

DYSMENORRHEA :: painful menstrual cramps

- **Pathophysiology**
 - 1°: During ovulatory cycles, prostaglandins (+vasopressin + leukotrienes) → contractions → pain
 - 2°: Associated with underlying pathology (endometriosis, fibroids, cancer, STDs, PID, IUDs)
 - Later onset in life, longer duration, occurs on non-menstrual days + no ↓pain as ↓flow
- **Presentation & symptoms**
 - Begins shortly before or during start of menses → peaks at 1-2 days
 - 1° symptoms: lower abdominal pain/cramping, backache
 - Associated symptoms: N/D (due to prostaglandins), upper leg pain, headache, fatigue
 - Pain should ↓ as menstrual flow ↓
- **Goals of therapy:** ↓pain, ↓pelvic discomfort, ↓SE
- **Non-drug therapy:** heat patch, life style modifications (aerobic exercise, smoking cessation)
- **Drug treatment**
 - **Analgesics:** NSAIDs ↓prostaglandin production
 - OTC (1st line): ibuprofen, naproxen
 - If failed (2nd line): generic agents, branded traditional NSAIDs, COX-2 selective NSAIDs
 - Scheduled dosing > prn (↓PG synthesis vs. merely analgesic effect)
 - AE: not many due to short term use, GI upset, bronchoconstriction (asthmatics), dizziness
 - **Contraceptives**
 - MOA: (–)ovulation, ↓prostaglandin, ↓uterine motility
 - Extended use (i.e. skipping placebos) help avoid menses & cramps (max 3 months in a row)
 - 1st line for sexually active patients: killing 2 birds with 1 stone
 - 2nd line for patients failing adequate trial of NSAIDs
 - Oral contraceptives > DepoProvera or Mirena due to their side effects
 - **Alternative therapies:** 3rd line (limited efficacy data)
 - Drugs: CCBs, transdermal nitroglycerin, fish oils, oral zinc
 - Non-drug: TENS nerve stimulation, acupuncture

PMS :: pre-menstrual syndrome :: physical ± mood changes

- During **luteal phase** (days 14-28 of menstrual cycle), onset 2 weeks prior to menstruation
 - Symptom free period during follicular phase (after menses)
- **Pathophysiology:** unknown, but think it is associated with abnormalities in 5-HT (maybe GABA & allopregnanolone too)
- **Symptoms**
 - Physical: breast tenderness/swelling, bloating/fluid retention, headaches, joint/muscle pains, sleep disturbances
 - Psychological: depressed, anxiety, mood swings, anger, irritability, ↓interest in activities, ↓concentration, appetite changes, overwhelmed, out-of-control feeling
- **Diagnosis**
 - Based on exclusion of underlying physiologic condition (lupus, thyroid disease, seizures) or psychological disorder (depression, bipolar, anxiety disorder)
 - Look for absence of symptoms in follicular phase and presence in luteal phase
 - ACOG/NIMH criteria
 - 1 affective/somatic symptom 5 days before menses in 3 cycles
 - Symptom relief 4 days after menses onset (no recurrence until ≥day 13)
 - No exogenous substance that causes symptoms
 - Consistent criteria ≥2 cycles
 - Cause identifiable social/economic dysfunction
- **Treatment goals:** ↓symptoms + ↑QOL + ↑well-being
- **Treatment**
 - **1st line: lifestyle modification & nutritional supplementation**
 - ↓Caffeine, ↓salt, ↓alcohol, ↓stress, ↓smoking
 - ↑tryptophan/complex carbs, ↑small frequent meals, ↑aerobic exercise, good sleep hygiene
 - Calcium 1000-1200 mg/day (taken daily, not just during symptoms)
 - Magnesium, vitamin E, vitamin B6
 - **2nd line_a: serotonergic antidepressants** (agents of choice)
 - Class effect, improves mood symptoms more than physical, wait several cycles for full effects
 - SSRIs: fluoxetine (Prozac/Sarafem), sertraline (Zoloft), paroxetine (Paxil CR)

- Others: nefazodone, venlafaxine, duloxetine, tricyclics (clomipramine, nortriptyline)
- Dosing options
 - Daily dosing: throughout cycle
 - Intermittent: low dose during luteal phase → slower onset but ↓SE
- **2nd line_s: oral contraceptives**
 - Yaz: ethinyl estradiol + drospirenone (24 active/4 placebo)
 - Use if trying to kill 2 birds with 1 stone (i.e. want contraception as well)
- **Symptom targeted therapy**
 - **Anxiety**
 - Anxiolytics with intermittent dosing: alprazolam, buspirone
 - **Fluid retention/bloating**
 - Diuretic if it's patient's chief complaint + ≥5lb weight gain
 - Spironolactone (agent of choice), metolazone, HCTZ, triamterene, pamabrom, caffeine
 - **Mastalgia** (breast tenderness)
 - Vitamin E, NSAIDs
 - **Headaches, joint/muscle pains**
 - Acetaminophen, NSAIDs (but may ↑bloating)
 - **Insomnia**
 - Sedatives prn: diphenhydramine, pyrilamine maleate, tarzodone, doxepin, melatonin
- **Menstrual cycle modulation (hormonal therapy)**
 - Directs therapy at the modulation or temporary ablation of hormonal changes that trigger PMS symptoms
 - Progesterone supplementation
 - Danazol: synthetic androgen that ↓ovarian function
 - GnRH agonists: "medical ovariectomy"
 - GnRH agonists + add-back: adding low dose estrogen+progesterone to ↓estrogen risks
 - GnRH agonists + anti-osteoporosis treatment: adding bisphosphonate to ↓bone loss
- **Surgical management** (last resort)
 - Bilateral oophorectomy: eliminates hormonal changes

PMDD :: pre-menstrual dysphoric disease :: severe form of PMS

- **Incapacitating symptoms**
 - **Diagnosis:** APA criteria
 - ≥5 symptoms consistent with PMS (≥1 dysphoric mood change)
 - 30% worse symptoms during luteal phase
 - Impairment of social/occupational function
 - Symptom-free week after menses
 - **Treatment**
 - 1st line: serotonergic agents + OCPs
 - Add on: symptom targeted therapy, lifestyle modification
 - Ovarian suppression/removal
- } Treatment details consistent with PMS as outline above