

Endometriosis

What is endometriosis?

Endometriosis is a perplexing disease affecting women in their reproductive years. It is a condition where the cells that line the uterus are also found in other areas of the body, mostly within the pelvis. The name comes from the tissue that lines the uterus, the endometrium. During the menstrual cycle, the thickness of the endometrium increases in readiness for the fertilised egg. If pregnancy does not occur, the lining is shed as a period.



Under normal hormonal influence, this tissue outside the uterus is built up each month and then breaks down in the same way as the lining of the uterus. The internal bleeding into the pelvis has no way of leaving the body, and this leads to inflammation, pain and the formation of scar tissue. In some women, endometrial deposits can also be found in more remote sites than the pelvis, e.g. in or on the bowel, the bladder, and even in locations outside the abdomen, e.g., in the lung.

Endometrial growths are generally not malignant; they are a type of normal tissue outside their usual location. However, in recent decades, there has been an increased frequency of malignancy recognized in relation with endometriosis.

The cause of the disease is unknown but there are several theories, such as retrograde menstruation, genetic predisposition to the condition, or a dysfunction of the body's immune system.

The most widely accepted theory is retrograde menstruation, i.e. some of the menstrual blood flows backwards down the fallopian tubes into the pelvis and endometrial cells, contained in the menstrual fluid, implant on organs or other areas in the pelvis. What remains unclear is why these endometrial cells implant in some women and not in others. The amount of pain is not necessarily related to the extent or size of growths. Tiny or "petechial" growths have been found to be more active in producing prostaglandins, which are thought to cause many of the symptoms of endometriosis.

Most patients present with a long list of symptoms, such as lethargy and tiredness, painful and irregular periods, pain starting before periods, prolonged bleeding, ovulation pain, pain during or after sexual intercourse, and in patients with extra-pelvic location, painful bowel movements, pain when passing urine and symptoms of irritable bowel syndrome. On the other hand, some women with the condition will have no symptoms at all. Infertility affects about 30-40 per cent of women with endometriosis and is a common result with progression of the disease. Endometriosis is best diagnosed by a laparoscopy. This is a minor operation in which a laparoscope is inserted into the abdomen via a small cut near the navel. This allows the gynaecologist to see the pelvic organs and any endometrial implants.

Who does endometriosis affect?

In industrialised countries, endometriosis is the second most common gynaecological condition. Roughly 10 per cent of women of childbearing age are affected which leads to the estimate that some 15 million women in Europe suffer from the condition. Endometriosis can occur at any time from the onset of menstrual periods until the menopause. Only very rarely is it first diagnosed after the menopause, but this is not unknown.

Present treatments:

There is a range of medical treatments which have been made available over the past 25 years. Unfortunately, none of the medications offer a cure for the condition, but they contribute in relieving pain symptoms, shrinking or slowing endometrial growth, and preserving or restoring fertility. The considerations about what type of treatment should be used depend on the age of the woman, the severity of the symptoms, and the desire to have children.

Analgesics of various classes are prescribed to treat abdominal pain. Hormonal treatment aims to stop ovulation and allow the endometrial deposits to regress and die. They either put the woman into a state of false pregnancy or menopause. Medicines used include testosterone derivatives, gonadotrophin-releasing hormone (GnRH) analogues, and contraceptives, either containing a combination of estrogen and progesterone, or progesterone alone.

In women not responding to pharmacotherapy, surgery may be necessary. Conservative surgery seeks to remove the endometrial growths. This is either done by laparoscopy or by a larger open operation – a laparotomy. Removal of the uterus and the ovaries should be the 'last resort' treatment and not contemplated until all other treatments have been tried.

What's in the development pipeline?

The antagonists of GnRH are new approaches being investigated for the treatment of endometriosis. In fact, researchers claim that this group of medicines, in contrast to the commonly used agonists of GnRH, may cause fewer sideeffects and be more effective. A class of medicines known as aromatase inhibitors may also constitute a novel approach in hormonal therapy of endometriosis. Initially used to treat breast cancer, they act by decreasing the body's supply of estrogen. They will be reserved for patients who have gone through menopause.

Selective estrogen receptor modulators (SERMs) have a positive effect in selective tissues such as the cardiovascular system, the muscles and the bones, but they do not have any negative effects in uterine and breast tissues. Animal models have shown that the application of SERMs prevents osteoporosis and estrogen-induced proliferation of the endometrium. Similarly, the possible use of selective progesterone receptor modulators (SPRMs) is under investigation. The compounds possess selective impacts on progesterone receptors, and thus it is expected that their use could decrease the growth of endometrial tissue outside the uterus. Both SERMs and SPRMs are in Phase 2 clinical trials.

The use of extracellular matrix modulators (EMMs) is also of increasing interest among scientists. The proliferating endometrium produces some specific enzymes. The isolation and destruction of these enzymes by EMMs may lead to another type of endometriosis treatment. Molecules of the beta2-adrenergics class are successfully

Endometriosis is a painful, distressing disease that affects women in their reproductive years. Various medicines for endometriosis have been introduced over the last 25 years, but there is no cure. Research continues into this perplexing disease.



used for preventing premature birth, and their effectiveness in relieving pain during endometriosis is also being studied in Phase 3 clinical trials.

The longer-term future:

Research in recent years has demonstrated a number of abnormalities of the immune system of women with endometriosis. The findings suggest immunological treatment approaches for endometriosis. The target would be to synchronise the activation of natural killer lymphocytes in conjunction with the T lymphocyte response against the extra-uterine endometrial growths.

Angiogenesis, i.e. the formation of new blood vessels, is also an important field of research to treat endometriosis. Any newly formed tissues – like endometrial cell growing outside the uterus – need additional blood supply. Without sufficient supply of oxygen and nutrients, the hormonal impacts on petechial growths have little effect. The idea is to limit the growth of the extra-uterine cells by checking their blood supply. Medicines which decelerate or arrest angiogenesis may also control fibrotic growths or formation of adhesions.

In 2004, Canadian research groups identified a major deficiency in a gene that plays a key role in controlling the inflammatory reaction associated with endometriosis. While the gene is present in endometrial cells in normal women, it is partially or totally absent in women with endometriosis. According to the scientists, this defective gene results in an inflammatory reaction in the endometrium and localised changes to the immune system in the tissue.

An assumption that has at times been made about endometriosis is that it is not a serious disease because it is not life-threatening like cancer, for instance. However, anyone who has ever met women with endometriosis learns that too many are suffering from severe pain, emotional stress, an inability to work and that they experience a poor quality of life because of their condition. Research is continuing that someday soon one will understand this perplexing disease and be able to end all the pain and frustrations that so often go with it.

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