Women's Health:
Take Home Points

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Reproductive Endocrinology

Amenorrhea

Types
• Primary Amenorrhea
  – Absence of menses by age 16
• Secondary Amenorrhea
  – Absence of menses for 3 months

Causes:
Pregnancy, Uterine or Outflow Tract Disorders, Ovulatory Disorders (genetic and anatomic abnormalities more likely with primary amenorrhea.)

Eval: βHCG, FSH, PRL, TSH

Hypothalamic Amenorrhea

• Causes
  – Energy Output > Energy Input
  – Weight loss, eating disorders, excessive exercise
  – Stress
  – Psychological, Physical
• Eval: rule out other cause, MRI, BMD
• Treatment
  – Weight gain, decrease exercise
  – Oral contraceptives/HRT (?)
  – Adequate calcium, vitamin D

Premature Ovarian Failure

• Elevated FSH, age < 40 yrs
• Causes:
  – Turner’s syndrome; X chromosome deletions, translocations; Fragile X premutations
  – Autoimmune
  – Chemotherapy or radiation therapy
  – Other rare
• Eval:
  – Karyotype, Fragile X premutation screen, anti-thyroid and anti-adrenal antibodies
• Treatment:
  – OCPs/HRT; calcium/vit D
**PCOS**

- Rotterdam definition
  - 2 out of 3 of the following must be present
    - Oligo- or anovulation
    - Clinical and/or biochemical signs of hyperandrogenism
    - Polycystic Ovaries
  - Exclusion of other causes (e.g. hyperprolactinemia, CAH, androgen secreting tumors)
- Other common features:
  - obesity; insulin resistance; infertility

**PCOS Management**

- Weight loss (diet/exercise)
- OCP
- Metformin
- Ovulation induction/IVF
- Hair removal/spironolactone
- Follow up of glucose, lipids, bp

**Menopause Management**

**Postmenopausal hormone therapy**

- Improves vasomotor symptoms
- (WHI data)
  - HRT: Increased risks of CHD, stroke, invasive breast cancer, DVT/PE, urinary incontinence; Reduced risks of fracture, colorectal cancer
  - ERT: Increased risk of stroke, reduced risk of fx
  - Both increased risk of dementia among women 65+
- Indications: vasomotor symptoms; in some cases GU atrophy (local therapy preferred)
- Contraindications: h/o DVT/PE, breast CA, CVD, endometrial cancer/unexplained vaginal bleeding, liver disease

**Raloxifene**

- Reduced risks of vertebral (not hip) fracture, invasive breast cancer
- Increased risk of DVT/PE
- No increased risk of endometrial cancer
- No sig effect on CHD risk

**Management of symptoms**

- Vasomotor
  - ERT/HRT- at lowest doses/shortest duration needed
  - Lifestyle- keep cool, weight control, exercise, don’t smoke, avoid excessive alcohol
  - Isoflavones- not generally effective in RCTs
  - Other possible medications -not FDA approved for this indication: SSRIs, SNRI, gabapentin, progesterational agents, clonidine
- GU
  - Topical estrogen; estradiol ring; topical lubricants
HPV and Cervical Cancer
Screening/Prevention

Updated Screening Guidelines 2012
• Initiate screening at age 21
• D/c screening at age 65 if well screened (3 neg Paps or 2 neg co-screens in past 10 years); otherwise continue screening
• After age 30, if 3 normal consecutive Paps, and NO history of CIN2/CIN3, DES or HIV, or other immunocompromise, may do Paps q 3 years or combined Pap/HPV q 5 years if both tests negative.
• More frequent screening needed in high risk women
• May d/c screening after hysterectomy for benign disease in women without prior CIN

HPV testing
• Below age 30
  – No role for HPV test in screening (high rate of positivity, and most infections are cleared and do not confer elevated risk)
  – Use only as reflex test to follow up ASCUS Pap in this age group (at age 21 and over)
• Age 30+:
  – Combined PAP/HPV test approved for primary screening

Medical Disorders
Complicating Pregnancy

Pre-Existing Hypertension
• Generally good pregnancy outcomes unless superimposed preeclampsia develops
• Antihypertensive therapy
  – generally can be tapered during pregnancy
  – Goal SBP < 150-160; DBP <100-110 mm Hg
  – Stop ACEIs and ARBs prior to conception
  – Methyldopa recommended 1st line (long term outcomes data)

Pre-existing diabetes mellitus
• Birth defect risk directly related to HbA1c at conception
• ADA goals at conception
  – HbA1C ≤ 7%; preprandial plasma blood glucose 80-110 mg/dl; 2-hour postprandial plasma blood glucose <155 mg/dl
• Treatment
  – Human insulin recommended; most experience with NPH and regular (Category B); Lispro and Aspart also used
  – Pump ok
  – Oral agents have been used in pregnancy
Hyperthyroidism

- Diagnosis in early pregnancy: should not be based solely on a low TSH level (may be a normal finding) but also on symptoms (eg weight loss or absence of weight gain, anxiety, palpitations) and elevated T4.
- Exam: enlarged thyroid (not normal for pregnancy)
- Risks: IUGR, SGA infant; preterm delivery; thyroid storm
- Treatment: Aim is NOT to normalize TSH; rather aim for high normal T4; use minimum dose anti-thyroid drug (PTU) that will control sx

Hypothyroidism

- Possible risks: poor fetal growth; possible effects on IQ; increased risk for preeclampsia in mother
- Requirement for thyroid hormone increases in pregnancy and returns to pre-pregnancy requirement postpartum
- Titrate thyroid hormone dose before and during pregnancy to maintain TSH <2.5

Oral and patch contraceptives

- Ortho Evra patch
  - Better compliance than OCP BUT higher estradiol levels, uncertain effect on DVT risk (may be increased)
  - Should not use continuously
- Drospirenone
  - 2 recent studies suggested increased DVT/PE risk versus levonorgestrel
  - FDA changed label to include warning re increased VTE risk

Long-acting reversible contraception

- IUD
  - Pregnancy rare (but ectopic pregnancy common if pregnancy occurs)
  - Safe/Effective in nulliparous women at low PID risk (though IUD expulsion, bleeding, pain slightly more common in nulliparous women)
  - Types
    - Levonorgestrel (Mirena)-
      - Overall less bleeding; often used in women with menorrhagia or dysmenorrhea; may have hormonal side effects
    - Copper IUD (Paragard)–
      - Increased bleeding (esp in first few months after insertion); more cramping/pain
      - Can be inserted within 5 d after single act of unprotected intercourse as emergency contraception
- Implantable contraception (Implanon; progestin only rod)
  - Highly effective, up to 3 years
  - Must be inserted by trained provider
  - Irregular cycles common

Osteoporosis and Metabolic Bone Disease


### Risk Factors for Fracture

- Advanced age
- Estrogen deficiency
- Prior fracture
- Anorexia nervosa
- Low body-mass index
- Low testo (men)
- Vitamin D defic
- Low calcium intake
- Medical conditions:
  - GI, CTD, CKD, Endocrine diseases
- Medications:
  - AIs, heparin, anticonvulsants
  - MTX, CTX, GnRH agonist
  - Lithium, cyclosporin, aluminum, terbinafine (premenopausal)
- Systemic corticosteroid use
- Parental hx of hip fracture
- Low BMD
- Current smoking
- Excess alcohol intake
- Vitamin D defic

### Bone density

- **T-score**
  - BMD compared with "young normal" adults; ( number of standard deviations (SD) above or below the mean)
  - Used to dx osteopenia (-1 to -2.5)
  - osteoporosis (below -2.5)

- **Z-score**
  - BMD compared with persons of same sex and age.
  - A low Z-score indicates possible secondary cause of osteoporosis.

### Vitamin D deficiency

- Extremely common
- Recommended intake of Vitamin D (Cholecalciferol) varies according to different guidelines 400-1000 IU/day or more

### Approved Drugs to Treat Osteoporosis

- **Raloxifene**
  - NO reduction in hip fx/ risk of VTE

- **Calcitonin**
  - NO reduction in hip fx

- **Bisphosphonates** (Alendronate, Risedronate, Ibandronate, Zolendronic acid)
  - Reduces spine and hip fractures
  - Concerns: GI, musculoskeletal pain ONJ, atypical femoral fractures (rare)

- **Teriparatide**
  - Anabolic; reduces fractures
  - Contraindicated if hypercalcemia, XRT, bone CA, elevated alk phos, Paget’s

- **Denosumab**
  - Reduces fractures
  - Concerns: hypocalcemia, musculoskeletal pain, skin infections, ONJ (rare)

### Osteomalacia

- Delayed mineralization of bone
- **Sx/Signs:**
  - Bone pain/ deformity, kyphoscoliosis, bowed legs, proximal muscle weakness
- **Labs:**
  - Calcium nl or slightly decreased
  - Phosphorus nl or slightly decreased
  - PTH increased or normal
  - Alkaline phosphatase increased

### Osteomalacia (cont..)

- **Causes:**
  - Vit D defic (eg nutritional, malabsorption )
  - Altered Vit D metabolism (renal/liver disease..)
  - Phosphate deficiency (eg nutritional, impaired renal reabsorption, oncogenic)
  - Acidosis (eg RTA, ureterosigmoidoscopy, carbonic anhydrase inhibitors)
  - Other mineralization inhibitors (eg etidronate, AI)
Paget’s disease

• Clinical findings
  – bone pain, skeletal deformities, pathologic fractures, increased cardiac output, nerve compression, osteogenic sarcoma (rare); often asymptomatic
• Labs
  – Calcium/phosphorus: usually normal (hypercalcemia may develop with immobilization); alkaline phosphatase elevated; urinary collagen crosslinks elevated
• Treatment
  – NSAIs, bisphosphonates (FDA approved)
  – Treatment indicated for pain, hypercalcemia, fx, high output CHF (rare), neurologic compromise,
    ? to prevent progression