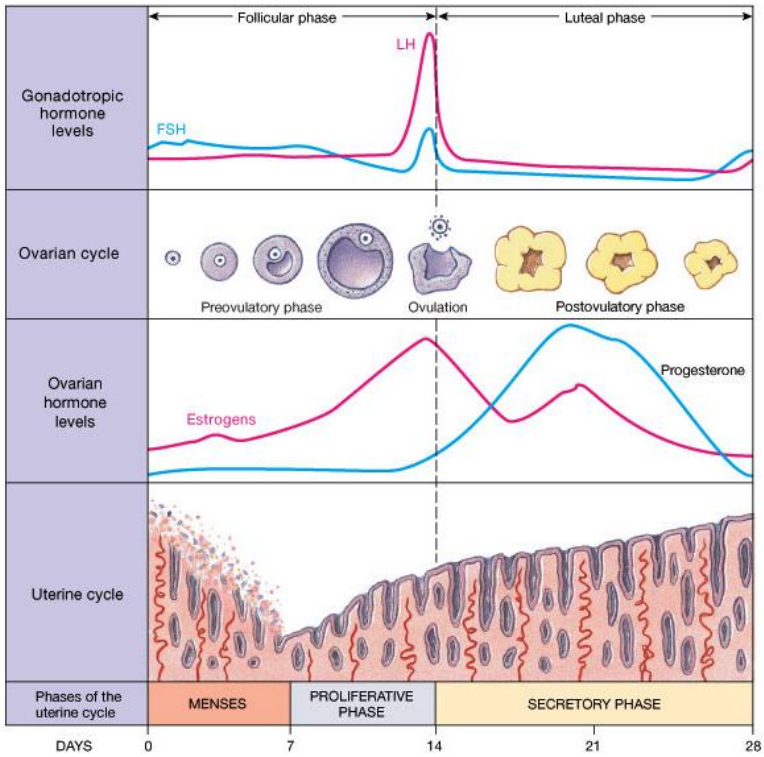
Endometriosis and PCOS

There are a number of cyclic changes that occur in the endometrium over the course of a women's cycle.

The proliferative phase begins at the end of menstrual flow and the glands are initially sparse and small. Increasing levels of estrogen increase the thickness of the stratum functionalis and the glands are more coiled and densely packed.

The secretory phase begins at ovulation and is the final phase of the uterine cycle as the endometrial lining reaches its maximum thickness. The glands become more coiled due to secretins rich is glycoprotein and glycogen.

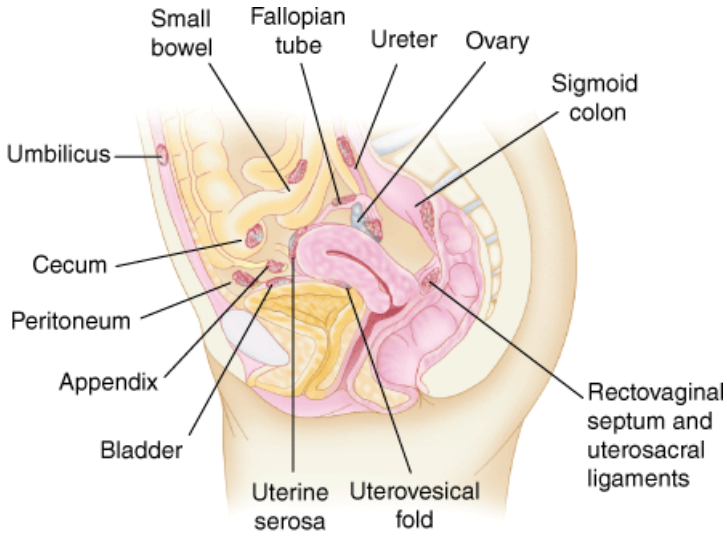


Endometriosis

This is the presence of endometrial tissue in ectopic locations and is often influence by hormonal changes in the same way as normal endometrial tissue inside the uterus. It affects 6-10% of women of reproductive age, with 35-50% of women experiencing pain, infertility or both.

Key symptoms

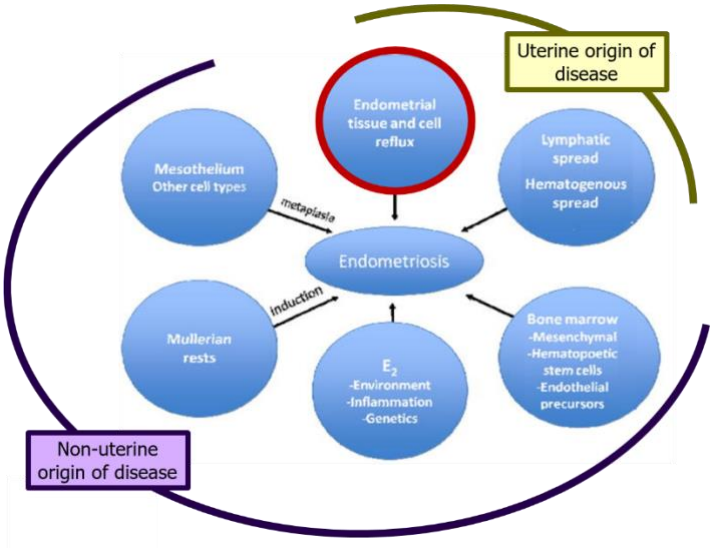
- Abdominal pain in different forms
  - Chronic pelvic pain
  - Dysmenorrhea
  - Dyspareunia (painful sexual intercourse)
  - Dyschezia
  - Constipation
- Infertility
- There is an average delay of 6.7 years between disease (and symptom) onset and diagnosis



Source: Schorge JO, Schaffer JI, Halvorson LM, Hoffman BL, Bradshaw KD, Cunningham FG: *Williams Gynecology*: http://www.accessmedicine.com

Theories of pathogenesis

Non-uterine Origin of Disease



stimulus driven reprogramming of female reproductive tract dependent on inciting factors and genetic susceptibilities eg endocrine disrupting chemicals, endogenous/exogenous estrogens. Supported by presence of endometriotic tissue in patients without menstrual endometrium (eg men undergoing high dose estrogen treatment)

- Coelomic metaplasia – transformation of normal peritoneal tissue to ectopic endometrial tissue
- Mullerian rests – cells residual from embryologic Mullerian duct migration maintains capacity to develop into endometriotic lesions under influence of estrogen beginning at puberty
- Extra-uterine stem/progenitor cells from bone marrow may differentiate into endometriotic tissue.

Uterine Origin of Disease

- Lymphatic or hematogenous dissemination of endometrial cells – endometriosis in lymph nodes and sites distant from uterus including bone, lung and brain
- Retrograde menstruation – intuitively attractive and supported by multiple lines of evidence

Endometrial cell survival

- 90% prevalence of retrograde menstruation
    - Additional steps required for development of ectopic endometrial implants (in 10% of women)
        - Escape from immune clearance
        - Attachment to peritoneal epithelium
        - Invasion of epithelium
        - Establishment of local neurovascularity
        - Continued growth and survival
- Genetic predisposition
    - Heritable component established
    - Several candidate factors including PTEN (tumor suppressor) and BCL-2 (anti-apoptosis)
- Estrogen dependence; progesterone resistance
    - Increase the expression of aromatase enzyme
    - Decrease the progesterone receptor expression
- Evasion from immune clearance due to impaired NK cell function and compromised macrophage function