

Dysmenorrhea

Clinical Cases Applicability: dysmenorrhea, pelvic pain, endometriosis, adenomyosis

Learning Objectives:

1. Understand the histology of the normal endometrium and myometrium
2. Understand the pathophysiology behind dysmenorrhea and endometriosis
3. Understand the pharmacological treatment of dysmenorrhea

What are the normal histology and function of the endometrium and myometrium?

Endometrium: Simple columnar epithelium with simple tubular glands; hormonally active; 2 layers (**figure 1**):

- 1) Stratum functionale: temporary layer at the luminal surface, responds to hormones, changes during the menstrual cycle
- 2) Stratum basale: deeper, permanent layer containing basal portion of the endometrial glands, retained during menses

Myometrium: highly vascular smooth muscle in interwoven layers, responsible for uterine contractions

What is the pathophysiology behind dysmenorrhea? (figure 2)

- 1° dysmenorrhea: painful menstruation without an associated underlying pathology
- 2° dysmenorrhea: painful menstruation caused by an identifiable underlying condition as endometriosis
- Prostaglandins (E2 and F2 α) released during endometrial sloughing \rightarrow myometrial contractions \rightarrow high intrauterine pressures \rightarrow uterine pressure exceeds arterial pressure \rightarrow uterine ischemia \rightarrow anaerobic metabolites accumulate \rightarrow stimulate type C pain neurons
- Prostaglandins (and other inflammatory mediators) \downarrow the resting membrane potential of pain receptors \rightarrow \downarrow neuronal firing threshold \rightarrow \uparrow sensitivity to pain

What is endometriosis?

- **Endometriosis:** presence of endometrial tissue outside the uterus often near the ovaries, fallopian tubes, cul-de-sac, broad ligament & the uterosacral ligament (**Adenomyosis:** presence of endometrial tissue within the myometrium)
- Deposits respond to hormonal stimulation, results in inflammation \rightarrow dysmenorrhea, dyspareunia, pain, infertility
- Symptoms range from minimal to debilitating, implants can be superficial, peritoneal, ovarian and deeply infiltrating
- Inflammatory cells break down RBCs \rightarrow pigmented lesions (the older the lesion, the more likely it is to be pigmented)

What causes endometriosis? Multifactorial! Combination of environmental (estrogen dominance, inflammation, escape from immune clearance) and genetic predisposition; Multiple hypotheses:

- 1) Retrograde menstruation theory: During menses, endometrial debris travels backwards through the fallopian tube \rightarrow peritoneal cavity \rightarrow implant onto various peritoneal structures; \uparrow rates in women with outflow tract anomalies
- 2) Stem cell theory: undifferentiated endometrial cells initially in the basalis layer displaced to an ectopic location (i.e. retrograde menstruation), and may give rise to endometriosis
- 3) Aberrant lymphatic or vascular spread of endometrial tissue
- 4) Coelomic metaplasia – pluripotent peritoneum can undergo metaplastic transformation to tissue identical to endometrium

How do we diagnose endometriosis?

- Typically diagnosed clinically, based on the history and physical exam (uterosacral ligament nodularity, fixed uterus, etc)
- Biomarkers: cancer antigen 125 (CA 125), +correlation with disease severity; BUT poor sensitivity with mild disease
- Imaging: Transvaginal ultrasound detects endometriomas, and helps exclude other causes of pain
- Gold standard: laparoscopy and histological confirmation – lesions can be red, white, black

How do we treat dysmenorrhea? How do we treat endometriosis?

Primary and secondary dysmenorrhea (e.g. from endometriosis):

- COX1 and COX 2 inhibitors such as NSAIDs initiated before expected menses and continued for 2-3 days \rightarrow \downarrow prostaglandins (**figure 3**)
- Hormonal contraception including oral contraceptives, intrauterine devices, etc. can be used \rightarrow atrophy of endometrium \rightarrow \downarrow amounts of arachidonic acid \rightarrow \downarrow prostaglandins

Endometriosis refractory to hormonal suppression & NSAIDs:

- GnRH agonists can be considered if pain refractory to hormonal contraception
- Surgical intervention (ablation, excision, hysterectomy) can be considered

Figure 1:

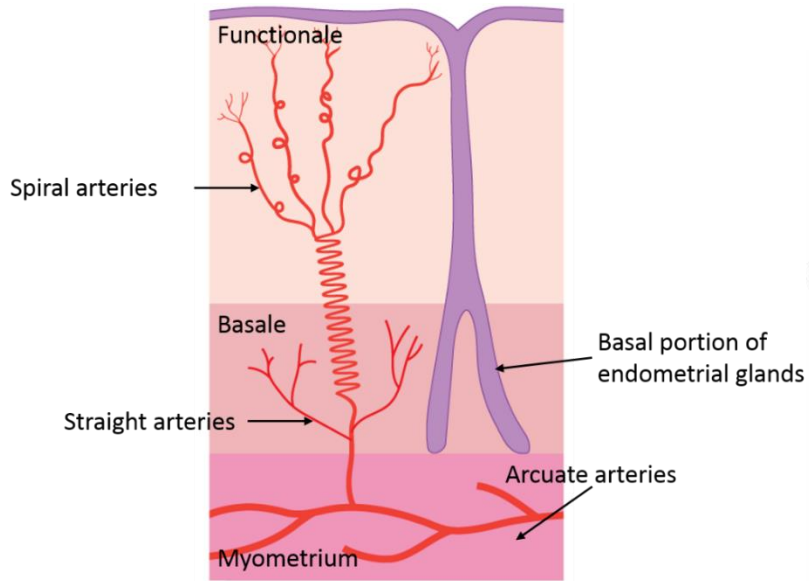


Figure 2:

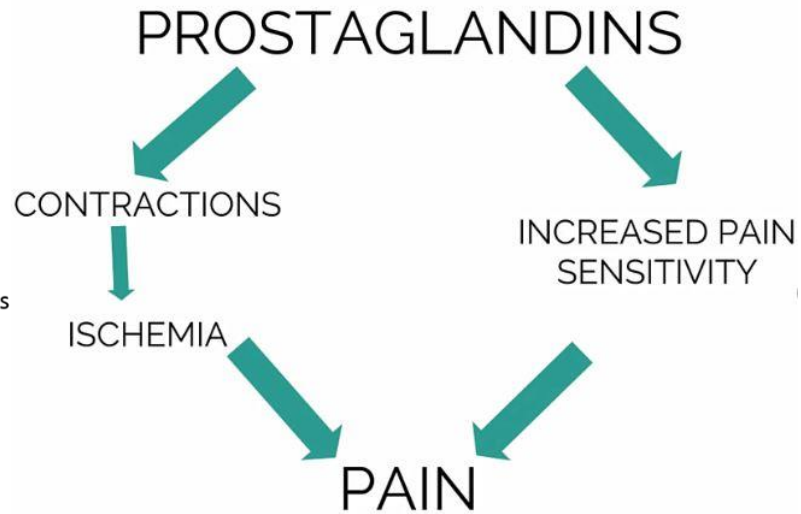


Figure 3:

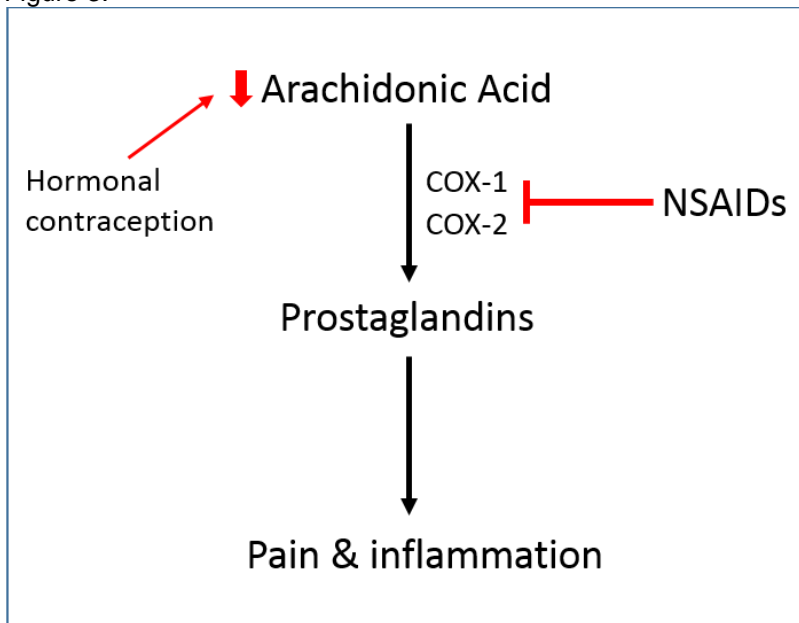


Figure 1: Aki Yao, Learning Design & Publishing, Medical School Information Services, University of Michigan

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