AMENORRHEA

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Overview

Amenorrhea (absence of menses) can be a transient, intermittent, or permanent condition resulting from dysfunction of the hypothalamus, pituitary, ovaries, uterus, or vagina. The menstrual cycle is susceptible to outside influences; thus, missing a single menstrual period is rarely important. In contrast, prolonged amenorrhea might be the earliest sign of a decline in general health or signal an underlying condition.

Diagnostic Considerations

Definitions[1,2]

- Primary Amenorrhea: No menses by age 14 in the absence of secondary sexual characteristics or no menses by age 16 with secondary sexual characteristics
- Secondary Amenorrhea: No menses for >6 months or 3 cycles after documented menarche
  - o → Secondary amenorrhea is pregnancy until proven otherwise

History[3-6]

The following features on history may indicate an underlying cause:

History	Potential etiology
Exercise, weight loss, current or previous chronic illness, illicit drug use	Hypothalamic amenorrhea
Menarche? Menstrual history (regularity of cycles)	Primary vs. secondary amenorrhea
Prescription drug use	Certain medications can cause amenorrhea e.g. Busulfan, Chlorambucil, Cyclophosphamide, Phenothiazines
Previous CNS chemotherapy or radiation	Hypothalamic amenorrhea
Previous pelvic radiation	Premature ovarian failure
Psychosocial stressors; nutritional and exercise history	Anorexia/Bulimia nervosa
Sexual activity/Last menstrual period	Pregnancy
Genetic defects	Chromosomal abnormalities e.g. Turner's syndrome (45,X) 46,XX gonadal dysgenesis and rarely, 46,XY gonadal dysgenesis
Pubic hair pattern e.g. Lack of pubertal development	Androgen insensitivity syndrome, ovarian or pituitary failure or a chromosomal abnormality
Menarche and menstrual history of mother/sisters AND pubertal history (i.e. growth delay)	Constitutional delay of growth/puberty
Anosmia	Kallman syndrome
Cyclic abdominal pain with no flow; breast changes	Outflow tract obstruction or Mullerian agenesis
Galactorrhea, headache and/or visual disturbances	Pituitary tumor; hyperprolactinemia
Signs/symptoms of hypo or hyperthyroidism	Thyroid disease
Hirsutism/acne	PCOS

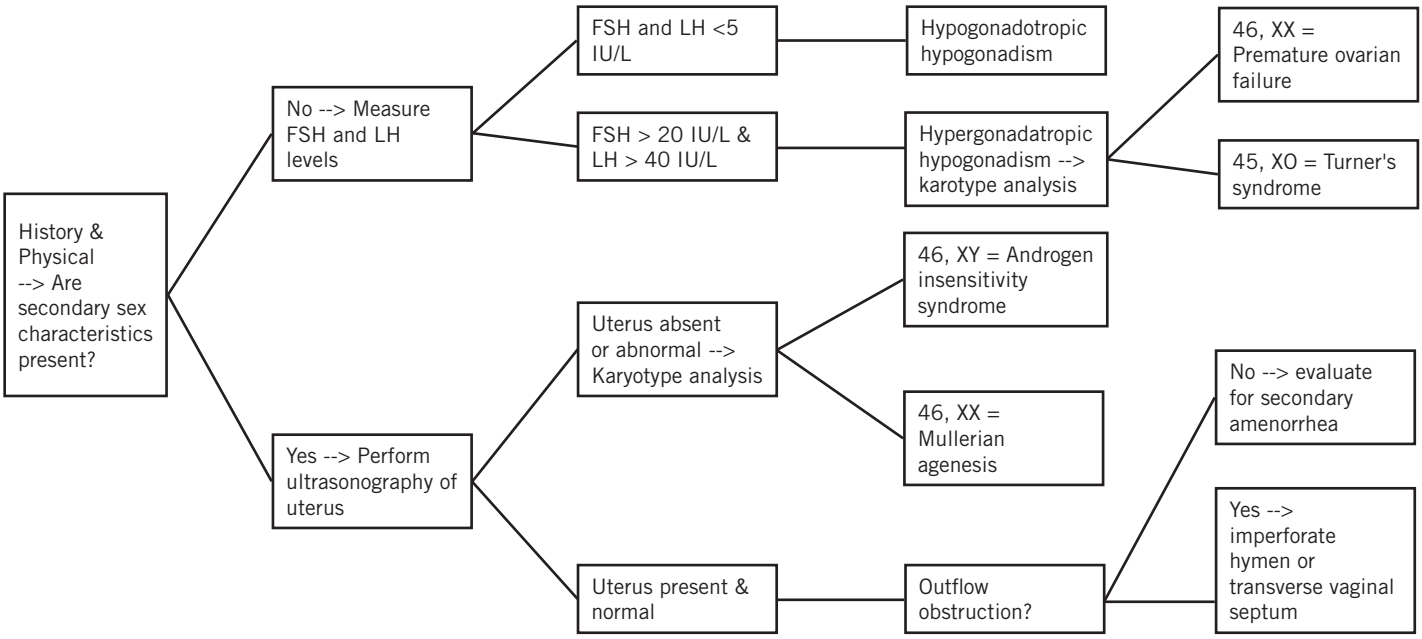
Physical exam[3-6]

The following findings on physical examination can elicit a possible underlying cause:

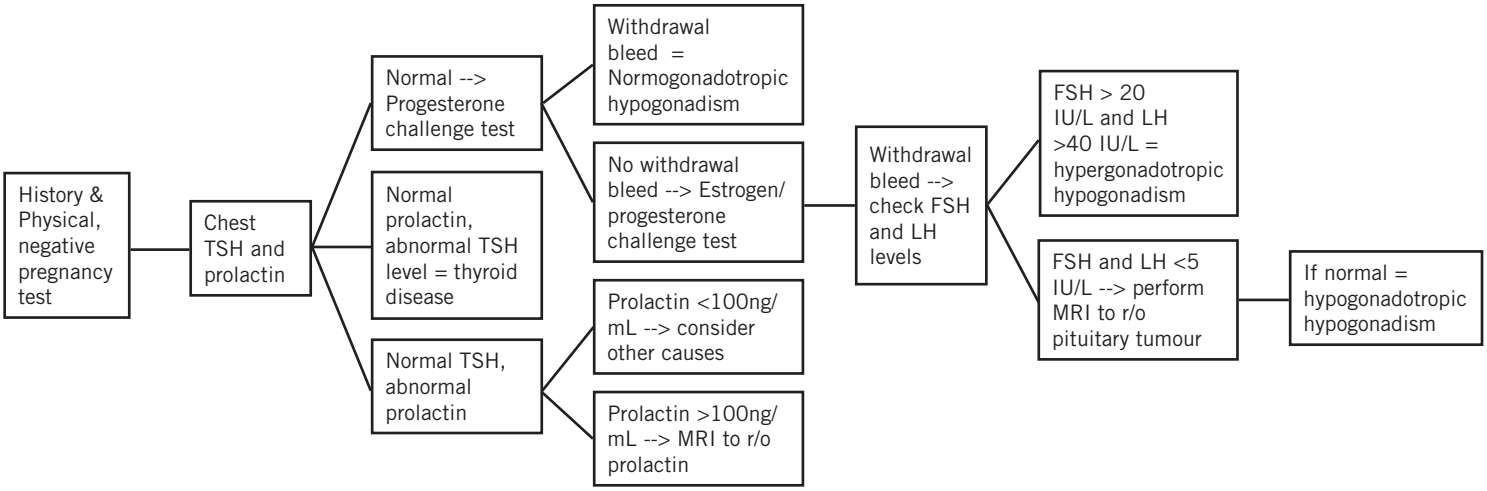
Findings	Potential Etiology
Anthropomorphic measurements	Constitutional delay of growth/puberty
BMI (obesity; BMI ≥30)	PCOS
Dysmorphic features (i.e. webbed neck, short stature, widely spaced nipples)	Turner's syndrome
Rudimentary or absent uterus and pubic hair	Mullerian agenesis
Stria, buffalo hump, significant central obesity, easy bruising, hypertension, proximal muscle weakness	Cushing's disease
Tanner staging	Primary vs. secondary amenorrhea
Thyroid examination – nodules, enlarged thyroid	Thyroid disease
Transverse vaginal septum; imperforate hymen	Outflow tract obstruction
Undescended tests; external genital appearance (vulvovaginal exam)	Androgen insensitivity syndrome, estrogen deficiency
Virilization; clitoral hypertrophy	Androgen-secreting tumor

Physical Examination[2,4,5]

Approach to Primary Amenorrhea[4-8]
*Adapted from Kiningham, Apgar, Schwenk (1996)



Approach to Secondary Amenorrhea[4,5,7,9]
*Adapted from Kiningham, Apgar, Schwenk (1996)



Pharmacologic Guidelines for Progestogen and Estrogen/Progestogen Challenge Tests[2]

Drug	Dosing	Duration
Progestogen challenge test		
Medroxyprogesterone acetate (Provera)	10 mg PO OD	7-10d
Norethindrone (Norlutate)	5 mg PO OD	7-10d
Progesterone	200 mg parenterally OD	Single dose
Progesterone micronized (Prometrium)	400 mg PO OD	7-10d
Progesterone micronized gel (4 or 8%) (Crinone)	Intravaginally q other day	Six applications
Estrogen/progestogen challenge test		
Conjugated equine estrogen (Premarin)	1.25 mg PO OD	21 days
or Estradiol (Estrace)	2 mg PO OD	21 days
→ followed by Progestational agent	*As noted above*	*As noted above*

Contraindications to Estrogen/Progesterone Challenge tests

- Hypersensitivity to medroxyprogesterone or any component of the formulation
- History of or current thrombophlebitis or venous thromboembolic disorders (including DVT, PE); cerebral vascular disease; severe hepatic dysfunction or disease; carcinoma of the breast or other estrogen- or progesterone-dependent neoplasia; undiagnosed vaginal bleeding; missed abortion, diagnostic test for pregnancy, pregnancy

Management Considerations[7,9]

Treatment depends upon cause

Hypothalamic dysfunction
- Stop drugs that may be contributing, stress reduction, adequate nutrition, decrease excessive exercise
- Clomiphene citrate (Clomid) if pregnancy desired
- Oral contraceptive pill to induce menstruation

Hyperprolactinemia
- Bromocriptine
- Consider referral to endocrine, may consider surgery for macroadenoma (depending on size, level of prolactin)

Premature ovarian failure
- Treat potential associated autoimmune disorders
- HRT to prevent osteoporosis and other manifestations of hypoestrogenic state

Hypoestrogenism
- Karyotype
- Removal of gonadal tissue if Y chromosome present

Polycystic ovarian syndrome
- Interrupt self-perpetuating cycle with OCP
- Decreasing peripheral estrone formation with weight reduction
- Enhance FSH secretion: clomiphene, hMG (Pergonal), LHRH, purified FSH
- Prevent endometrial hyperplasia from unopposed estrogen using progesterone (Provera) or OCP

If pregnancy is desired, may need medical induction of ovulation
- Clomiphene citrate (Clomid) = drug of choice
- Human menopausal gonadotropin (Pergonal)

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm