

Endometriosis — Causes and Symptoms

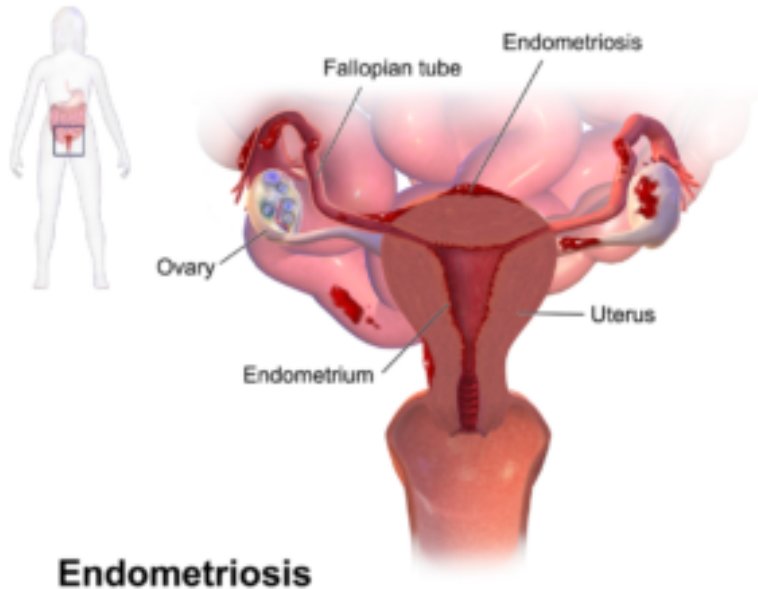
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Endometriosis is a common disease in which ectopic normal endometrial tissue is implanted outside the uterus. The ovaries along with other pelvic organs can be involved. While laboratory investigations have a limited utility in the diagnosis, imaging and laparoscopic evaluation can be used to confirm the diagnosis of endometriosis. Medical treatment of endometriosis involves hormonal manipulation with oral contraceptive pills, danazol, GnRH analogs, and progesterone supplementation. Surgical treatment can be either conservative or radical, depending on whether reproduction is wished to be preserved or not.



Definition of Endometriosis

Patients with endometriosis have histologically and functionally normal **endometrium** implanted in organs other than the uterus. These organs and locations include the ovaries, the cul-de-sac, the broad ligament, rectum and sigmoid colon, and the urinary tract and the degree of implantation vary, from superficial to deep into the organ involved. Thoracic endometriosis is associated with recurrent pneumothoraces at times of a menstrual period, termed **catamenial pneumothorax**.



[Image:](#) "Endometriosis." by Blausen.com staff. "Blausen gallery 2014". Wikiversity Journal of Medicine. DOI:10.15347/wjm/2014.010. ISSN 20018762. - Own work. License: [CC BY 3.0](#)

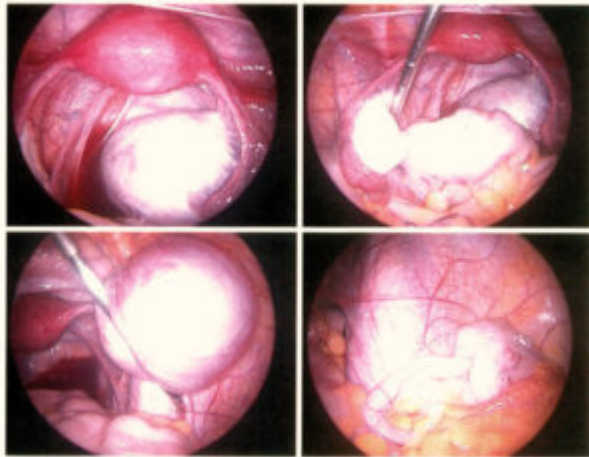
Epidemiology of Endometriosis

Endometriosis is a common condition encountered in approximately **10%** of the population in the United States. The diagnosis of endometriosis is dependent on **biopsy** and **histological examination**, which makes any figures to estimate its incidence an underestimate.

In certain populations, the prevalence of endometriosis is known to be high. For instance, up to 50% of women who are **infertile** have endometriosis. Additionally, 80% of women with **chronic lower abdominal pain** or **painful intercourse** have endometriosis as their etiology.

The prevalence of endometriosis is not different between different ethnicities. The typical age of these patients ranges **between 25 and 30 years**. Additionally, the location of endometriosis involvement seems to be age dependent. For example, women who are older than 35 years of age tend to have involvement of organs outside the pelvis, while women who are younger than 20 years usually have some form of an anatomical abnormality in their reproductive tract.

Etiology of Endometriosis



[Image](#): "Ovarian cyst / Endometriosis" richie graham - originally posted to Flickr as jensute. License: [CC BY 2.0](#)

The etiology of endometriosis is not known but several **risk factors** have been identified.

Family history of endometriosis seems to put the patient at an increased risk of developing the disease suggesting a strong **genetic predisposition**.

Additionally, women who started their **menarche at an early age**, with menstrual cycles less than 27 days and with menstruation flow above 7 days are at an increased risk of developing the disease. This later observation can be explained by the fact that endometriosis is a condition that is **highly dependent on estrogen** and that is why the symptoms of the disease disappear in menopausal women.

Also, younger women who have **anatomical abnormalities in their reproductive tract** are at an increased risk of developing endometriosis. These anatomical abnormalities make endometrium shedding during normal menstruation more difficult and eventually lead to **endometrial metastasis and implantation** to other adjacent organs.

Finally, some postulates that endometriosis is an **autoimmune disorder** and evidence of immune dysregulation does exist in these patients. These patients have increased **humoral immune response**, antibodies against the endometrium in their serum, and decreased cellular immunity response manifested as impaired T-cell and natural killer cell responses.

Pathophysiology of Endometriosis

Once the endometrial tissue **metastasizes** to other organs, the **lower pelvic organs** are the most likely to be involved. This is thought to be related to gravity effect as these lower organs are more likely to have the deposits on them than organs in the upper abdomen.

It is important to note that this **endometrial tissue is normal** in function and histology, which differentiates it from endometrial cancer. Endometrial implants respond as normal endometrium to the cyclic hormonal changes.

Just like the **normal menstruation**, the ectopic endometrial tissue will also shed due to the cyclic hormonal changes and this would eventually lead to an **inflammatory process** that is characterized by **abnormal T and B cell function** and **elevated interleukin-6**. These pro-inflammatory responses eventually lead to **fibrosis**.

Eventually, the extensive inflammatory process leads to adhesions which distorts the normal anatomy of the pelvic organs and their relationship to each other. The ultimate result of these abnormalities would be **infertility**, **painful intercourse**, and **chronic pelvic pain**.

Clinical Presentation of Endometriosis

Patients with endometriosis commonly complain of **chronic lower abdominal pain** that is maximum few days before the menstruation and that eventually improves after menstrual flow ends.



Image: "Localisation of endometriosis" by Endometriosis_loc_ger.svg: *Female_anatomy.svg: Tsaitgaist derivative work: Hic et nunc (talk). License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Additionally, **painful sexual intercourse**, **back pain**, **painful menstruation**, and **dysuria** or **urinary frequency** are commonly seen in these patients. The different locations of pain can be related to the organs involved in the disease and the presence of intraabdominal adhesions.

Dysuria and urinary frequency are signs of **urinary tract infection** which happens when the adhesions kink the ureters or direct invasion of the urinary tract happens.

In some patients, **acute severe lower abdominal pain** results at the time of the menstruation which is thought to be due to shedding of the ectopic endometrial tissue due to the cyclic hormonal changes.

Women with endometriosis usually have a family history of the disease, long duration of menstrual flow and an **improvement of the symptoms during pregnancy**. Family history of endometriosis increases the risk by approximately 10 times suggesting a **strong genetic factor** in the disease.

Diagnostic Work-up for Endometriosis

Pelvic infections and **urinary tract infections** can complicate endometriosis. A **complete blood count** to check white blood cells count might be helpful in excluding these diagnoses. Additionally, **sexually transmitted diseases** can cause pelvic

inflammatory disease and pain and should be excluded by the appropriate **blood and smear tests**.

Recently, it was found that patients with endometriosis have **elevated Thomsen-Friedenreich T antibodies** which support the hypothesis of autoimmune pathology. Looking for these antibodies can help in the diagnosis of endometriosis. **Elevated CCR1** is also found in women with endometriosis.

Cancer antigen 125 is neither specific nor sensitive for endometriosis but is usually slightly elevated in women with huge ectopic implants.

Imaging studies are the most helpful modality to diagnose endometriosis and to exclude other differential diagnoses.

Transvaginal ultrasound is superior to transabdominal or endorectal ultrasonography in assessing pelvic organs involvement and identification of the cystic nature of the endometrial ectopic implants. The **common chocolate cysts of the ovaries** can be identified with transvaginal ultrasound. **Endorectal ultrasound** is useful in the assessment of rectal and cul-de-sac involvement.

Magnetic resonance imaging (MRI) is useful in the identification of rectal and cul-de-sac disease and is usually more sensitive than ultrasound for detection of localized disease. Unfortunately, MRI is less useful for diffuse endometriosis.

The gold standard to diagnose endometriosis is to perform a **laparoscopy**. In laparoscopy, blue, black, red, white or non-pigmented lesions can be identified. Laparoscopic evaluation of endometriosis has to be systematic in order to not miss the lesions and the different organs known to be involved need to be checked in this order: the ovaries, cul-de-sac, the broad and uterosacral ligaments, the rectum and sigmoid colon, the bladder and finally the distal ureter.

A **biopsy** is usually indicated and it shows normal and well-differentiated endometrial glands and stroma. Due to the proinflammatory response, fibrosis can be also found in the histologic examination.

Treatment of Endometriosis

Treatment of endometriosis is dependent on the patient's expectations and goals. If **surgery** is not preferred, **medical therapy** is usually indicated but the patient has to understand that the recurrence rate after medical therapy is relatively high, in up to 50% of the cases.

Combined oral contraceptive pills are the mainstay treatment for endometriosis and the results are usually good. They suppress the ovaries and alter the normal cyclic hormonal pattern which leads to pain relief.

It is recommended that the four placebo pills that allow for menstrual flow at the end of the cycle be omitted for the first four months. This is known to further decrease pelvic pain and improve the clinical outcome eventually. Additionally, combined oral contraceptive pills are known to lower the risk of ovarian cancer in this population.

Different progesterone preparations have been successfully used in the treatment of endometriosis but the side effects are usually more common compared to combined oral contraceptive pills. For instance, **medroxyprogesterone acetate injections** or oral pills are associated with **weight gain and depression**.

Gonadotropin-releasing hormone analogs improve pain symptoms in patients with endometriosis but they do not affect fertility. On the other hand, women with endometriosis who are on combined oral contraceptive pills are known to achieve pregnancy after the discontinuation of the treatment in up to 50% of the cases.



Image: "Cyst resection (right ovary)." by Hic et nunc - Own work.
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Danazol inhibits the sudden surge of follicle-stimulating hormone/ luteinizing hormone which happens during the menstrual cycle and is responsible for the initiation of menstrual flow. Even though very effective, Danazol is associated with **hyperandrogenism**.

When surgery is preferred or medical therapy fails to control the symptoms, surgical treatment is usually indicated. **Drainage** of the ovarian cysts, **laparoscopic laser ablation** of the endometrial lesions, **uterine nerve ablation** for pain control and **removal of the cysts** by laparoscopy have been all used in the treatment of endometriosis with good results.

Usually, **nerve ablation** is reserved for patients with severe pelvic pain that is not responsive to other treatments. These surgeries are called conservative because they preserve reproduction.

Women who do not wish to get pregnant in the future and who have severe abdominal pain but are still young to be in artificial menopause might benefit from **semiconservative surgery**, in which the uterus is removed along with any ectopic lesions and cysts. The ovaries are preserved which **prevents premature menopause**.

Women who are near their menopause might benefit from **radical surgery** in which the uterus and both ovaries are removed. These older patients are more likely to have **excessive adhesions** and they benefit from **adhesiolysis** as well.

Hormonal replacement therapy with or without progesterone in addition to estrogen is indicated just as it is in normal women going into menopause and this does not seem to affect the rate of recurrence which is estimated to be 15%.

References

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