

## Differential Diagnosis of Amenorrhea

Disease	Present in Primary Amenorrhea?	Present in Secondary Amenorrhea?	LH	FSH	E <sub>2</sub>	Notes
Hypothalamus						
Hypothalamic amenorrhea	Yes	Yes	↓ or normal	↓ or normal	↓	Exercise, weight loss, stress, chronic illness
Hypogonadotropic hypogonadism	Yes	Yes	↓ or normal	↓ or normal	↓	Anosmia may be present
Hypothalamic tumors	Yes	Yes	↓ or normal	↓ or normal	↓	May present with short stature, diabetes insipidus, or both; brain imaging necessary
Hypothalamic infection or infiltration (e.g., tuberculosis, syphilis, sarcoidosis)	Yes	Yes	↓ or normal	↓ or normal	↓	May present with short stature, diabetes insipidus, or both; brain imaging necessary
Pituitary						
Hypogonadotropic hypogonadism	Yes	Yes	↓ or normal	↓ or normal	↓	
Pituitary tumors (e.g., prolactinoma)	Yes	Yes	↓ or normal	↓ or normal	↓	Brain imaging; prolactin may be elevated
Pituitary infection or infiltration	Yes	Yes	↓ or normal	↓ or normal	↓	
Sheehan's syndrome	No	Yes	↓ or normal	↓ or normal	↓	Generally presents after delivery; manifestations can be acute or present slowly
Ovary						
Gonadal dysgenesis	Yes	Yes	↑	↑	↓	45,XO = Turner's syndrome; mosaic forms also exist

Pure gonadal dysgenesis	Yes	Yes	↑	↑	↓	Karyotype either 46,XX or 46,XY; testosterone may be increased
Premature ovarian failure	No	Yes	↑	↑	↓	Autoimmune syndromes, 47,XXX, galactosemia, idiopathic; autoimmune polyglandular syndrome type I may present as primary amenorrhea
Polycystic ovary syndrome	Yes	Yes	↑ or normal	Normal	Normal	Hyperandrogenism; history of oligomenorrhea since menarche; testosterone and DHEAS may be normal or increased; LH/FSH ratio not clinically useful
Ovarian tumors	No	Yes	↓	↓	↑ or normal	T may be normal or increased; look for acute virilization
Ovarian enzymatic deficiency (e.g., 17 $\alpha$ -hydroxylase deficiency)	Yes	No	↑	↑	↓	Sexual infantilism; may have hypertension secondary to increased deoxycorticosterone

#### Uterus

Müllerian agenesis	Yes	No	Normal	Normal	Normal	May have cyclical pelvic pain
Asherman's syndrome (uterine synechiae)	No	Yes	Normal	Normal	Normal	History of instrumentation (primarily dilation and curettage)

#### Other

Adrenal tumors	No	Yes	↓	↓	↑ or Normal	Hyperandrogenism. Testosterone, DHEAS, urinary 17-ketosteroids may be increased. DHEAS is the most sensitive single test of adrenal androgens
Thyroid disease	Yes	Yes	Normal	Normal	Normal	

Testicular feminization (androgen resistance)	Yes	No	↑	↑ or normal	↑	Normal or near-normal breast development, short vagina, elevated testosterone, XY karyotype
Late-onset congenital adrenal hyperplasia	Yes	Yes	Normal	Normal	Normal	May have hirsutism, acne; screen with early morning proliferative phase 17-hydroxyprogesterone
Chronic illness	Yes	Yes	↓	↓	↓	

DHEAS = dehydroepiandrosterone sulfate; FSH = follicle-stimulating hormone; LH = luteinizing hormone; T<sub>3</sub> = triiodothyronine; T<sub>4</sub> = thyroxine.

Table from Physicians' Information and Education Resource (PIER), *Amenorrhea* module.