



# Endometriosis

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## Key facts

- Endometriosis is a disease where tissue similar to the lining of the uterus grows outside the uterus, causing pain and/or infertility (1).
- Endometriosis affects roughly 10% (190 million) of reproductive age women and girls globally (2).
- It is a chronic disease associated with severe, life-impacting pain during periods, sexual intercourse, bowel movements and/or urination, chronic pelvic pain, abdominal bloating, nausea, fatigue, and sometimes depression, anxiety, and infertility.
- The variable and broad symptoms of endometriosis mean that healthcare workers do not easily diagnose it and many individuals suffering from it have limited awareness of the condition. This can cause a lengthy delay between onset of symptoms and diagnosis (3).
- At present, there is no known cure for endometriosis, and treatment is usually aimed at controlling symptoms (4).
- Access to early diagnosis and effective treatment of endometriosis is important, but is limited in many settings, including in low- and middle-income countries.
- There is a need for more research and awareness raising around the world to ensure effective prevention, early diagnosis, and improved management of the disease (2,5).

## Introduction and definition

Endometriosis is a disease characterized by the presence of tissue resembling endometrium (the lining of the uterus) outside the uterus (1). It causes a chronic inflammatory reaction that may result in the formation of scar tissue (adhesions, fibrosis) within the pelvis and other parts of the body. Several lesion types have been described (1,6):

- superficial endometriosis found mainly on the pelvic peritoneum

- **cystic ovarian endometriosis (endometrioma) found in the ovaries**
- **deep endometriosis found in the recto-vaginal septum, bladder, and bowel**
- **in rare cases, endometriosis has also been found outside the pelvis**

Symptoms associated with endometriosis vary, and include a combination of:

- **painful periods**
- **chronic pelvic pain**
- **pain during and/or after sexual intercourse**
- **painful bowel movements**
- **painful urination**
- **fatigue**
- **depression or anxiety**
- **abdominal bloating and nausea**

In addition to the above, endometriosis can cause infertility. Infertility occurs due to the probable effects of endometriosis on the pelvic cavity, ovaries, fallopian tubes or uterus. There is little correlation between the extent of endometrial lesions and severity or duration of symptoms: some individuals with visibly large lesions have mild symptoms, and others with few lesions have severe symptoms. Symptoms often improve after menopause, but in some cases painful symptoms can persist. Chronic pain may be due to pain centres in the brain becoming hyper-responsive over time (central sensitisation), which can occur at any point throughout the life course of endometriosis, including treated, insufficiently treated, and untreated endometriosis, and may persist even when endometriosis lesions are no longer visible. In some cases, endometriosis can be asymptomatic.

### **What is the cause of endometriosis?**

Endometriosis is a complex disease that affects some women globally, from the onset of their first period (menarche) through menopause regardless of ethnic origin or social status. The exact origins of endometriosis are thought to be multifactorial, meaning that many different factors contribute to its development. Several hypotheses have been proposed to explain origins of endometriosis. At present endometriosis is thought to arise due to:

- **Retrograde menstruation, which is when menstrual blood containing endometrial cells flows back through the fallopian tubes and into the pelvic cavity at the time that blood is flowing out of the body through the cervix and vagina during periods. Retrograde menstruation can result in endometrial-like cells being deposited outside the uterus where they can implant and grow.**
- **Cellular metaplasia, which is when cells change from one form to another. Cells outside the uterus change into endometrial-like cells and start to grow.**
- **Stem cells giving rise to the disease, which then spreads through the body via blood and lymphatic vessels.**

Other factors may also contribute to the growth or persistence of ectopic endometrial tissue. For example, endometriosis is known to be dependent on estrogen, which facilitates the inflammation, growth, and pain associated with the disease. However, the relationship between

estrogen and endometriosis is complex since the absence of estrogen does not always preclude the presence of endometriosis. Several other factors are thought to promote the development, growth, and maintenance of endometriosis lesions. These include altered or impaired immunity, localized complex hormonal influences, genetics and potentially, environmental contaminants (2,7).

### **Health, social and economic benefits of addressing endometriosis**

Endometriosis has significant social, public health and economic implications. It can decrease quality of life due to severe pain, fatigue, depression, anxiety, and infertility. Some individuals with endometriosis experience debilitating endometriosis-associated pain that prevents them from going to work or school (8,9). In these situations, addressing endometriosis can reduce absence from school or increase an individual's ability to contribute to the labour force. Painful sex due to endometriosis can lead to interruption or avoidance of intercourse and affect the sexual health of affected individuals and/or their partners (9). Addressing endometriosis will empower those affected by it, by supporting their human right to the highest standard of sexual and reproductive health, quality of life, and overall well-being.

### **Prevention**

At present, there is no known way to prevent endometriosis. Enhanced awareness, followed by early diagnosis and management may slow or halt the natural progression of the disease and reduce the long-term burden of its symptoms, including possibly the risk of central nervous system pain sensitisation, but currently there is no cure.

### **Diagnosis**

A careful history of menstrual symptoms and chronic pelvic pain provides the basis for suspecting endometriosis. Although several screening tools and tests have been proposed and tested, none are currently validated to accurately identify or predict individuals or populations that are most likely to have the disease. Early suspicion of endometriosis is a key factor for early diagnosis, as endometriosis can often present symptoms that mimic other conditions and contribute to a diagnostic delay. In addition to medical history, referral from the primary health care level to secondary centers where additional investigations are available may be needed. For instance, ovarian endometrioma, adhesions and deep nodular forms of disease often require ultrasonography or magnetic resonance imaging (MRI) to detect. Histologic verification, usually following surgical/laparoscopic visualization, can be useful in confirming diagnosis, particularly for the most common superficial lesions (1,2). The need for histologic/laparoscopic confirmation should not prevent the commencement of empirical medical treatment.

### **Treatment**

Treatment can be with medications and/or surgery depending on symptoms, lesions, desired outcome, and patient choice (4). Contraceptive steroids, non-steroidal anti-inflammatory

medications, and analgesics (painkillers) are common therapies. All must be carefully prescribed and monitored to avoid potentially problematic side effects. Medical treatments for endometriosis focus on either lowering estrogen or increasing progesterone in order to alter hormonal environments that promote endometriosis. These medical therapies include the combined oral contraceptive pill, progestins, and GnRH-analogues. However, none of these treatments eradicates the disease, they are associated with side effects, and endometriosis-related symptoms can sometimes - but not always - reappear after therapy discontinuation. The choice of treatment depends on effectiveness in the individual, adverse side effects, long-term safety, costs, and availability. Most current hormonal management is not suitable for persons suffering from endometriosis who wish to get pregnant, since they affect ovulation.

Surgery can remove endometriosis lesions, adhesions, and scar tissue. However, success in reducing pain symptoms and increasing pregnancy rates are often dependent on the extent of disease. In addition, lesions may recur even after successful eradication, and pelvic floor muscle abnormalities can contribute to chronic pelvic pain. Secondary changes of the pelvis, including the pelvic floor, and central sensitisation may benefit from physiotherapy and complementary treatments in some patients. Treatment options for infertility due to endometriosis include laparoscopic surgical removal of endometriosis, ovarian stimulation with intrauterine insemination (IUI), and in vitro fertilization (IVF), but success rates vary (4). Other comorbidities may occur alongside endometriosis, requiring diagnosis and management. Multidisciplinary treatment addressing different symptoms and overall health should involve different specialists, such as pain specialists, pelvic physiotherapists, complementary and alternative medicine specialists, general practitioners, and psychologists, in addition to gynaecologists, to be most effective (2,10).

### **Addressing current challenges and priorities**

In many countries, the general public and most front-line healthcare providers are not aware that distressing and life-altering pelvic pain is not normal, leading to a normalisation and stigmatisation of symptoms and significant diagnostic delay (2,3). Patients who could benefit from medical symptomatic management are not always provided with treatments due to limited awareness of endometriosis among primary healthcare providers. Due to diagnostic delays, prompt access to available treatment methods, including non-steroidal analgesics (painkillers), oral contraceptives and progestin-based contraceptives is often not achieved. Due to limited capacity of health systems in many countries, access to specialised surgery for those who need it is sub-optimal. In addition, and especially in low and middle-income countries, there is a lack of multi-disciplinary teams with the wide range of skills and equipment needed for the early diagnosis and effective treatment of endometriosis. Although primary health care professionals should play a role in screening and basic management of endometriosis, tools to screen and accurately predict patients and populations who are most likely to have the disease are lacking. In addition, many knowledge gaps exist, and there is need for non-invasive diagnostic methods

as well as medical treatments that do not prevent pregnancy.

Subsequently, some of the current priorities related to endometriosis include:

- Raising awareness about endometriosis among health care providers, women, men, adolescents, teachers and wider communities. Local, national and international information campaigns to educate the public and healthcare providers about normal and abnormal menstrual health and symptoms are needed.
- Training all healthcare providers to improve their competency and skills to screen, diagnose, manage, or refer patients with endometriosis. This can range from basic training of primary healthcare providers to recognize endometriosis, to the advanced training of specialist surgeons and multidisciplinary teams.
- Ensuring that primary health care plays a role in screening, identifying and providing basic pain management of endometriosis, in situations where gynaecologists or advanced multidisciplinary specialists are unavailable.
- Advocating for health policies that ensure access to at least a minimum level of treatment and support for patients with endometriosis.
- Setting up referral systems and care pathways consisting of well-linked primary healthcare centres and secondary and tertiary centres with advanced imaging, pharmacologic, surgical, fertility and multi-disciplinary interventions.
- Strengthening capacity of health systems to achieve early diagnosis and management of endometriosis by enhancing availability of equipment (e.g. ultrasound or magnetic resonance imaging) and pharmaceuticals (e.g. non-steroidal analgesics, combined oral contraceptives and progestin-based contraceptives).
- Increasing research on the pathogenesis, pathophysiology, natural progression, genetic and environmental risk factors, prognosis, disease classification, non-invasive diagnostic biomarkers, personalized treatments and other treatment paradigms, role of surgery, novel targeted therapeutics, curative therapies, and preventive interventions in endometriosis (2,5).
- Accelerating collaborative global action to improve access to reproductive health care for women globally, including in low- and middle-income countries.

## WHO response

The World Health Organization (WHO) recognizes the importance of endometriosis and its impact on people's sexual and reproductive health, quality of life, and overall well-being. WHO aims to stimulate and support the adoption of effective policies and interventions to address endometriosis globally, especially in low and middle-income countries. WHO is partnering with multiple stakeholders, including academic institutions, non-state actors and other organizations that are actively involved in research to identify effective models of endometriosis prevention, diagnosis, treatment, and care. WHO recognises the importance of advocating for increased awareness, policies and services for endometriosis, and collaborates with civil society and endometriosis patient support groups in this regard. WHO is also collaborating with relevant stakeholders to facilitate and support the collection and analysis of country- and region-specific endometriosis prevalence data for decision making.

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