

Basic Pathology: pp. 689-695

- Know the most common causes of chronic endometritis (p 608).
- Know how endometriosis gets transported to adjacent pelvic structures and to distant sites (p 609).
- What percent of women with atypical endometrial hyperplasia progress to endometrial carcinoma (p 610)?
- What are the risk factors for endometrial cancer? (p 612)
- What is the route of spread for endometrial cancer? (Handout, from staging factors)

Endometritis: Acute - neutrophils in endometrium, post-partum, retained products of conception

Chronic- plasma cells in endometrium

Adenomyosis: Endometrial glands and stroma deep into the uterine wall (myometrium). May be painful.

Endometriosis: Endometrial glands and stroma proliferating away from the endometrium often found on uterine serosa, fallopian tubes, cul-de-sac, ovaries, appendix, bowel wall, etc. "Powder burns, chocolate cysts." Affects fertility due to adhesion formation. Cyclic bleeding and pain (dysmenorrhea, dyspareunia, dysuria, pain on defecation, etc).

Dysfunctional uterine bleeding: Uterine bleeding without a distinct anatomic lesion:

1. Failure to ovulate: anovulatory cycles
 - a. Dysfunction of hypothalamic-pituitary axis-adrenal or thyroid disorders
 - b. Ovary tumor making increased estrogen
 - c. Malnutrition (anorexics), obesity (peripheral conversion of steroid hormones to estrogens)
 - d. Severe physical/emotional stress
2. Inadequate luteal phase: Corpus luteum can't tow the mark-makes too little progesterone
3. Contraceptive use-abnormal ratios of estrogen and progesterone

Endometrial Hyperplasia: Too much estrogen drives the endometrial glands to proliferate excessively. Results: varying degrees of endometrial hyperplasia ranging from simple hyperplasia to complex hyperplasia to atypical hyperplasia. Continued estrogen stimulation results in endometrial cancer-20-25% of women with atypical hyperplasia progress to endometrial cancer. Risk of developing endometrial hyperplasia is increased in obese, hypertensive, diabetic women.

Signs and symptoms: excessive and irregular uterine bleeding (metromenorrhagia)

Tumors of endometrium and myometrium:

1. Endometrial polyps
2. Leiomyomas
3. Endometrial carcinoma
4. Leiomyosarcoma
5. Malignant mixed müllerian tumor

Endometrial polyps: occur at any age, common at menopause, clonal stromal cells 6p21 cytogenetic rearrangement; produce uterine bleeding, uncommonly progress to cancer. May prolapse.

Signs and symptoms: Irregular uterine bleeding/spotting.

Leiomyoma: Benign smooth muscle tumors of uterus, most common benign tumor in women, found in 30-50% of women. (Called “fibroids” by clinicians). More frequent in African-American women. Driven by hormones, shrink with menopause (usually). May parasitize to other organs. May prolapse. May autoinfarct, especially during pregnancy. Often multiple.

Signs and symptoms: menorrhagia, with or without metrorrhagia

Leiomyosarcoma: Malignant smooth muscle tumor, arises spontaneously. Usually solitary.

Malignant characteristics include increased mitotic activity, cellular atypia and necrosis.

Endometrial Carcinoma (EMCA): In the US and many other Western countries, this is the most frequent cancer of the female genital tract. Mean pt age-59, range 55-65. Risk factors: obesity [increased synthesis of estrogen in fat depots from adrenal and ovarian precursors, (androstenedione converted into estrone)], diabetes, hypertension, infertility (pts tend to be single, nulliparous, anovulatory cycles), previous hx of endometrial hyperplasia. Increases in women with a hx of breast cancer and in Lynch II syndrome (colon/ovary/endometrial cancers). Uncommon in Japanese women (? dietary factors, increases in 1st and 2nd generation Japanese immigrants). Some evidence that Tamoxifen (used in treatment or prophylaxis for breast CA) increases pt's risk of EMCA.

20% of EMCA develops in women without a significant previous hx. The latter tend to be more aggressive tumors and less responsive to treatment modalities.

Signs and symptoms: Irregular uterine bleeding in pre- perimenopausal woman; uterine bleeding in post-menopausal woman, pelvic mass.

Staging in endometrial carcinoma: i.e. how does it spread?

Stage I	confined to endometrium (Ia), inner 2 (Ib) or outer 2 of uterus (Ic)
Stage II	endocervical involvement
Stage III	invades uterine serosa, vaginal mets, (+) pelvic/para-aortic lymph nodes, abdominal involvement
Stage IV	bladder/bowel involvement, distant metastasis

(+) denotes positive for malignancy, i.e. tumor present in lymph nodes

Survival is directly proportional to pathologic stage at diagnosis. The more aggressive the tumor, the deeper it will invade the uterus and the worse the prognosis. Women with tumors confined to the endometrium have a survival rate of 94%; with inner 1/3 myometrial wall invasion-91%; with 1/3-2/3 myometrial wall invasion-84%; with greater than 2/3 myometrial wall invasion-59%. Only 36% of women with (+) aortic lymph nodes are alive 5 years after diagnosis.

Treatment: Total abdominal hysterectomy (uterus), bilateral salpingo-oophorectomy (fallopian tubes and ovaries), omentum, pelvic/paraortic lymph nodes.

Post-op: +/- radiation therapy, chemotherapy for high stage tumors or vaginal recurrence