Amenorrhea in the Adolescent

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Objectives

• Diagnostic criteria for primary and secondary amenorrhea
• Evaluation of patients with primary and secondary amenorrhea
Menarche

- Mean age 12.5 years (range 9-16 years)
- Occurs one year after peak growth velocity and two years after onset of breast buds
- By menarche most girls have completed 75% of pubertal development and achieved 98% of growth potential

Adolescent Menstrual Cycle

- Early menstrual cycles are annovulatory
- Ovulation reflects synchronization and maturation of H-P-O axis
- Cycle lengths vary - 21-45 days
- Duration is 2-7 days
- Average blood loss - 30-40 ml
Primary Amenorrhea
• Absence of menarche by age 15 years with normal growth and development
• Absence of menarche, breast development and pubic hair by age 13 years
• Failure to undergo menarche within 3 years of beginning pubertal development

Secondary Amenorrhea
• Absence of menses for greater than three months in female with established menstruation

Question 1 - Amenorrhea
Evaluation for primary amenorrhea is indicated for all of the following except:
a) Absence of menarche in a 15 year old female with normal pubertal growth and development
b) Amenorrhea x 6 months in previously menstruating 12 yr old
c) Failure to undergo menarche within 5 years of beginning pubertal development
d) Absence of menarche and absence of breast development and pubic hair by age 15 years
Etiology of Amenorrhea

- Hypothalamic
  - Constitutional delay of puberty
  - Kallman Syndrome
  - Isolated GnRH insufficiency
  - Chronic disease
    - Inflammatory Bowel Disease
    - Cystic Fibrosis
    - Systemic Lupus Erythematosus
    - Diabetes

- Pituitary disorders
  - Prolactinoma
  - Craniopharyngioma
  - Idiopathic hypopituitarism
  - CNS Infection
Etiology of Amenorrhea

- Ovarian disorders
  - Gonadal Dysgenesis (46 XX, 46 XY)
  - Turner's Syndrome (45,XO)
  - Polycystic Ovary Syndrome
  - Ovarian failure
    - Infection, radiation, chemotherapy
    - Autoimmune disease
    - Idiopathic premature ovarian failure

Etiology of Amenorrhea

- Structural or End Organ Defects
  - Genital tract obstruction
    - Imperforate hymen
    - Vaginal septum
  - Asherman Syndrome
  - Mullerian Agenesis (46,XX)
  - Androgen Insensitivity Syndrome (46,XY)

Etiology of Amenorrhea

- Other Etiologies
  - Pregnancy
  - Hormonal contraception
  - Endocrinopathies
    - Diabetes mellitus
    - Thyroid disease
    - Adrenal disease
Evaluation of Amenorrhea

• History
  – Pubertal growth and development
  – Systemic disease
  – Family history
  – Environmental stress
  – Psychiatric illness
  – Medications / drug abuse

Evaluation of Amenorrhea

• History cont.
  – Diet
  – Exercise habits
  – Change in weight
  – Sexual history
  – History of androgen excess
  – Galactorrhea

Evaluation of Amenorrhea

• Physical Exam
  – Vital signs
  – Growth charts
  – Sexual maturity rating
  – Body habitus
  – Signs of hirsutism or virilization
Evaluation of Amenorrhea

- Physical Exam cont.
  - Careful palpation of thyroid, abdomen, groin
  - Breast exam
  - External genitalia or pelvic exam
  - Neuro exam- cranial nerves, visual fields

Evaluation of Amenorrhea

- Laboratory
  - Pregnancy test
  - CBC with diff
  - Sedimentation rate
  - Thyroid function tests
  - Prolactin

Evaluation of Amenorrhea

- Laboratory cont
  - FSH and LH
  - Karyotype
  - Bone age film of wrist
  - Testosterone, DHEA-S
  - Fasting glucose & insulin
  - Pelvic / abdominal CT Scan or MRI
Amenorrhea with Delayed Puberty

History and physical exam
- CBC
- ESR
- TSH, T4
- Proctolin
- Bone age

Elevated TSH
Low T4
Hypothyroidism

Proctolinoma

Head MRI

FSH, LH
Delayed bone age
Other labs/PE WNL

Elevated prolactin
Prolactinoma
Hypothyroidism

Normal or low

Karyotype
Consider head MRI

Turner syndrome (45XO)
Gonadal Dysgenesis (Abnormal X)
Ovarian failure (46XX)
Autoimmune orchitis
Radiation or chemotherapy
Resistant ovary syndrome

CNS Lesion
Chronic disease
Eating disorder
Excessive exercise
Psychosocial stress

Abnormal
Normal

Amenorrhea with Delayed Puberty

History and physical exam
- CBC
- ESR
- TSH, T4
- Proctolin
- Bone age

Elevated TSH
Low T4
Hypothyroidism

Proctolinoma

Head MRI

FSH, LH
Delayed bone age
Other labs/PE WNL

Elevated prolactin
Prolactinoma
Hypothyroidism

Normal or low

Karyotype
Consider head MRI

Abnormal
Normal

Amenorrhea with Delayed Puberty

History and physical exam
- FSH, LH
- Karyotype

Elevated
Normal or low

Consider head MRI
Amenorrhea with Delayed Puberty

- Elevated FSH & LH
  - Abnormal
  - Normal

  - Turner syndrome (45XO)
  - Gonadal Dysgenesis (Abnormal X)
  - Ovarian failure (46XX)
  - Autoimmune oophortis
  - Radiation or chemotherapy
  - Resistant ovary syndrome

- Normal or low FSH
  - Consider head MRI
  - Abnormal
  - Normal

- CNS Lesion
- Chronic disease
- Eating disorder
- Excessive exercise
- Psychosocial stress

Question 2 - Amenorrhea

- A 12 yr old female gymnast presents with lack of pubertal development. She is Tanner 1 for breast development and pubic hair and has not undergone menarche. Height and weight are at the 10%. Family history reveals that her mother and sister were “late bloomers” and underwent menarche at age 15 yrs. Her history and physical exam are all within normal limits.

- Diagnosis to consider include:
  - a) Inflammatory bowel disease
  - b) Excessive exercise
  - c) Constitutional delay of puberty
  - d) All of the above
Question 3 - Amenorrhea

- The study most likely to be abnormal in constitutional delay of puberty is:
  a) Bone age
  b) TSH
  c) ESR
  d) Prolactin

Question 4 - Amenorrhea

- A 14 year old female presents for evaluation of primary amenorrhea. On exam you notice that she is <5% for height. Physical exam also reveals a web neck, widely spaced nipples, low hair line and a short fifth metacarpal. The best study to confirm your diagnosis is:
  a) LH
  b) Karyotype
  c) TSH
  d) Bone age

Amenorrhea with Normal Pubertal Development

- History and physical exam
- Pregnancy test
- TSH, Prolactin
- Withdrawal bleeding
- Progesterone challenge
- No withdrawal bleeding
- Anovulatory cycles
- PCOS
- FSH, LH
- Normal or low
- High
- Karyotype
- Turner mosaic (45,X0/46,XX)
- Mixed Gonadal Dysgenesis
- Ovulation failure (46,XX)
- Achondroplasia
- Radiation or chemotherapy
- Resistant ovary syndrome
- Consider head MRI
- Abnormal
- Normal
- Chronic disease
- Eating disorder
- Excessive exercise
- Psychosocial stress

Adapted from Pletcher, J.R. Pediatric Clinics of N America Vol 46.
No. 3 WB Saunders Co. 1999, p514
Amenorrhea with Normal Pubertal Development

History and physical exam
Pregnancy test
TSH, Prolactin
Progesterone Challenge
Abnormal pelvic exam
Pelvic ultrasound

Progesterone Challenge
Withdrawal bleeding
Anovulatory cycles
PCOS

Estrogen & Progesterone challenge
FSH, LH
Asherman’s Syndrome
Outlet obstruction

Positive response
No response
Amenorrhea with Normal Pubertal Development

- Turner mosaic (45,XO/46,XX)
- Mixed Gonadal Dysgenesis
- Karyotype Normal or low
- Consider head MRI
- Abnormal or normal
- CNS lesion
- Chronic disease
- Eating disorder
- Excessive exercise
- Psychosocial stress
- Autoimmune oophoritis
- Radiation or chemotherapy
- Resistant ovary syndrome
- Ovarian failure (46,XX)
- Turner mosaic

Question 5 - Amenorrhea

- A 15 year old female presents with a 2 month history of amenorrhea, fatigue and dizziness. Menarche began at age 12 and menses have previously been regular. Physical exam is normal including Tanner 5 breast and pubic hair. The most important initial study would be:
  a) Lutenizing hormone (LH)
  b) Progesterone challenge
  c) Pregnancy test
  d) Prolactin level

Question 6 - Amenorrhea

- A 16 year old female presents to your office with a 12 month history of secondary amenorrhea. She joined the cross country team one year ago and in an effort to improve her athletic performance she began to “eat more healthy.” She subsequently lost 20 lbs. Exam reveals a very thin female with a height at the 50%. Weight has fallen from 25% one year ago, to less than the 5%. The study most likely to be abnormal is:
  a) Prolactin
  b) MRI of the head
  c) TSH
  d) Bone density
Question 7 - Amenorrhea

• A 16 yr old female presents for evaluation of primary amenorrhea. History is unremarkable. Physical exam reveals a young woman who is at the 50% for height and weight and Tanner 5 for breasts and pubic hair. External genitalia are normal but attempts at performing a digital exam or introducing a Q-tip into the vagina are unsuccessful. The next step in the evaluation would be:
  a) Progesterone challenge
  b) MRI of the head
  c) Ultrasound of the pelvis
  d) Testosterone level

Amenorrhea with Hirsutism & Normal Pubertal Development

- History and physical exam
  - Pregnancy test
  - TSH, Prolactin
  - Free & Total Testosterone
  - DHEAS
  - 17 Hydroxyprogesterone

Congenital Adrenal Hyperplasia
  - Adrenal-SCCing Tumor

If obese, consider:
  - Fasting Glucose
  - Fasting Insulin

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Amenorrhea with Hirsutism & Normal Pubertal Development

- Congenital Adrenal Hyperplasia
- Androgen Secreting Tumor
- Progesterone Challenge
- Withdrawal bleeding
- Overan Hyperandrogenism
- Polycystic Ovary Syndrome
- Fasting Insulin
- 2 Hour Glucose Tolerance test

Question 8 - Amenorrhea

A 17 yr old female presents with amenorrhea x 6 months. She has a history of infrequent menses since menarche at age 12 years. Exam is remarkable for obesity and mild hirsutism. Pregnancy test is negative. Labs: TSH, prolactin, DHEA-S, 17-hydroxyprogesterone are WNL. Testosterone is mildly elevated. The next step in the management of this patient would be:

a) CT Scan of abdomen
b) Progesterone challenge
c) Karyotype
d) Estrogen and progesterone challenge

Bibliography