The Most Important Differential Diagnoses for Secondary Amenorrhea

Definition of Amenorrhea

The absence of menstruation occurs physiologically before menarche, during pregnancy and lactation, as well as postmenopausal. If no menstruation has occurred at the completion of the 16th year, a so-called primary amenorrhea occurs. Possible causes are, inter alia, an atresia of the hymen, vaginal septa, competitive sports, the Ullrich-Turner syndrome, malnutrition, the adrenogenital syndrome or the polycystic ovary syndrome.

A secondary amenorrhea is the absence of menstruation for a period of at least 3 months after a previously regular cycle without an existing pregnancy. 3 to 5 percent of women experience secondary amenorrhea in any specific year. Secondary amenorrhea can result from abnormalities at the levels of hypothalamus, pituitary, ovary, uterus, and outflow tract.

Differential Diagnoses

Background knowledge for secondary amenorrhea

You will find a broad division into the respective disciplines – naturally with numerous overlaps - to allow you to assign the differential diagnoses quickly and thus lose none of your precious time in exams.

Be careful: do not only identify the disease, but also a few background facts. In an exam situation, this method proves that you have a comprehensive understanding and the tutors will be satisfied more quickly than if they have to “worm everything out of your nose”. A rough classification is also beneficial in your future clinical practice!

Endocrinology and internal medicine

Congenital adrenal hyperplasia (Overproduction of androgens by disturbed Kortisolbildung in the adrenal cortex)
For 21-hydroxylase deficiency of the woman, a female genotype is seemingly a male phenotype. Uterus and ovaries are, however, set up (pseudohermaphroditism femininus).

**Acromegaly**

In addition to an increase in the extremities, vision problems, joint pain, fatigue, the amenorrhea is also a symptom of acromegaly.

**Sheehan's syndrome**

In the case of postpartum hypopituitarism, there is a complete or partial failure of the anterior pituitary. In addition to many other symptoms during FSH/LH deficiency, an amenorrhea occurs.

**Inflammatory bowel disease**

Especially during Crohn’s disease, amenorrhea can occur during the active thrust.

**Diabetes mellitus I and II**

Amenorrhea may occur especially in poorly controlled blood glucose levels.

**Hyperprolactinemia**

Additional distribution of the hormone prolactin may be caused by a pituitary adenoma (prolactinoma) or medication (eg. metoclopramide).

**Hypothyroidism**

The amenorrhea is here grouped among symptoms like loss of libido and fertility problems. Hyperthyroidism in Graves’ disease may also be the reason.

**Gynecology**

**Endometriosis**

Scattered endometrial tissue is found intra-/extra-genital or extra-abdominal. Besides menstruation ailments like spotting, menorrhagia, metrorrhagia or hypermenorrhea it can also cause amenorrhea.

**Polycystic ovary syndrome**

Multiple cysts in the ovaries lead to increased androgen production with anovulatory cycles and virilization (DD: congenital adrenal hyperplasia)

Ovarian tumor

Clinical symptoms are pelvic pain, palpable/visible protrusions.

**Menopause praecox**

A complete ovarian failure before the age of 40. There are various reasons (eg. autoimmune/metabolic diseases, radiotherapy/chemotherapy).

**Asherman's syndrome**

Asherman’s syndrome results from obliteration of the uterine cavity by adhesions that prevent normal growth and shedding of the endometrium. Common causes include Gynaec procedure/curettage and genital tuberculosis in endemic areas.
Psychiatry/Psychosomatics

Psychogenic

By a changing rhythm of life and/or change of the environment, e.g. through travelling and/or extreme change in climate, menstruation may not occur over a longer period.

Anorexia nervosa

A secondary amenorrhea may occur as a result of complications of eating disorders, including anorexia nervosa and bulimia. The cause is a hormonal imbalance with increased cortisol secretion. The body creates a sort of “natural contraceptive protection” because it would not be able withstand a pregnancy. Often the patients perceive this more as a relief, which complicates the compliance with the therapy additionally.

Depression

In a manifest or depressive episode menstruation may not occur for months or years.

Side Effects

Anabolaabbusus

Hyperandrogenism, often combined with extreme performance sports.

Cushing’s syndrome

The most common cause of hypercortisolism is the exogenous glucocorticoids. Symptoms among others include not only androgenisation of women but also truncal obesity, peripheral muscle wasting, osteoporosis and arterial hypertension.

Radio-/chemotherapy

Irreversible damage to the ovaries leads to premature menopause (climacteric praecox).

Psychiatric medication

Tricyclic antidepressants and neuroleptics, especially risperidone, are potential polluters of amenorrhea (NW: hyperprolactinemia), as are corticosteroids (see Cushing’s syndrome).

Additional Tips

In practical work you do not have to be familiar with every single disease including diagnosis and treatment – as opposed to situation in your medical exams. However, you must be able to consider and decide whether colleagues from other fields should be consulted, and if so, which.

With just a few non-invasive means, such as medical history, physical examination, complete blood cell counts, based hormone parameters and sonography, your diagnostic skills will be much improved.

Before any further diagnostic evaluation, however, you should always do a β-HCG-test to exclude pregnancy!

Structural abnormalities of uterus and outflow tract should be ruled out in initial
evaluation that should also include testing for Hyperandrogenism and abnormal FSH levels (Hyperandrogenism is often suggestive of PCOS and rarely 21 hydroxylase deficiency. Elevated FSH levels are commonly seen in ovarian insufficiency. Reference: Harrison’s 20/e)

Patients with normal reproductive structure and either low or normal FSH levels should be ruled out for abnormal Prolactin levels (High prolactin levels seen due to both drugs and prolactinomas). The patients who turn out normal for Prolactin levels should be evaluated for other causes such as abnormal TSH, short stature, primary amenorrhea, eating disorders and other chronic diseases

References


**Legal Note:** Unless otherwise stated, all rights reserved by Lecturio GmbH. For further legal regulations see our [legal information page](#).