Pre-Post Reproductive years, “The Change”

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Dysmenorrhea: Definition

Painful menstruation that prevents a woman from performing normal activities

* Primary dysmenorrhea – no readily identifiable cause
* Secondary dysmenorrhea – identifiable organic cause
Pain
- Onset within 2 years of menarche
- Begins a few hours before or just after onset of menses
- Lasts 48 – 72 hours
- Described as “cramp-like”
- Strongest over lower-abdomen
- Radiates to back or inner thighs

Associated symptoms
- Nausea and vomiting
- Fatigue
- Diarrhea
- Lower backache
- Headache
Primary Dysmenorrhea: Conventional Treatment

* Medical
  * NSAIDs
  * Hormonal contraceptives (e.g. OCPs, IUD, Vaginal rings, Patches)
  * Progestins (e.g. Medroxyprogesterone acetate)
  * Tocolytics (e.g. Salbutamol)
  * Analgesics

* Other Measures
  * Transcutaneous nerve stimulation
  * Acupuncture
  * Psychotherapy
  * Hypnotherapy
Secondary Dysmenorrhea: Symptoms

- **Pain**
  - Develops in older women (30’s to 40’s)
  - Not limited to menses

- **Associated symptoms**
  - Dyspareunia
  - Infertility
  - Abnormal uterine bleeding
# Secondary Dysmenorrhea: Symptoms

<table>
<thead>
<tr>
<th>Condition</th>
<th>Signs and Symptoms</th>
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<tbody>
<tr>
<td>Endometriosis</td>
<td>Pain extends to premenstrual and postmenstrual phase</td>
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<tr>
<td></td>
<td>Deep dyspareunia</td>
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<tr>
<td></td>
<td>Tender pelvic nodules (e.g. uterosacral ligaments)</td>
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<td>Onset in 20’s – 30’s</td>
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<tr>
<td>Pelvic inflammation</td>
<td>Pain initially menstrual, with each cycle extends into premenstrual phase</td>
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<tr>
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<td>Intermenstrual bleeding</td>
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<td>Pelvic tenderness</td>
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<td>Fever, chills, malaise</td>
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<tr>
<td>Adenomyosis,</td>
<td>Pain ± menorrhagia</td>
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<td></td>
<td>Uterus symmetrically enlarged, mildly tender, “boggy”</td>
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<tr>
<td>Uterine fibroids</td>
<td>Pain ± menorrhagia</td>
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<td>Firm, irregularly enlarged uterus</td>
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<td>Ovarian cysts</td>
<td>Mid-cycle, unilateral pain</td>
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<tr>
<td>Pelvic congestion</td>
<td>Dull, ill-defined pelvic ache</td>
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<tr>
<td></td>
<td>Pain worse premenstrually and relieved by menses</td>
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<td>History of sexual problems</td>
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</table>
Secondary Dysmenorrhea: Conventional Treatment

* Management consists of treatment of the underlying disease
* Treatment used for primary dysmenorrhea often helpful
Treatment

- Progesterone topical or suppository
  - Typical dose depends on the severity of the case.
  - 200mg to 400mg daily from day 13 to 27 of cycle is good starting dose.
  - Max dose is 2.4gm of progesterone per day to control the symptoms and then reduce down to physiologic dose
- Reduce estrogen with aromatase inhibitor or vitamins as an adjunctive therapy.
Treatment

Other related treatments:

- Due to heavy blood loss and excess inflammation
  - Methylcobalamin 6.25mg
  - Hydroxocobalamin 6.25mg
  - Folinic Acid 5mg
  - P5P 6.25mg

Inject 1ml weekly for 4 weeks then 1ml every month.
Menopause

- Marks the end of reproductive life
- Cessation of menses for 12 months
- Clinical diagnosis (not labs)
- Result of egg depletion and estrogen production by the ovary due to...
- Natural aging or surgery
Why is understanding menopause important?

% Increase in US population aged over 55

Source: US Bureau of the Census, International Database
Summary of Key Physical Changes

* Vasomotor instability
* Metabolic Changes
* Coronary Artery Disease
* Accelerated bone loss
* Skin changes
* Urogenital atrophy
* Cognition
* Libido
THE 7 MENOPAUSAL DWARFS

ITCHY

BITCHY

SLEEPY

SWEATY

FORGETFUL

PSYCHO
Menopause is related to health

- increased risk for developing two significant diseases: osteoporosis and heart disease
The Basics: Perimenopause

Overview:
* Years immediately preceding and following the last menstrual period
during this time the following processes are occurring within a woman's body:
  * ovaries release eggs less regularly
  * ovaries gradually produce less estrogen and other hormones
  * fertility decreases
  * menstrual cycles shorten, there are fewer ovulations, and more cycle irregularity
Perimenopause

- Follows period of declining fertility
- Precedes menopause
- Clinical diagnosis based on menstrual cycle pattern.
  - cycle irregularity (shortening then lengthening)
  - increasing symptoms
- Duration 2 to 8 years (average 5 years)
Perimenopause - Symptoms:

Highly Variable

* Vasomotor instability (85%)
* Sleep disturbances
* Mood disturbances
* Changes in sexual desire
* Difficulty in concentration
* Somatic symptoms:
  * Fatigue, palpitations, headache, increased migraine, breast pain and enlargement.
* Oligo- → Anovulation
  * heavier or irregular cycles.
* joint and muscle aches, frequent urination
* similar symptoms as experienced with premenstrual syndrome (PMS)
Managing Perimenopause

Goals:

* Patient education
* Prevention of endometrial cancer
* Individualized symptomatic relief
  * Menstrual control
  * Minimizing hot flashes
  * Mood disturbances
Peri/menopause Treatment

- Bio-identical hormones
  - Estradiol
  - Estriol
  - Testosterone
  - DHEA
  - Pregnenolone
  - Cortisol
  - Thyroid
  - Insulin
- OTC herbs and supplements
Peri/menopause Treatment

Factors to consider

* Daily vs Rhythmic hormonal treatment
* What dosage form is right for your patient
  * Capsules
  * Sublingual drops/tablets/troches
  * Topical/mucosal cream/gel
  * Transdermal cream/gel
  * Suppositories
  * IM injections
Dosage forms

* Capsules – swallow by mouth. Some may cause drowsiness and some has huge 1st pass. May also increase metabolite concentration and have to be careful if they are toxic.

* Suppository – can be used either rectally or vaginally

* Sublingual drops/tablets/troches – must place under the tongue until absorbed. (caution: part of the medication will be swallowed and taste will vary based on the dosage

* IM injections – Need to take weekly shots. No other added advantage.

* Pellets – Minor surgical procedure required to insert the pellets and may last for 3 to 6 months (only for estradiol & testosterone)
Dosage Forms - cont

* Topical creams – All creams has limitation as to the final concentration of the cream.
  * All creams are oil-in-water emulsions and depending on the oil phase of the cream there is only so much hormones you can incorporate inside.
  * The best area to apply the medication is as close to ovaries as possible (vaginally).
  * Cosmetically very appealing

* Trans-dermal creams – Most work on the concept of making small micelles with liposome and can incorporate larger concentration of hormones than creams
  * Actively drives the medication through the skin
  * Takes a little longer to absorb and may not be cosmetically appealing (a little sticky)
Dosage Forms - cont

* Gel – most gels are alcohol based. Water based gel cannot dissolve hormones and may not deliver hormones via skin.
* Alcohol based gels may cause dry skin and cannot be used for vaginal application.
* Ideal to delivery large amount of hormones
* Fast absorbing and actively drives the medication through the skin.
Typical Rx for Peri-Menopause

* Progesterone SB (*Saccharomyces boulardii*) 150 to 200mg caps @ bedtime (if insomnia) OR

* Progesterone 5 to 10% cream daily from day 13 to 27 of cycle

* Biestrogen 0.625 to 1.25mg cream (only if low estradiol level and symptomatic)

* Androgen added if symptomatic and confirmed low hormone levels
Typical Rx for Menopause

* Biestrogen 1.25 to 2.5mg cream daily (Day 1 to 25)
* Progesterone SB (*sacchromycesis boulardii*) 150 to 200mg caps @ bedtime (Day 6 to 30)
* Testosterone 0.5 to 1mg cream daily
* Pregnenolone/DHEA 25/5 to 25/10mg caps daily

Also evaluate the need to regulate thyroid and adrenal function for optimum results.
Typical Rx for Menopause (secondary to hysterectomy)

<45yrs old vs >45yrs old

* Progesterone 30 to 80mg topical cream OR
* Progesterone 100mg to 200mg SB daily at bedtime from day 13 to 27 of cycle/month.
* Biestrogen 0.625 to 1.25mg topically daily from day 1 to day 21 of cycle/month
* Testosterone 0.5mg to 1mg topically daily
* Pregnenolone/DHEA 25/5 to 25/10mg topically or orally daily
Perimenopause Case 1

- Patient: LB
- Age: 32 years old - Female
- Marital Status: Single
- Occupation: Receptionist
* Allergies: Lidocaine
* Medications, OTC, Vitamins: Alprazolam, Ambien
* Medical Conditions: Insomnia
* Cancer History/Family History: No history of cancer
* Pregnancies: 3 children
- Alcohol: none
- Tobacco: none
- Caffeine: none
* Mammogram/Pap Smear: negative (within past 6 months)
* Sexually active: Yes
* Menstrual cycle: Period lasts 4-6 days, heavy periods, irregular cycle
* Hot flashes 1/10
* Night sweats 2/10
* Vaginal Dryness 2/10
* Depression 3/10
* Anxiety 4/10

* Irritability 5/10
* Insomnia 10/10
* Low Libido 1/10
* Fuzzy Thinking 5/10
* Fatigue 5/10
* Estradiol 110 pg/ml
* Progesterone 0.8 ng/ml
* Testosterone 45 ng/dl
* DHEA-S 175 mcg/dl
* Vitamin D3 67 ng/ml
Treatment

* Progesterone 100mg – 1 capsule po qhs on day 14-28 of cycle
* Pregnenolone/DHEA 25/5mg – 1 c po daily
* Estriol 2mg/gm. Apply 1 gm intravaginally daily prn dryness.
* Glandular adrenal support vitamins 1 po QAM and if needed 1 @ 2pm.
Perimenopause Case 2

* Patient: TS
* Age: 42 years old - Female
* Marital Status: Married
* Occupation: Physician
* Allergies: Pollen, Dust
* Medications, OTC, Vitamins: Alprazolam, Calcium, Multivitamin, Fluoxetine
* Medical Conditions: Depression, Anxiety
* Cancer History/Family History: No history of cancer-
* Past Surgeries: Tubal ligation 6 years ago
* Pregnancies: 2 children
- Alcohol: none
- Tobacco: none
- Caffeine: none
* Mammogram/Pap Smear: negative (within past 6 months)
* Sexually active: Yes
* Menstrual cycle: Period lasts 6 days, heavy periods, approx 28-30 day cycle, regular
- Hot flashes 0/10
- Night sweats 0/10
- Vaginal Dryness 2/10
- Depression 10/10
- Anxiety 9/10
- Irritability 8/10
- Low Libido 7/10
- Fuzzy Thinking 5/10
- Fatigue 5/10
* Estradiol 96 pg/ml
* Progesterone 0.6 ng/ml
* Testosterone 15 ng/dl
* DHEA-S 153 mcg/dl
* Vitamin D3 29 ng/ml
* Progesterone 100mg/ml – 1ml inner thighs po qhs on day 13-27 of cycle
* Pregnenolone/DHEA 25/5mg – 1 c po daily
* Testosterone 1mg/0.1ml – 0.1ml inner labia daily
* Vitamin D3/K2 5000 IU – 1 c po daily
Menopause Case 1

* Patient: JM
* Age: 53 years old - Female
* Marital Status: Married
* Occupation: Cashier
* Allergies: Sulfa, Morphine
* Medications, OTC, Vitamins: Vitamin B12, Vitamin D3
* Medical Conditions: Arthritis, Depression
* Cancer History/Family History: No history of cancer
* Past Surgeries: Tubal ligation 15 years ago
* Pregnancies: 4 children
* Alcohol: 2 glasses of red wine/week
* Tobacco: 2 cigarettes/day
* Caffeine: 2 cups coffee/day
* Mammogram/Pap Smear: negative (within past 6 months)
* Sexually active: Yes
* Exercise: Walk 3x a week

* Last menstrual cycle: 2 years ago
* When cycling: Period lasted 4 days (irregular, heavy periods)
* Hot flashes 9/10
* Night sweats 7/10
* Vaginal Dryness 5/10
* Depression 6/10

* Anxiety 2/10
* Irritability 0/10
* Low Libido 10/10
* Fuzzy Thinking 8/10
* Fatigue 5/10
<table>
<thead>
<tr>
<th>Substance</th>
<th>Level</th>
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<tbody>
<tr>
<td>Estradiol</td>
<td>12 pg/ml</td>
</tr>
<tr>
<td>Progesterone</td>
<td>&lt;0.5 ng/ml</td>
</tr>
<tr>
<td>Testosterone</td>
<td>7 ng/dl</td>
</tr>
<tr>
<td>DHEA-S</td>
<td>40 mcg/dl</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>21 ng/ml</td>
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Treatment

* Biestrogen 1.25mg/0.1ml – 0.1ml inner labia daily
* Progesterone 100mg/ml – 1ml inner thighs po qhs on day 13-27 of cycle
* Pregnenolone/DHEA 25/5mg – 1 c po daily
* Testosterone 1mg/0.1ml – 0.1ml inner labia daily
* Vitamin D3/K2 5000 IU – 1 c po daily
Menopause Case 2

* Patient: DC
* Age: 45 years old - Female
* Marital Status: Married
* Occupation: Beauty Salon Owner
* Allergies: None
* Medications, OTC, Vitamins: Multivitamin daily
* Medical Conditions: N/A
* Cancer History/Family History: Mother had breast cancer, Sister had ovarian cancer
* Past Surgeries: Hysterectomy 2013
* Pregnancies: 2 children
* Alcohol: 3 glasses of red wine/week
* Tobacco: 0 cigarettes/day
* Caffeine: 0 cups coffee/day
* Sexually active: Yes
* Exercise: Walk 3x a week
* Last menstrual cycle: 2 years ago (hysterectomy)
* When cycling: Period lasted 5 days, 28 day cycle (regular, heavy periods)
* Hot flashes 10/10
* Night sweats 10/10
* Vaginal Dryness 8/10
* Depression 8/10

* Anxiety 9/10
* Irritability 10/10
* Low Libido 8/10
* Fuzzy Thinking 8/10
* Fatigue 9/10
* Estradiol  <0.1 pg/ml
* Progesterone  <0.5 ng/ml
* Testosterone  15 ng/dl
* DHEA-S  100 mcg/dl
* Vitamin D3  28 ng/ml
Treatment

* Biestrogen 2.5mg/0.1ml – 0.1ml inner labia daily
* Progesterone 150mg SB caps 1 po QHS
* Pregnenolone/DHEA 25/5mg – 1 c po daily
* Testosterone 1mg/0.1ml – 0.1ml inner labia daily
* Vitamin D3 5000 IU – 1 c po daily
Conclusion

* Pre & Post reproductive years in women life is about the same number.
* Learning effective way to manage hormonal intervention can dramatically improve quality of life.
* Managing of hormones need to take into account for all the hormones from Cortisol, thyroid, insulin, gonadal, pituitary and hypothalamic hormones.
* Strive to achieve proper endocrine balance for patients to feel the best.