Objectives

At the conclusion of this presentation, the participants will be able to:
1. Explain (review) the physiology of the normal menstrual cycle
2. Differentiate primary vs secondary amenorrhea.
3. Identify the etiology of primary and secondary amenorrhea.
4. Recognize the female athlete triad components.
5. Determine the appropriate PPE history, PE, and laboratory workup for functional hypothalamic amenorrhea.
6. Utilize the Triad Cumulative Risk Assessment to determine return to play.
7. List the treatment options in female athlete triad.

Amenorrhea is the absence of menstrual bleeding.

Prepubertal

Postmenopausal

Pregnant
Amenorrhea in reproductive age women...

- Primary
  - Failure of menses by 16 years of age
- Secondary
  - Cessation of menses after menarche
- Oligomenorrhea
  - Cycle > 35 days

Menstrual Cycle

- Regular cycles designed for fertilization and pregnancy
  - Average length is 28 days
- Cycle components:
  - Follicular phase
  - Ovulation
  - Luteal phase
Primary Amenorrhea

- Average age of menarche in the U.S. is 12.6 years
  - Range 9 - 15 years
- Pathophysiology of primary amenorrhea
  - Hypothalamic dysfunction
  - Pituitary dysfunction
  - Ovarian causes
  - Congenital and anatomic abnormalities
  - Receptor and enzyme defects

Primary Amenorrhea

- Etiologies
  - Hypothalamic causes
    - Kallman Syndrome: congenital absence of GnRH and anosmia
    - Hypogonadotropic hypogonadism
    - Compression of pituitary stalk by tumor
    - Decreased GnRH release
      - Stress
      - Anorexia nervosa
      - Weight loss
      - Extreme exercise
      - Hyperprolactinemia (prolactin inhibits GnRH)

Functional Hypothalamic Amenorrhea

- Eating disorders
- Exercise
- Prolonged physical or mental stress
Amenorrhea - Pituitary Causes

- Tumors:
  - Hyperprolactinemia
  - Iron deposition in pituitary: hemosiderosis
    - Impairs pituitary function
    - Decreased FSH and LH
  - Gene mutations

Amenorrhea - Ovarian Causes

- Turner Syndrome (XO karyotype): ovarian dysgenesis
- Polycystic Ovarian Syndrome (PCOS)
  - 1 in 5 cases of amenorrhea is caused by PCOS
  - Causes abnormal follicular growth and secretion of androgens

Amenorrhea - Congenital and Anatomic Abnormalities

- Imperforate hymen or other outflow tract obstruction
- Vaginal or uterine agenesis
- Transverse vaginal septum
- Uterine scarring with adhesions
Amenorrhea - Receptor and Enzyme Defects
- Congenital adrenal hyperplasia
- Androgen insensitivity syndrome
- Mutations of LH and FSH receptors (rare)
- Aromatase deficiency (rare)
- Lead to virilization in females

Secondary Amenorrhea
- Low or normal FSH levels (66%)
- High FSH levels (12%)
- High prolactin (13%)
- Anatomic disorders (7%)
- Hyperandrogenic states (2%)

Low or normal FSH levels (66%)
- Chronic anovulation/PCOS
- Hypothyroidism
- Cushing syndrome
- Pituitary tumor
- Functional hypothalamic amenorrhea
High FSH levels (12%)
- Primary ovarian insufficiency (premature ovarian failure)
- Menopause before age 40
- Turner Syndrome (XO karyotype): ovarian dysgenesis

Hyperandrogenic states (2%)
- PCOS
  - Triad of weight gain (relative insulin resistance), hyperandrogenism, irregular menses or infertility
  - Absence of galactorrhea
  - Ovarian tumor

Functional Hypothalamic Amenorrhea
- Female Athlete Triad
  - Low energy availability with or without disordered eating
  - Menstrual dysfunction
  - Impaired bone health
Markers of the Triad: A continuum.

**Menstruation**
- Menstrual Dysfunction
  - Decreased GnRH secretion
  - Shortened luteal phase and prolonged follicular phase
  - Decreased estradiol
  - Oligo- or amenorrhea
  - 30 kcal/kg threshold for maintaining menstrual function

**Bone Mineral Density**

**Energy Availability**

**Low Energy Availability**
- Low energy availability: lack of adequate caloric needs for their exercise or training
- Exercise history
  - Number of hours athlete spends in practice/exercise
    - Formal practice
    - Additional time: related activities (conditioning, running, and lifting)
    - Season vs Offseason
- Nutritional assessment
  - Number of calories per day
- Disordered Eating:
  - Eating Disorder Inventory (EDI), the Athletic Milieu Direct Questionnaire (AMDQ), the Female Athlete Screening Tool (FAST), and the American Physiological Screening Test for eating disorders among Female College Athletes (PST), Low Energy Availability in Females Questionnaire

**Optimal Bone Health**

**Optimal Energy Availability**

**Triad Circles**

10/7/2016
Impaired Bone Health

- Decreased estrogen affects calcium resorption and bone accretion
- Peak bone mass: between 20 and 30 years
- Peak bone mineral content: between 9 and 20 years
- Bones of the lower extremities, pelvis, and vertebrae: most common
- Stress fractures and overt fractures
- DEXA scan normal reporting of osteopenia and osteoporosis postmenopausal women:
  - T-score or the standard deviations (SDs) below the mean
  - Premenopausal athletes, adolescents and children:
    - Z-score or BMD by chronologic age and gender
    - Most athletes have a higher BMD than non-athletes
    - Work up athletes with Z-score < 1.0

High Risk Athletes

Disordered eating:
- Do you worry about your weight?
- Do you limit the foods you eat?
- Do you lose weight to meet image requirements for sports?
- Does your weight affect the way you feel about yourself?
- Do you feel you have lost control over what you eat?
- Do you make yourself vomit or use laxatives or diuretics?
- Have you suffered from an eating disorder?
- Do you ever eat in secret?

Screening in the Pre-participation Exam
Screening in the Pre-participation Exam

- Menstrual dysfunction:
  - How old were you when you had your first menstrual period?
  - Do you have monthly menstrual cycles?
  - How many menstrual cycles have you had in the past 12 months?

- Skeletal health
  - Have you ever had a stress fracture?
  - Have you ever been told you have low bone density (osteopenia or osteoporosis)?

Physical Exam

- Height, weight, BMI
- Pulse, BP (supine and standing), and temperature
  - Bradycardia, orthostatic hypotension
- Cardiac exam
- Oral, salivary glands, and thyroid exam
  - Parotid enlargement, thyroid enlargement
- Skin, hand and finger exam
  - Cold extremities, dry skin, lanugo hair, knuckle scars
- Stage sexual maturation
- Consider pelvic exam in female athletes with menstrual dysfunction
  - Vaginal atrophy
**Laboratory Assessment**

- CBC with differential
- CMP
- Electrolytes, calcium, glucose, LFTs
- LH, FSH, Beta hCG
- Vitamin D
- Prolactin
- TSH, T4
- Estradiol, testosterone (free and total), DHEA-S
- Progesterone challenge test
- UA
- DEXA scan, if indicated
- +/- 17 (OH) progesterone and/or pelvic ultrasound

**Progesterone Challenge Test**

- Progesterone challenge test (secondary amenorrhea)
- Indirectly determines whether ovary is producing estrogen
- Give progesterone for 10 days, then stop
- If estrogen produced, menses

**Uterine pathology or outflow tract disorder**

- Low to N gonadotropins
- Neg Progesterone challenge
- Painless pelvic pain
- Consider FSH (producer not producing estrogen)

**History and PE**

- History and physical examination
- Relevant symptoms and history
- Physical examination findings

**Disorders of sexual differentiation**

- Consider specific investigation of endocrine disorder
- Chronic anasarca/PCOS
- POI
- Specific investigation of endocrine disorder
- Abnormal TSH, prolactin, DHEA-S, 17 (OH) progesterone
Treatment Aimed at Low EA

- Non-pharmacological therapy:
  - Energy status normalized
  - Modifications of diet and exercise
    - Include the athlete, coach, parents
    - Referrals:
      - Sports dietician, exercise physiologist, healthcare provider, athletic trainer, MH practitioner if necessary
  - Optimize calcium and vitamin D intake

Treatment Aimed at Low EA

- Pharmacological Therapy
  - If ED or co-morbid depression, anxiety, OCD
    - SSRIs
  - Estrogen replacement generally not recommended
  - Bisphosphonates - not approved
    - Only initiate through consultation with endocrinologist

Patient education is the key to successful outcomes
### Triad Cumulative Risk Assessment to Determine Return to Play

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Low Risk = 0 pts each</th>
<th>Moderate Risk = 1 pt each</th>
<th>High Risk = 2 pts each</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low EA with or without DE/ED</td>
<td>No dietary restriction</td>
<td>Some dietary restriction; current/past fit of DE</td>
<td>Symptoms DSM V criteria for ED</td>
</tr>
<tr>
<td>Low BMI</td>
<td>BMI &gt;18.5 or &gt;95% EW</td>
<td>BMI 17.5 - 18.5 or &gt;95% EB or 15 to 10% weight loss/month</td>
<td>BMI &lt;17.5 or &lt;85% EB or &gt;10% weight loss/month</td>
</tr>
<tr>
<td>Delayed Menarche</td>
<td>&lt; 15 years</td>
<td>15 to 16 years</td>
<td>&gt; 16 years</td>
</tr>
<tr>
<td>Oligo- or amenorrhea</td>
<td>&gt; 9 menses/year</td>
<td>6-9 menses/year</td>
<td>&gt;6 menses/year</td>
</tr>
<tr>
<td>Low BMD</td>
<td>Z-score = -2.0</td>
<td>Z-score = -1 to -2</td>
<td>Z-score = -2.0</td>
</tr>
<tr>
<td>Stress Fr/Reaction</td>
<td>None</td>
<td>1</td>
<td>+1 or 2 or 1 in high risk area</td>
</tr>
<tr>
<td>Cumulative Risk</td>
<td>____ points +</td>
<td>____ points +</td>
<td>____ points +</td>
</tr>
</tbody>
</table>

Cumulative Risk ________ points + _______ points + _______ points = _______ Total Score

### Triad Cumulative Risk Total

- Full clearance:
  - Cumulative risk score 0-1 point
- Provisional/Limited clearance:
  - Cumulative risk score 2-5 points
- Restricted from training and competition:
  - Cumulative risk score >/= 6 points

### Prognosis

- Energy status
  - Recovers in days to weeks
- Menstrual dysfunction
  - Recovers in months
- BMD
  - May take years to recover
  - >95% of total BMD acquired by age 18 years
  - 90% of female athletes with low BMD at baseline had low BMD at 3 year follow up
References


Questions?