycles in order to track follicular growth, or they'll begin ovulation predictor kits at home once ovulation occurs again, either indicated by a positive test or may trigger injection is given to stimulate ova.

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Position the patient proceeds with the insemination method. If they're going with timed intercourse, intercourse typically begins on again that first day of the positive ovulation predictor kit, and then every other day for a total of 3.

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Times. Now we'll.

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Move on and talk about ovulation. Induction. Ovulation induction involves the use of medications to help induce ovulation.

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And with the goal of increasing the likelihood of pregnancy, and this includes three major.



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The verse being clomiphene citrate AKA Clomid, which is the selective estrogen receptor modulator, typical dosing is between 25 and 100 milligrams. It's important to note that Cloman can't interfere with endometrial lining.

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And has a 7 to 8% risk of multiples, meaning giving birth to twins, triplets, etc. And the next medication often used is called letrozole or femara and it's an aromatase inhibitor. Typical dosing for this is between 2.5 and 10 milligrams and it may be more effective than clomid in patients with PC.

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Yes, there is also a lower risk of multiple gestations than clomid and less impact on uterine lining. Clomid and Femara are administered on days 2 through 6 of the cycle.

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And we try and monitor follicle development if possible. As mentioned above, it's recommended that patients have intercourse on the first day of their positive ovulation predictor kit and every other day for three times in total, in order to optimize chances of pregnancy. Sometimes an HCG trigger shot like overdrill and overill are used to make the bodies LH surge.

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Which causes an egg to mature and be released from the follicle. The last group of medication used for ovulation induction are.

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This typically involves injectable FSH or a combo of FSH. LH during a number of protocols for the type, dosing and timing of ovulation induction with kinetic tropicans and the protocol used will depend on each individual patient's situation and healthcare providers preferences. There is a high risk of multiples when using the gonadotropin, so an ultrasound.

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Is used to monitor follicular growth because multiple large follicles increases the risk of multiples and ovarian hyperstimulation.

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Syndrome.

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Next, we'll talk about in vitro fertilization or IVF. This is a process by which ovulation is stimulated and egg is retrieved and then fertilized outside the womb. Prior to IVF, the patient and their partner will complete a litany of blood tests, including blood typing, Pap smear, STI testing that includes HIV, syphilis, hepatitis C.



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And hepatitis B testing. Certain genetic testing is also recommended to screen for things like cystic fibrosis, carrier status and other genetic conditions based on family history. During IVF, a patient undergoes controlled ovarian stimulation using injectable gonadotropins to stimulate follicular.

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Growth. But medications are given to prevent ovulation, and this includes GnRH antagonists and medroxyprogesterone acetate. Now, the idea being that we want the follicle to grow, but we want to be able to retrieve the egg before it's expelled from the ovary during ovulation. Once the follicles are around 20mm in size.

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The patient will take a trigger injection. Now, HCG is usually used for older patients or people who have responded poorly in the past to IVF. And Lupron is, as mentioned before, usually preferred for PCOS patients or people with many follicles.

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To prevent OHSS or ovarian hyperstimulation syndrome, 36 hours post trigger injection, the patient undergoes an egg retrieval. This is a 10 to 20 minute procedure that's typically performed in office under anesthesia and it's a transvaginal probe with a long 17 gauge needle with a suction tubing.

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Is inserted into the vagina. The needle goes through the vaginal wall into the ovary, puncturing each follicle and draining the fluid and oocyte inside. Once oocytes are retrieved, they're fertilized in the lab, using partner or donor sperm, and the fertilization occurs in two ways, the first being conventional insemination.

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And this is when healthy sperm and mature eggs are mixed and incubated overnight. The next is intracytoplasmic sperm injection, or ICSI. In ICSI, a single healthy sperm is injected directly into each mature egg, and this is often used when semen quality or number is a problem.

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Lower fertilization attempts during prior IVF cycles.

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Failed. Once fertilized, zygote is cultured for five to six days until it reaches the blastocyst stage, which again, a blastocyst is a rapidly dividing ball of cells, and it's considered the stage before it's an official embryo. At this point, the blastocyst is either preserved for future use or used for immediate transfer. If freezing embryo is, patients can opt to do genetic testing.

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Using trophoblast biopsy which can tell patients the sex of the embryo.



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And aneuploidy and presence of specific genetic mutations like bracca, huntingtons risks and complications of IVF include things like multiple births, premature delivery and low birth weight, ovarian hyperstimulation syndrome, miscarriage, which the rate of miscarriage for women who conceived using IVF with fresh embryos is similar to that of women who conceived.

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Around 15 to 25%, but that risk increases with maternal age, other risk and complications of IVF include complications from the egg retrieval procedure that includes infection, bleeding, possible perforation of either the bowel, the bladder, blood vessels or ovarian torsion. Atopic pregnancy is another complication about two to 5% of women who use IVF.

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Will happen at topic pregnancy and of course, stress is definitely a complication.

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Using IVF can be financially, physically and emotionally draining.

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Lastly, we'll talk about embryo transfer. Now. This is the process of transferring an embryo, either fresh or previously frozen, into the uterus of the patient or their gestational carrier. Transfer cycles can be natural or medicated.

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A natural embryo transfer is when the transfer is timed using a patient's natural menu.

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Cycle and occurs during the luteal phase. A medicated embryo transfer is where medications are used to mimic a natural menstrual cycle, meaning a patient has three weeks of exogenous estradiol and then five days of progesterone prior to embryo transfer. Progesterone helps prepare the uterine lining for implantation and is usually continued until pregnancy test results return.

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Or sometimes for several weeks after if indicated.

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The procedure is performed the patient oblique, although sometimes patients are medicated, the Valium using a transabdominal ultrasound, a catheter, is advanced past the cervix to the upper uterine cavity and the embryo that's contained in a special.

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Nice fluid is injected into this area. The number of embryos transferred is typically based on age and the number of eggs retrieved. Since the rates of implantation is lower for older women, more embryos are



usually transferred, is successful, and embryo will implant into the lining of the uterus about 6 to 10 days after egg retrieval. And it takes about 9:00 to 12:00.

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Before pregnancy can be detected, the society for reproductive Technology, or SART National Summary report for 2020 states that for women under 35, the percentage of live births via IVF is around 54.5%.

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For women who are between 35 and 37, the success rate drops to 39.8 for 38 to 40. It drops to 26.1% for 41 to 42, it drops down to 13.3%, and for women greater than 42, the success rate drops to just 4%. Factors that affect the success rates of IVF.

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Include things like decreased ovarian reserve, poor embryo quality and the age of the patient.