

## EXPLORING THE ENIGMA OF ENDOMETRIOSIS: INSIGHTS FROM TRADITIONAL CHINESE AND WESTERN MEDICINE

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**Abstract:** Endometriosis (EMs) is a complex gynecological condition characterized by the presence of endometrial tissue outside the uterine cavity. This disorder is associated with various distressing symptoms, including chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility. Despite extensive research, the precise etiology of EMs remains elusive. Clinical manifestations categorize EMs into subtypes like "dysmenorrhea," "menorrhagia," "dysentery," and "infertility," shedding light on diverse presentations. Stasis of blood plays a pivotal role in EMs pathogenesis, impeding the normal flow of menstruation and obstructing key meridians, such as the uterus, Chong meridian, and Ren meridian. The incidence of EMs is on the rise, severely impacting women's quality of life. Recent advances in both traditional Chinese and Western medicine have offered promising treatment modalities, providing substantial relief to patients. This review compiles contemporary literature to provide an overview of the evolving understanding and therapeutic progress in EMs, offering valuable insights into the management of this challenging condition.

**Keywords:** Endometriosis, gynecological condition, chronic pelvic pain, dysmenorrhea, infertility, traditional Chinese medicine, literature review, treatment modalities.

### 1. Introduction

Endometriosis (EMs) refers to a disease caused by the appearance of growth-functional endometrial tissue in other parts of the body than the lining of the uterine cavity. The main symptoms include chronic pelvic pain, dysmenorrhea, dyspareunia and infertility. The pathogenesis of EMS has not yet been elucidated. According to its clinical manifestations, it can be classified as "dysmenorrhea", "menorrhagia", "dysentery", and "infertility". The main pathogenesis of endometriosis is stasis blood, which causes stasis blood of the "leaving menstruation" and blocks the uterus, Chong meridian, Ren meridian. In recent years, the incidence of EMs has shown a significant upward trend, which seriously affects the quality of life of women. With the continuous in-depth study of EMS in traditional Chinese and western medicine, more and more reliable treatment methods have been proposed, which greatly

relieve the suffering of patients. Based on the literature research in recent years, this paper expounds the understanding and treatment research progress of EMs.

## 2. Understanding of Western medicine

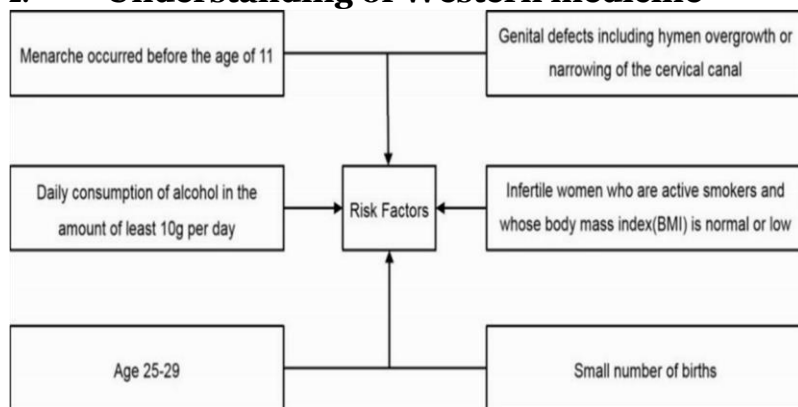


Figure 1: Risk factors for endometriosis

EMs can lead to pelvic pain and infertility, which seriously affects the health and quality of life of women. It is an aggressive and relapsing disease, which is very troublesome. Its formation is related to genetic factors, immune and inflammatory factors, environmental factors, angiogenesis factors, etc <sup>[1]</sup>. The risk factors are shown in Figure 1. About its origin, there are mainly the theory of retrograde blood flow implantation, body cavity epithelial metaplasia, and stem cell theory.

### 2.1. Retrograde blood flow implantation theory

Sampson proposed the theory of implantation in 1921, which suggested that endometrial glandular epithelial and stromal cells could be retrograde in menstrual blood flow and seeded on the ovary or other pelvic organs <sup>[2]</sup>. It does not explain retrograde menstrual bleeding, which occurs in 90% of women of reproductive age but in only a minority (10%-15%), nor does it explain extrapelvic endometriosis. Lang Jinghe <sup>[3]</sup> puts forward the "determinism of eutopic endometrium", which holds that ectopic endometrium can form lesions in the pelvis and abdomen, and must go through a "trilogy" of adhesion, invasion and angiogenesis to achieve "root, growth and disease". The eutopic endometrium is the seed, the allotopic endometrium is the soil, and other factors act as sunlight and rain.

### 2.2. The theory of body cavity epithelial metaplasia

Various types of cells and tissues metamorphose into ectopic endometrioid tissues under the repeated stimulation of continuous ovarian hormones or menstrual blood and chronic inflammation <sup>[4]</sup>.

### 2.3. Stem cell theory

More and more studies have shown that stem cells have a certain relationship with the occurrence of EMs <sup>[5]</sup>. At first, some scholars thought that menstrual blood reflux, Estrogen therapy and other factors provide a suitable local microenvironment for stem cells from different sources to differentiate <sup>[6]</sup>. With the deepening of research, it has been found that the abnormal differentiation and proliferation of endometrial stem/progenitor cells may lead to the occurrence of endometriosis. The pathogenesis is shown in Figure 2.

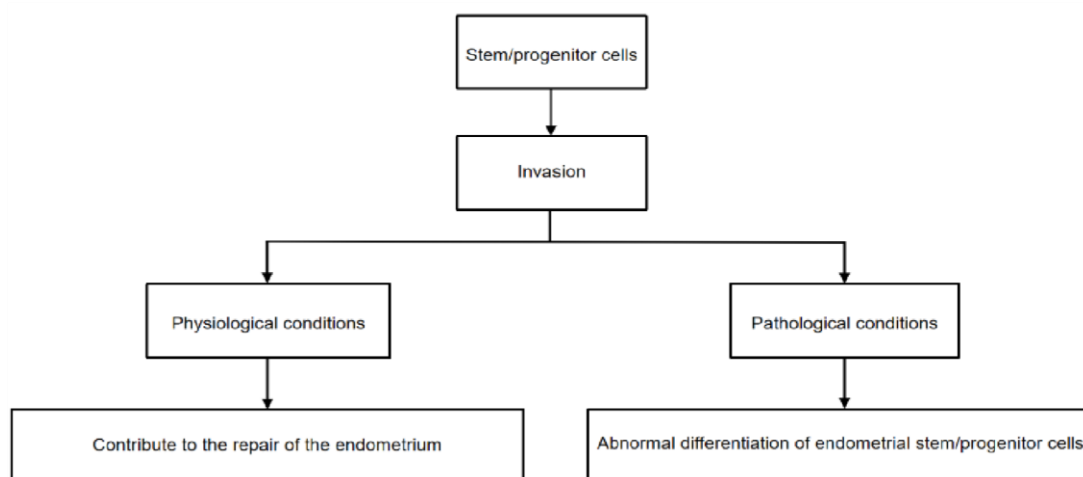


Figure 2: The pathogenesis

### 3. Understanding of Chinese Medicine

There is no disease name for endometriosis in ancient books. According to its clinical manifestations, it is mostly classified as "dysmenorrhea", "infertility", "irregular menstruation" and "abdominal mass". Its core pathogenesis is "blood stasis", which is closely related to the dysfunction of the liver, spleen, and kidney. The main syndrome types are blood stasis due to Qi stagnation syndrome, Qi deficiency and blood stasis syndrome, cold coagulation and blood stasis syndrome, kidney deficiency and blood stasis syndrome, dampness-heat and blood stasis syndrome, and phlegm and blood stasis syndrome.

### 4. Treatment with Western medicine

The fundamental purpose of treating EMs is to "reduce and remove lesions, relieve and control pain, treat and promote fertility, prevent and Reduce recurrence ".The main treatment methods include surgical treatment and drug therapy, among which drug therapy is currently the preferred way to treat the clinical symptoms of EMs and prevent postoperative recurrence.

#### 4.1. Drug therapy

Drug therapy is mainly divided into hormone therapy and non-hormone therapy. Hormone therapy mainly includes the combination of estrogen and progesterone, aromatase inhibitors, and GnRH-a. Non-hormonal therapy mainly includes immunomodulators, antiangiogenic drugs, and antioxidants. The prominent features of EMs are estrogen dependence and progestin resistance. After natural and induced menopause, ectopic endometrial lesions can gradually atrophy and be absorbed, so highly effective oral progestins combined with small doses of estrogen can be used to achieve a "pseudopregnancy state"; the mechanism is shown in Figure 3. Multiple studies have shown that aromatase is not detected in normal human endometrium, while it is overexpressed in both normal and ectopic endometrium of patients with endometriosis [7-10]. The mechanism of aromatase inhibitors is to inhibit the activity of aromatase, thereby reducing the local estrogen production [11]. GnRH-a can promote the release of LH and FSH in the short term and then continue to inhibit the secretion of gonadotropin by the pituitary gland, resulting in a significant decrease in ovarian hormone levels and temporary amenorrhea, but there will be menopausal symptoms such as hot flashes, vaginal dryness, decreased libido and bone loss. Anti-angiogenic drugs mainly inhibit angiogenesis by clearing VEGF receptors and reducing the secretion of VEGF and fibroblast growth factor, thereby inhibiting the growth and invasion of EMs lesions.

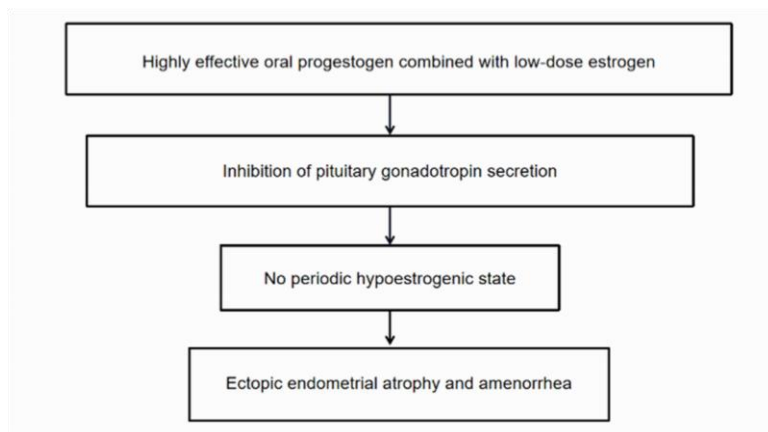


Figure 3: The mechanism

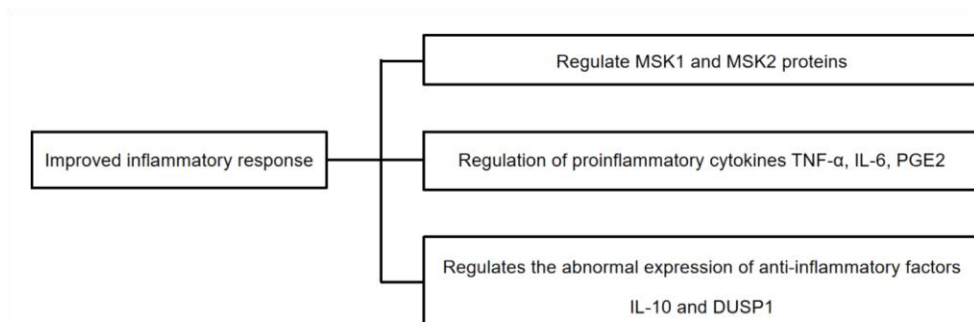
#### 4.2. **Surgical treatment**

The purpose of surgical treatment is to remove the lesion and restore the anatomy. Conservative surgery, which preserves the uterus and at least one ovary, is currently the preferred treatment for women who wish to have children. According to a study, 11.8% of women who underwent resection of EMs lesions reported no improvement in pain, 22.6% of patients underwent further surgery, and the incidence of postoperative pain, recurrent pain, and adverse events was not low. Even if the lesions were removed, there was a risk of developing malignant tumors such as ovarian cancer [12]. Radical surgery is suitable for patients over 45 years old. Patients who do not receive estrogen supplementation after surgery have almost no recurrence.

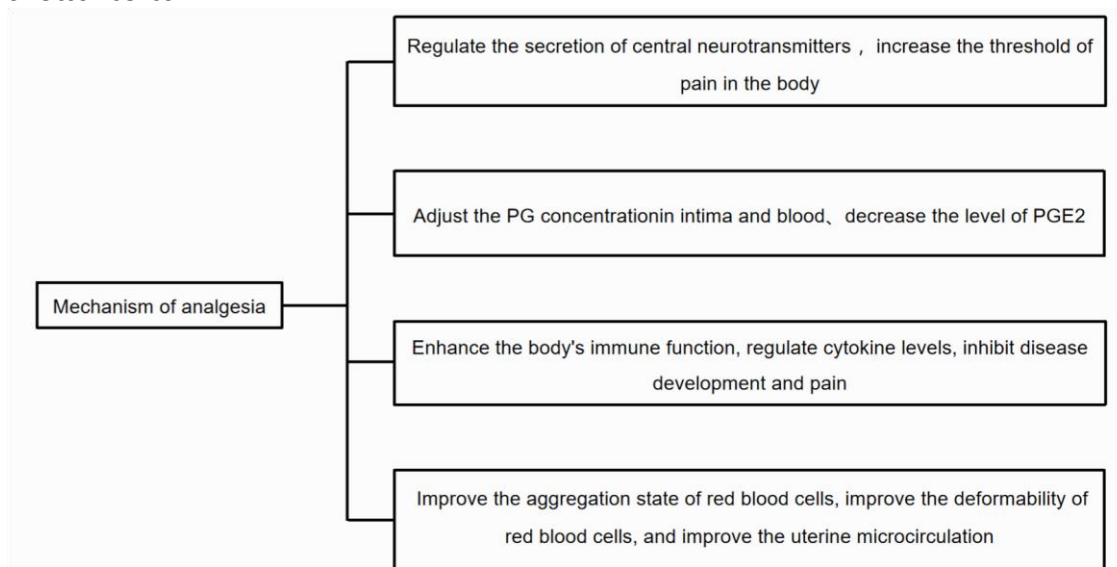
### 5. **TCM (traditional Chinese medicine) therapy**

#### 5.1. **Internal treatment of TCM**

The treatment principle of Qi stagnation and blood stasis type endometriosis is moving Qi to relieve pain, activating blood to resolve stasis. Through network data mining technology, it was found that Angelica sinensis and Chuanxiong Rhizoma, Sanling sinensis and Zedoary rhizoma, Wulingzhi sinensis and Typhimurium, Radix paeoniae alba and Angelica sinensis appeared frequently [13]. The core drug pairs of Qi deficiency and blood stasis type are Astragalus and Codonopsis, Atractylodes and Poria [14]. Professor Qi Cong's Yiqi Huoxue prescription uses Radix astragali and Codontirrhizae radix as its prescription to promote Yang circulation, dissipate pathogenic factors, replenish Yang and benefit Qi. It was found that Yiqi Huoxue Prescription can cause morphological changes in ectopic endometrioid tissues in the rat EMs model [15]. Cold coagulation and blood stasis type is usually treated with Shaofu Zhuyu decoction and Wenjing decoction [13], the study found that Shaofu Zhuyu decoction had a therapeutic effect on EMs rats with cold coagulation and blood stasis syndrome [16]. The mechanism is shown in Figure 4. Kidney deficiency and blood stasis type is mainly treated by tonifying kidney and activating blood. Li Xiao found that Bushen Huoxue recipe can effectively reduce the clinical symptoms of EMs patients, reduce local inflammatory response, and improve endometrial receptivity [17]. The dampness-heat and stasis type mainly uses Chinese herbs with the effects of clearing heat, removing dampness and blood stasis, and has the advantages of improving microvascular circulation, anti-inflammatory, analgesic and regulating immune function [18], Zheng Weilin [19] found that the traditional Chinese medicine of clearing heat and removing blood stasis could improve hemorheology, inhibit platelet aggregation, interfere with angiogenesis and inhibit the production of inflammatory mediators. The combination of phlegm and blood stasis is mainly treated by promoting blood circulation to remove blood stasis and dissipating phlegm and eliminating symptoms, Liu Xiaojie [20] found that Xiaozheng decoction has a good effect on EMs with phlegm and blood stasis junction, and modern pharmacology suggests that Xiaozheng decoction has the effects of improving pelvic microcirculation, regulating immune function, anti-inflammation, analgesia, and inhibiting ectopic endometrial hyperplasia.



*Figure 4: Mechanism of Shaofu Zhuyu decoction in the treatment of EMs rats* **5.2. External treatment**



*Figure 5: The mechanism of acupuncture on pain in EMs patients*

Acupuncture for pain relief is one of the characteristics and advantages of traditional Chinese medicine. Studies have found that acupuncture can significantly reduce adverse reactions caused by gestrotriene and improve the levels of IL-1 $\beta$ , TNF- $\alpha$ , VEGF and MMP-2 in patients with EMs <sup>[21]</sup>; The mechanism of acupuncture on pain in EMs patients as shown in Figure 5 <sup>[22]</sup>. Chinese medicine enema is very common in EMs treatment, Zhou Yahong <sup>[23]</sup> found that traditional Chinese medicine enema could decrease the concentration of CA125 and IL-6 in the peritoneal fluid, reduce the local inflammatory reaction, and improve the pain of patients with EMs. The acupoint application method has also achieved good effect in the treatment of EMs. This method not only reduces the occurrence of adverse reactions in the treatment of ovarian endometriosis, but also can directly act on the lesion site.

## 6. Summary

Modern medicine considers EMs as a hormone-dependent disease, and hormone therapy is commonly used. Although it can achieve the therapeutic effect in a short time, there are many adverse reactions, such as osteoporosis and infertility. Traditional Chinese medicine believes that the core pathogenesis of EMS is blood stasis. The basic treatment principle is to promote blood circulation and remove blood stasis, and the syndrome differentiation and treatment are carried out according to the different symptoms and signs of the patients. In the future, the treatment of EMs should be integrated with traditional Chinese medicine and western medicine, through a variety of ways of medication and multi-method treatment, so as to alleviate the symptoms, reduce the occurrence of adverse reactions and reduce the recurrence rate. In addition, in the meantime of standardized treatment, maintaining a good lifestyle is also very important for the prevention and rehabilitation of EMs.



## References

- Smolarz B, Szyłło K, Romanowicz H. Endometriosis: Epidemiology, Classification, Pathogenesis, Treatment and Genetics (Review of Literature) [J]. *Molecular Sciences*, 2021, 22(19):10554.
- [2] Sampson JA. Metastatic or Embolic endometriosis, due to the Menstrual Dissemination of Endometrial Tissue into the Venous Circulation [J]. *Am J Pathol*, 1927, 3(2):93-110.
- Dai Yi, Lang Jinghe, Zhu Lan, Leng Jinhua. The present and future of diagnosis and treatment of endometriosis [J]. (*Scientia Sinica*), 2021, 51(8):1017-1023.
- Ferguson BR, Bennington JL, Haber SL. Histochemistry of mucosubstances and histology of mixed müllerian pelvic lymph node glandular inclusions. Evidence for histogenesis by müllerian metaplasia of coelomic epithelium [J]. *Obstet Gynecol*, 1969, 33(5):617-25.
- Cousins FL, O DF, Gargett CE. Endometrial stem/progenitor cells and their role in the pathogenesis of endometriosis. *Best Pract Res Clin Obstet Gynaecol*, 2018; 50:27-38.
- Nikoo S, Ebtekar M, Jeddi-Tehrani M, et al. Menstrual blood-derived stromal stem cells from women with and without endometriosis reveal different phenotypic and functional characteristics. *Mol Hum Reprod*, 2014; 20(9): 905-918.
- Bulun SE, Fang Z, Imir G, et al. Aromatase and endometriosis [J]. *Semin Reprod Med*, 2004, 22(1):45-50.
- Noble LS, Simpson ER, Johns A, et al. Aromatase expression in endometriosis [J]. *Clin Endocrinol Metab*, 1996, 81(1): 174-179.
- Kitawaki J, Noguchi T, Amatsu T, et al. Expression of aromatase cytochrome P450 protein and messenger ribonucleic acid in human endometriotic and adenomyotic tissues but not in normal endometrium [J]. *Biol Reprod*, 1997, 57(3): 514-519.
- Velasco I, Rueda J, Ación P. Aromatase expression in endometriotic tissues and cell cultures of patients with endometriosis [J]. *Mol Hum Reprod*, 2006, 12(6): 377-381.
- Gheorghisan-Galateanu AA, Gheorghiu ML. Hormonal therapy in women of reproductive age with endometriosis: an update. *Acta Endocrinol (Buchar)*, 2019, 15(2):276-281.
- Singh SS, Gude K, Perdeaux E, et al. Surgical outcomes in patients with endometriosis: a systematic review [J]. *Obstet Gynaecol Can*, 2019. pii: S1701-2163(19) 30730-3.
- Ni Jianli, Shen Yu. Laws of Compound Traditional Chinese Medicine in the Treatment of Dysmenorrhea Based on Data Mining [J]. (*Jilin Journal of Chinese Medicine*), 2019, 0(3):385-388. [14] Gan Dongling. Discussion on syndrome-medicine law of traditional Chinese medicine treating endometriosis based on Data Mining Technology [D]. *Guangxi University of Traditional Chinese Medicine*, 2021.
- Hu Tianqi. Study on the Therapeutic effect and Mechanism of Yiqi Huoxue recipe on Endometriosis Model Rats [D]. *Shanghai University of Traditional Chinese Medicine*, 2020.
- Chen Yuanhuan, Mao Haiyan, Wu Quansheng, Zhang Xiaohua, Shen Jian, Feng Peng, Huang Cancan, Ji Xiujia. Mechanism of Shaofu Zhuyu Decoction in treatment of endometriosis-

*associated dysmenorrhea with syndrome of cold coagulation and blood stasis based on MSK1/2[J].(China Journal of Chinese Materia Medica), 2022,47(17):4674-4681.*

*Li Xiao, Zhou Yanyan. Bushen Huoxue recipe on endometrial receptivity in patients with kidney deficiency and blood stasis type of endometriosis-induced infertility [J].(Shaanxi Journal of Traditional Chinese Medicine), 2018,39(3):341-344.*

*Yang Dongxia, Wang Ning, Huo Yuxia, Shen Ruxia, Jing Jiabin, Wu Manli, Li Hongmei, Ma Baozhang. Research Progress in Treatment of EMs from Dampness-Heat and Blood Stasis [J].(Acta Chinese Medicine and Pharmacology), 2021,49(7):116-120.*

*Zheng Weilin, Liang Xuefang, Xu Zheng, Cao Lixing. Neuroangiogenesis Mechanism of Endometriosis-associated Pain in Traditional Chinese and Modern Medicine [J].(Chinese Archives of Traditional Chinese Medicine), 2018,36(9):2138-2142.*

*Liu Xiaojie. Clinical Study on the Curative Effect of XiaoZheng Decoction in Treating Endometriosis [D]. Shandong University of Traditional Chinese Medicine, 2011.*

*Zuo Dongdong, Han Fengjuan, Peng Yan, Guo Xuman, Fu Yang. Effect of Acupoint Catgut Embedding on the Levels of IL-1 $\beta$ ,TNF- $\alpha$ ,VEGF and MMP-2 in Patients with Endometriosis of Kidney Deficiency and Blood Stasis[J].(Journal of Clinical Acupuncture and Moxibustion), 2020,36(4):44-49.*

*Sun Kefeng, He Meirong, Li Na, Shi Simao. Pain Mechanism of EMs and Analgesic Mechanism of Acupuncture and Moxibustion in Treating Ems [J]. (Journal of Clinical Acupuncture and Moxibustion), 2019, 35(11):91-95.*

*Zhou Yahong, Mao Liyun, Wen Lina. Clinical Observation on Curative Effects of Retention Enema with Chinese Medicine in Treating Endometriosis and Influence on CA125 and IL-6 in Peritoneal Fluid [J]. (Journal of Nanjing University of Traditional Chinese Medicine), 2014, 30(6): 516-519.*