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Hello and welcome to another.

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Episode of the APAOG podcast.

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I'm the shows host and creator, Morgan, Bechtel, and today we'll be diving into The Dirty details of endometriosis. We'll talk about its discovery heavy on the air quotes, its proposed pathophysiology, common symptoms, complications, diagnosis, and treatment options.

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Endometriosis is a condition that plagues many uterus owners and can cause physical and psychological pain. It's my hope that by educating patients and providers on the subject that will help dispel the shroud of mystery that seems to surround this condition and show that there is hope to be had so.

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Listen close as we discuss the ins and outs of endometriosis.

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Let's start by defining what endometriosis is. Endometriosis is the presence of endometrial tissue, meaning the tissue that makes up the inner layer of the uterus that's located outside the uterus.

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Globally, endometriosis affects approximately 10% of patients of reproductive age. It's estimated that approximately 50% of patients who present with infertility and about 21% of patients present with chronic pelvic pain have endometriosis. The peak prevalence of endometriosis occurs in those between 25 to 35 years of age.

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It was a man, as history often records named John A Sampson, who coined the term endometriosis after in 1927. He discovered that while operating on a woman during her menstruation period, that peritoneal lesions were bleeding. Upon further testing, he was able to show that these lesions were, in fact, endometrial tissue growing outside of the uterus.

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Doctor Sampson was also the first to propose the theory for the pathogenesis of this condition, called retrograde menstruation, meaning that endometriosis occurred as a result of the menstrual tissue being regurgitated back up the fallopian tubes and into the peritoneal cavity.

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Other mechanisms have been proposed, such as peritoneal menoplasia.

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Transportation through the veins or lymphatics the presence of embryonic vestiges and transformation of bone marrow and endometrial stem cells. But menstrual regurgitation with the subsequent implantation of these endometrial cells under facilitating circumstances, can still explain most ectopic locations.

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As stated before, retrograde menstruation is the most common theory of ectopic endometrial.

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Cells evidence supporting retrograde menstruation comes from the observation that the incidence of endometriosis is increased in girls with genital tract obstructions that prevent the drainage of menses through the vagina and therefore increases total reflux. However, while up to 90% of females that have retrograde menstruation most don't develop endometriosis.

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Which kind of suggests that there's additional factors that are involved. The endometrial lesions are typically located in the pelvis, but they can occur in multiple sites, including the bowel, the diaphragm, and the pleural cavity. Symptoms of endometriosis include significant dysmenorrhea or painful periods.

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Heavy and regular bleeding, chronic abdominal pain, pelvic pain and again chronic meaning it's lasting longer than six months and this pain may even radiate to the back or upper thighs. Patients can also have painful bowel movements or urination during menses. Patients can also have dyspareunia, or pain of sex, as well as fatigue and depression.

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Once endometriosis is established, the process appears to cause symptoms through inflammatory changes now endometriosis related pelvic pain is associated with increased production of inflammatory and pain mediators as well as neurologic dysfunction.

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An increase in nerve fibers and an imbalance of sympathetic and sensory nerve fibers have been demonstrated in individuals with endometriosis. Related pain, proposed mechanisms for pain symptoms include estrogen acting as neuromodulator that selectively repulses the sympathetic axons while preserving the sensory innervation.

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Also, inflammation that stimulates peripheral nerve sensitization and chronic pain inducing changes in the central nervous system. Now it's important to note that up to 20% of patients have a silent endometriosis, meaning they have no symptoms and are often not diagnosed until they experience infertility.

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It is also important to note that the severity of symptoms does not correlate to the severity of the disease.

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Now, there are certain signs on physical exam that might suggest endometriosis, and this includes a fixed or retroverted uterus tender uterosacral ligaments, and a uterosacral and or cul-de-sac nodularities, endometriosis can lead to several complications, including infertility, subfertility, and ectopic pregnancy.

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The mechanism for subfertility appears to involve anotomic distortion from pelvic adhesions and endometriomas and or production of substances like prostanoids cytokines, growth factors that are hostile to normal ovarian function, ovulation, sperm motility, fertilization, implantation, etcetera. This results in scarring of the fallopian tubes, reduced ovarian reserve.

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And impaired oocyte quality for those who do get pregnant, there appears to be an increased risk of pregnancy complications. There was a meta analysis of 33 studies that included over 3 million pregnancies.

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That reported that among those who conceived spontaneously endometriosis was associated with placenta previa, cesarean delivery, preterm birth and low birth weight. In two large retrospective population based studies, including over 82,000 and 91,000 total births, respectively.

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Individuals with endometriosis have an increase.

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risk of preterm birth, preeclampsia, and cesarean birth, when compared to individuals without endometriosis there appears to be an increased risk of ovarian cancer, particularly endometroid and clear cell types in individuals with ovarian endometriosis, but not for patients with peritoneal or deeply infiltrating endometriosis. It's unclear if the increased risk of ovarian cancer.

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Applies to superficial ovarian endometriosis lesions, endometriomas, or both. Some ovarian endometriosis lesions harbor genetic changes.

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That may be found in ovarian cancer illusions, future molecular analysis of surgical ovarian endometriosis specimens may help to identify patients at higher risk of developing ovarian cancer, while the relative risk of ovarian cancer may be increased, the absolute risk of developing ovarian cancer from ovarian endometriosis remains low.

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While, there appears to be an association between endometriosis and an endometrial ovarian cancer.

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Endometriosis is not considered a pre malignant lesion and surveillance for ovarian cancer is not recommended in patients with endometriosis. There is no high quality data indicating that prophylactic removal of endometriosis lesions reduces the risk of endometrial ovarian cancer. However, the use of oral contraceptive pills does decrease.

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The risk of ovarian cancer in all users.

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Although we've discussed the signs and symptoms and complications of endometriosis, how do we diagnose the?

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Dang thing, well, the diagnosis is an initially made via clinical suspicion as there's no current pathognomonic laboratory findings for endometriosis. However, there is some more research being done into different serum and endometrial inflammatory markers in order to find kind of a a better non invasive test. But for now none available.

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A transvaginal ultrasound is commonly used to evaluate individuals with suspected endometriosis. If it's not appropriate or available, other acts of ultrasounds like transabdominal or transperineal or MRI, may be helpful.

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Transvaginal ultrasound is generally preferred, though, as it's more readily available and lower cost compared with MRI, although sensitivity and specificity are similar, particularly for rectovaginal and endometriosis. However, the sensitivity and specificity of ultrasound is dependent in part on the sonographer endometriomas can be seen on ultrasound as well as other signs, such as fixed pelvic organs or uterosacral thickening, but these are often missed unless the sonographer is trained specifically for endometriosis, the gold standard diagnosis is laparoscopy to visualize the lesions and take samples for biopsy. Typical indications for surgical exploration include:

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The evaluation of severe pain or other symptoms that limit function, persistent pelvic pain that does not respond to medical therapy, treatment of anatomic abnormalities such as symptomatic ovarian cysts, rectovaginal nodules or bladder lesions. Given that endometriosis lesions, excluding endometriomas, can regress in response to hormonal treatment, laparoscopy is not typically performed during initial hormone treatment for patients with a clinical diagnosis of endometriosis. In order to minimize the risk of under diagnosis of the disease.

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More on the treatment of endometriosis in a bit.

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We stage the disease based off of the American Society for Reproductive Medicine or the ASRM scoring system. So stage 1 is considered minimal disease, which is characterized by isolated implants and no significant adhesions. Stage 2 is considered mild endometriosis and it consists of superficial implants that are no less than 5 centimeters in aggregate and are scattered on the peritoneum and ovaries. Again, no significant adhesions are present.

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Stage 3 is where we get to moderate disease and this patient exhibits multiple implants, both superficial and deeply invasive. They have peritubular and periovarian lesions that might be evident. Lastly, stage 4 is considered severe disease and is characterized by multiple superficial and deep implants including large ovarian.

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Endometriomas filmy and dense adhesions are also usually present, so you have a patient who you suspect has endometriosis. What treatment options can you offer them? The first line for pain, of course, is NSAIDs as the pain is suspected to be inflammatory in nature.

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Next, we utilize combined oral contraceptive pills, usually starting with a pill that contains 20 micrograms of ethanol-estradiol, given in a continuous dose fashion. While both cyclic and continuous dose hormonal regimens appear to be effective at reducing endometriosis related pain, 2 systemic reviews, one with meta analysis.

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Reported that continuous combined oral contraceptive regimens were more effective at reducing pain.

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Symptoms than cyclic combo contraception regimen. Other hormonal contraceptives include DMPA or depot-medroxyprogesterone acelate, norethindrone acetate, and levonorgestrel or etonogestrel IUDs can be

used for more details on these treatment options, see are two-part episode from Season 1 on contraceptives.

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It's super important that patients who may want children in the future to be started on some form of the suppressive therapy. Again, typically the combined oral contraceptives and they they stay on it until they want to try to get pregnant. This can slow disease progression by preventing the cyclic growing and sloughing of the endometrial lesions.

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If hormonal contraception has been trialed or is not an option for this patient, think you know, maybe stroke, breast cancer, etcetera, GnRH analogs meaning agonist and antagonists are utilized now quick reminder that GnRH stands for gonadotropin-releasing hormone, the hormone that's made by the hypothalamus that causes the pituitary gland to release luteinizing hormone and follicle stimulating hormone, which in turn tells the ovaries to make estrogen and progesterone.

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More on the function of these hormones in the menstrual cycle episode from season 1 GnRH agonists work by desensitizing the GnRH receptors on the pituitary gland. The constant activation of the GnRH receptors effectively wears out the receptors to the point where the production of GnRH by the hypothalamus is suppressed. Medications in this drug class

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include buserelin, goserelin and leuprolide and they come in various forms including nasal sprays or injections with daily, weekly and monthly administration options. Now it can take several weeks to notice symptom improvement and these medications are.

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Generally used for less than six months, and definitely no more than a year. Unlike combined oral contraceptives, which only slow progression of the disease, GnRH agonist can actually reduce the number and size of endometriotic lesion. However, any scarring or damage that's already been done will not be reversed. Now there's GnRH antagonist which.

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These medications work by blocking the GnRH receptors. Medications in this drug class include elagolix and relugolix, both which are available in pill form now. The benefit of these drugs is that they work immediately. There's no, you know, couple week long waiting period to to see benefit.

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The side effect of GRnH analogs includes decreased bone mineral density and sinus symptoms of hypogonadism. Remember, that's hot flashes, night sweats, vaginal dryness, etcetera.

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These symptoms occur due to the increase in estrogen and progesterone. Providers can use add back therapy of supplemental estradiol and norethindrone with the GnRH meds in order to try to prevent bone mineral density loss and the symptoms of hypogonadism. Other options for treatment include aromatase.

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inhibitors for those of you who may not know, including me when I started researching this episode, aromatase is an enzyme that is found in a lot of places. But you know more commonly in the fatty tissues that is responsible for a key step in the biosynthesis of estrogens. And it's thought to be more abundant in the endometrial implants. It's thought by stopping the action of aromatase., the cycle of new endometrial tissue growth is essentially halted.

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Now, some examples of aromatase inhibitors include and you're going to have to forgive me because I'm going to put you this one amino glutethimide vidrosol, formestane, anastrozole and letrozole like the GRnH analogs. Long term use of the aromatase inhibitors is associated with an increased risk of osteoporosis and bone.

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Fractures and it's considered as treatment for only the severe cases of endometriosis. Another option for the treatment of severe endometriosis cases includes laparoscopic debulking surgeries.

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This is often a last resort option given the invasive nature and risk of complications of the surgery, but it can be very useful and even necessary for reducing patient symptoms. It's important to try and see a surgeon who specializes in endometriosis. Some studies have shown that surgery to remove endometriosis can be more damaging to fertility than the endometriosis itself.

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This is due to damage of the ovaries during surgery, which of course negatively impacts ovarian reserve and lastly, a hysterectomy can also be performed as a last resort treatment for endometriosis.

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like any chronic medical condition, a multidisciplinary approach to the treatment of endometriosis is often required for pelvic pain and dyspareunia. Patients may benefit from pelvic floor, PT, or sessions with a sexual therapist, a referral to a reproductive endocrinologist is also recommended to evaluate the patient's potential risk to fertility.

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And or referral to counseling services is preferred to help patients manage not only their chronic pain, but also the stress that comes with living with their chronic illness.