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Disorders of the Uterus

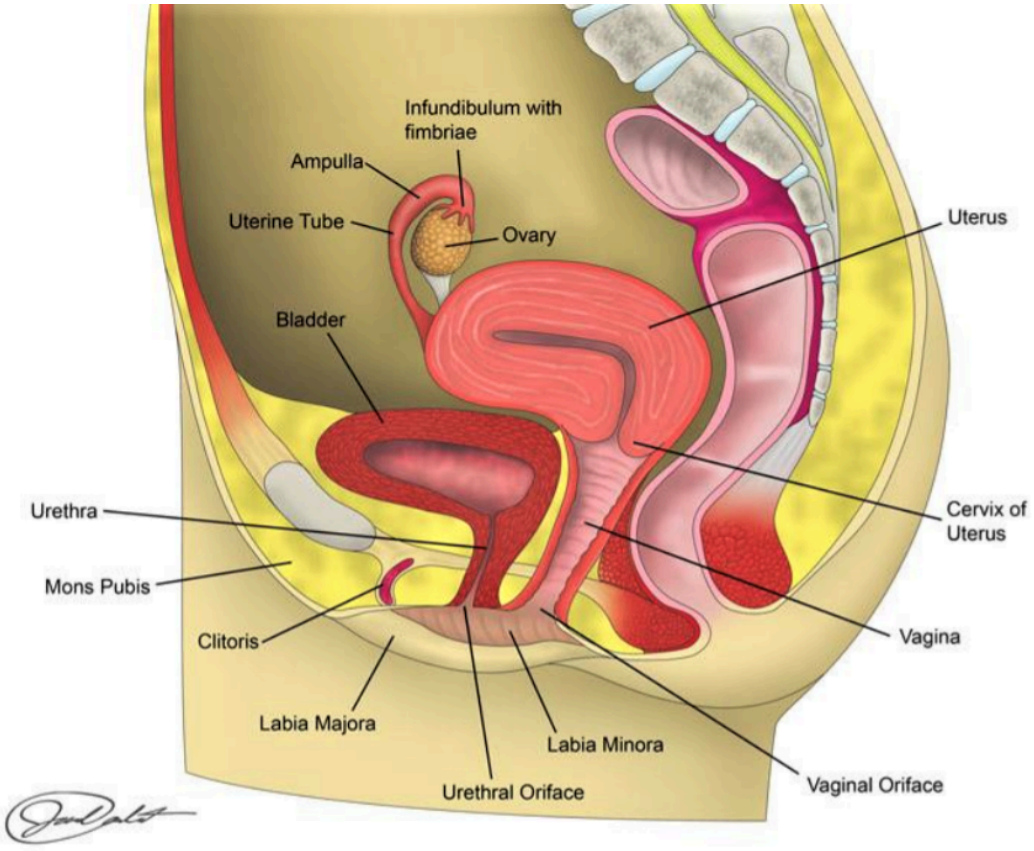
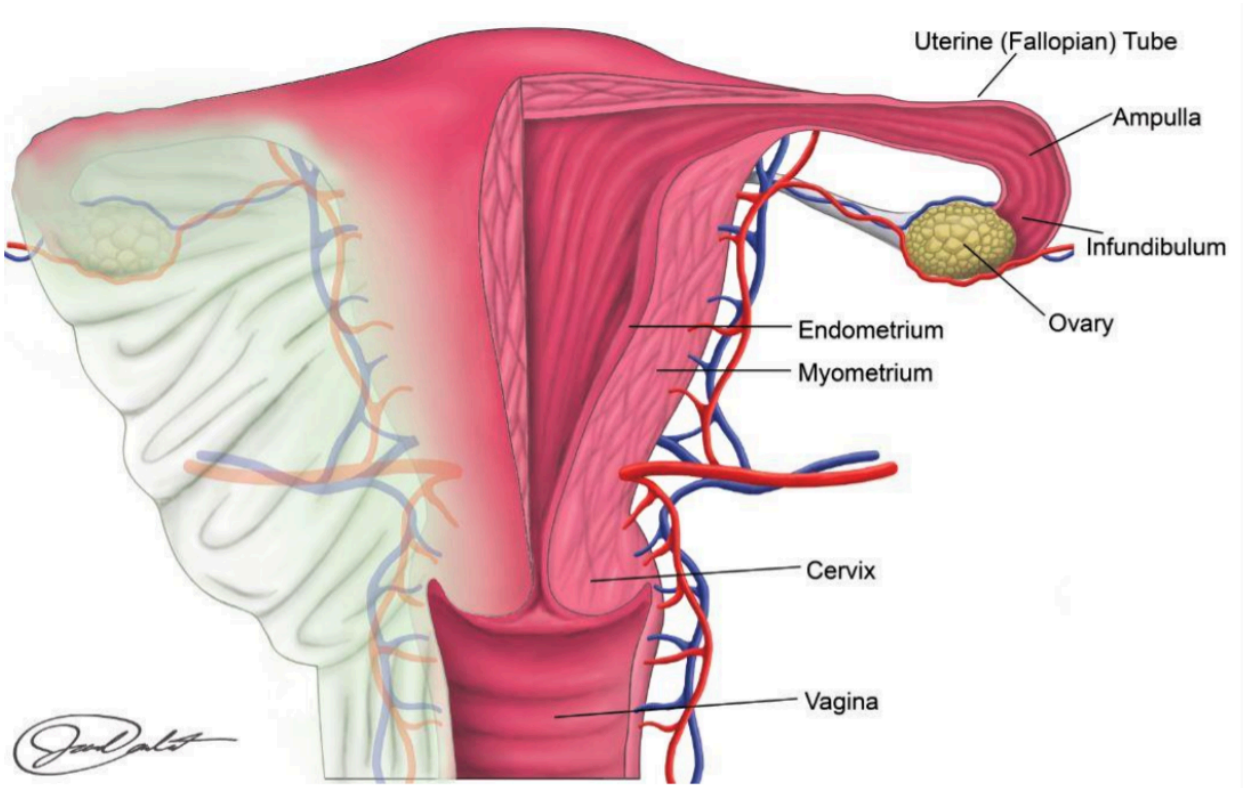


Image by Jared Cardinet BYU-Idaho W15



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Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) is inflammation of the female reproductive organs due to bacterial infection. Some microorganisms such as *Gonococcus, Staphylococcus, Streptococcus, Chlamydia,* and some anaerobes can ascend through the lower reproductive organs (vagina and cervix) to the uterus. From there, infection can spread to the fallopian tubes, ovaries, and pelvic cavity.

Common predisposing factors for PID include being less than 25 years of age, being younger than 15 years old at first intercourse, use of IUD or oral contraceptives, multiple sex partners, frequent vaginal douching, and a history of sexually transmitted diseases (STDs). Common symptoms of PID include abdominal pain, dyspareunia (painful intercourse), purulent cervical discharge, vaginal discharge, burning with urination, irregular menstruation, fever, and increased WBC count. PID is diagnosed by observation of these symptoms and cervical tenderness upon examination.

Problems due to chronic or untreated PID include scarring that can lead to chronic pain, infertility, and complications with pregnancy. The most common treatment of PID is antibiotics.

Endometriosis

Endometriosis is defined as ectopic endometrial tissue located outside of the uterus. Common locations of this ectopic endometrial tissue include the ovaries, uterine ligaments, fallopian tubes, peritoneum, bladder, rectum, and intestines. This inappropriately deposited endometrial tissue responds to the hormones that regulate the uterine cycle. Therefore, during the proliferative phase, this endometrial tissue will grow and during menses it can break down, bleed, and cause inflammation.

Risk factors for developing endometriosis include a family history of the disease, early age of menarche, and shorter menstrual cycles. Common clinical features and symptoms of endometriosis include dysmenorrhea, pelvic pain, and infertility.

We do not know exactly what causes endometriosis or how endometrial tissue travels to areas where it does not belong; however, there are three theories that explain this phenomenon:

1. **The regurgitation/implantation theory:** This theory basically implies that sloughed off tissue moves in a retrograde fashion to deposit fragments of endometrial cells on extra-uterine structures. Retrograde menses is not uncommon in women, but it is unknown why endometrial fragments would successfully implant in some women and not others.
2. **The vascular or lymphatic theory:** This theory suggests that endometrial cells enter the lymph or vascular circulation where they travel to extra-uterine structures and implant. Again, it is unknown why these traveling cells would have more success implanting in extra-uterine tissues in some women more than others.
3. **The metaplastic theory:** This theory suggests that dormant endometrial progenitor cells are deposited in multiple extra-uterine areas during development. These cells are then removed or restricted from completing their maturation to become functional endometrial cells in some women, but in others they are allowed to mature and develop leading to endometriosis.

Ectopic endometrial tissue is different from the endometria of a healthy uterus in that it releases inflammatory mediators including high levels of prostaglandin E2 (PGE2). Endometrial tissue also expresses high levels of aromatase which is required for estrogen synthesis. It is known that PGE2 increases the activity of aromatase, thus facilitating increased estrogen synthesis at the site of endometrial tissue. This increased estrogen then signals increased endometrial proliferation.

Common treatment for endometriosis include NSAIDs, progesterone and progestin-based contraceptives, and both GnRH analogs and antagonists. NSAIDs help reduce pain by inhibiting the production of prostaglandins, including PGE2, which stimulates nociceptors; and PGF-2α, which stimulates uterine cramping. Progesterone and progestins (synthetic progesterone analogs) directly and potently inhibit the release of GnRH. Normally, GnRH stimulates FSH and LH release which subsequently stimulate estrogen production from the ovaries. During the proliferative phase, estrogen, a potent mitogen stimulates emdometrial growth. Thus, decreased GnRH will diminish estrogen productions and suppress endometrial growth. In a similar fashion, both GnRH analogs and GnRH antagonists suppress estrogen synthesis. GnRH must be released in a pulsatile manner for proper FSH and LH release. When GnRH analogs are used, the GnRH is not pulsatile, but continuous; and although this causes an initial increase in FSH and LH, the constant stimulation of GnRH receptors ultimately desensitizes the pituitary to GnRH stimulation and FSH and LH levels fall. Similarly, GnRH antagonists block the GnRH receptors on the pituitary resulting in the same effect. Like progestin treatment, decreased FSH and LH levels results in decreased estrogen and its stimulatory effect on endometrial growth.

Adenomyosis

Adenomyosis is characterized by the abnormal deposit of endometrial tissue within the myometrium (muscle layer) of the uterus. In a way, adenomyosis is a subtype of endometriosis, but it is specific to the myometrium rather than extra-uterine tissues. This condition is also called endometriosis interna.

The cause of adenomyosis is unknown, but it is associated with uterine trauma. The current theory is that trauma may introduce a break in the barrier between the endometrium and the myometrium. Unlike endometriosis previously discussed, adenomyosis is more common in multiparous women (women who have had multiple children) in their late 4^{th} or 5^{th} decade. This may be because they have had more opportunities to experience uterine trauma.

The symptoms of adenomyosis can vary widely from no symptoms at all to severe and debilitating pain. The pain is worse during menstruation, which is generally heavy. Symptoms resolve with menopause.

Treatments for adenomyosis are generally divided into uterine sparing or non-sparing techniques. Uterine sparing strategies involve hormone manipulation similar to the treatments used for endometriosis. There are surgical techniques as well that involve ablation or resection of endometrial tissue. Uterine non-sparing treatment involves removal of the uterus in a procedure known as a **hysterectomy**. Treatment options will depend on the patient's age, fertility options, and severity of symptoms.

Endometrial Cancer

Endometrial cancer is the most common gynecological (female reproductive tract) cancer among women. It is more prevalent in postmenopausal women ages 55 to 65 years old. The major symptom of endometrial cancer is unexpected postmenopausal bleeding. Endometrial cancer is also possible in premenopausal women and often presents with abnormal bleeding in between periods. The bleeding is typically not painful. An endometrial tissue biopsy is needed to confirm cancer. Catching the cancer early leads to a much better prognosis because the cancer growth is relatively slow in its early stages. Later signs of endometrial cancer can include cramping, pelvic pain, and enlarged lymph nodes.

There are two types of endometrial cancer:

1. **Type 1 endometrial cancer** arises in women with estrogen excess. It is the most common type and tends to develop in women who are perimenopausal and have the following risk factors that lead to increased estrogen, which then stimulates endometrial proliferation: Estrogen replacement therapy, obesity, anovulation, ovarian androgen excess, chronic progesterone deficiency, nulliparity (never had children), polycystic ovarian syndrome, diabetes, early menarche, and late menopause.
2. **Type 2 endometrial cancer** occurs in older women in a setting of endometrial atrophy. Estrogen excess is not found. This type of endometrial cancer tends to have a poorer prognosis than type 1.

Uterine Leiomyoma

Uterine leiomyomas (also called **fibroids**) are the most common female reproductive tumor. They are benign, non-cancerous neoplasms of smooth muscle origin. These tumors can be seen as irregular projections on the surface of the uterus. In cases where they grow large enough, they may impinge or obstruct other nearby structures or tissues.

Leiomyomas are often asymptomatic and may only be discovered during pelvic examinations. In rarer cases, leiomyomas cause heavier bleeding during menses, increased urinary frequency, rectal pressure and constipation, abdominal pressure and extension, and sometimes abdominal or pelvic cavity pain.

Uterine leiomyomas can increase in size during pregnancy or exogenous estrogen therapy. Rarely, leiomyomas can interfere with zygote implantation. These tumors tend to regress with menopause. In cases where they cause excessive bleeding, pain, or other symptoms, surgery may be performed to remove the tumor and save the uterus for future pregnancies. A hysterectomy may be performed as well.