Secondary Amenorrhea

Background
1. Definition
   - Transient intermittent or permanent absence of menses for more than 3 cycles or 6 months
2. Primary amenorrhea
   - Absence of menses by age of 16 if
     - Secondary sexual characteristics present
   - Absence of menses by 14 years of age if
     - No secondary sexual characteristics
   - No menses 2 years after sexual maturation is complete

Pathophysiology
1. Hypothalamus
   - Low GnRH
     - Causes low gonadotropins and anovulation
     - Low or normal LH, absent LH surge, low estradiol, FSH:LH ratio similar to prepuberty levels
   - Eating disorders
     - 10% below ideal body weight
     - Anorexia nervosa
   - Stress
     - Emotional, physical
   - Female athlete triad
     - Amenorrhea
     - Disordered eating
     - Osteopenia
2. Pituitary
   - Common cause of galactorrhea
   - 20% of amenorrheic patients have a pituitary cause
3. Thyroid
   - Possible Sx of thyroid disorders
4. Ovary
   - Hyperandrogenism
     - Abnormal estrogen and/ or progesterone levels
     - Chronic anovulation
     - Endometrial atrophy
   - PCOS
     - Causes 20% of amenorrhea, often with obesity and signs of hyperandrogenism
     - Signs and symptoms = hirsutism, new acne, amenorrhea
   - Ovarian failure
     - Lack of estrogen production
     - May be normal in Menopause (45-55 yo)
     - Premature if <40 yo
5. Uterus
   - Ashermann's syndrome
     - Caused by postpartum hemorrhage, infection, or previous uterine instrumentation (D&C)
6. Medications
   - OCP, danazol, high-dose progestin, metoclopramide
   - Antipsychotics

**Diagnostics**

1. Systems approach most effective
2. History
   - Recent OCP use
   - Weight change
   - Stress, illness
   - Exercise, participation in athletics
   - Headaches, vision change
   - Body image
3. Physical exam
   - Signs of pregnancy
   - BMI
   - Breast discharge
   - Hirsutism
   - Acne
4. Laboratory testing
   - Urine pregnancy test
   - FSH, T4, TSH (SOR:B)
   - Prolactin
     - Recheck if abnormal
   - DHEA-S and testosterone
     - Check if hyperandrogenism suspected
   - Progesterone challenge (SOR:C)
     - 10mg medroxyprogesterone acetate orally for 5 days
     - Withdrawal bleed: chronic anovulation (PCOS, ovarian failure, hypothalamic dysfunction)
     - No bleed: "prime" the endometrium with estrogen 0.625 mg x 35 days, with MPA days 26-35
       - If no bleed, may confirm Ashermann's
5. Diagnostic imaging
   - Pelvic ultrasound
   - Cranial MRI
     - Indicated with confirmed abnormal prolactin
Differential Diagnosis
1. See Pathophysiology

Therapeutics
1. Directed at underlying pathology
   o BMI
     ▪ Maintain appropriate weight (SOR:B)$^{3,4}$
   o HRT
     ▪ Recommended regardless of diagnosis, if amenorrhea persists >6 months
     ▪ Reduces risks of osteoporosis, hypercholesterolemia
   o Calcium
     ▪ 1500mg/d if hypoestrogenism to prevent bone loss (SOR:A)
   o OCP
     ▪ Replace estrogen and prevent pregnancy, unless contraindicated
   o Bromocriptine
     ▪ Hyperprolactinemia

Follow-Up
1. Varies with etiology

References
1. Polycystic Ovary Syndrome - September 1, 2000 - American Family physician

Evidence-Based Inquiry
1. What's the best way to manage athletes with amenorrhea?

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