# Amenorrhoea

Amenorrhoea is define as the absence of menstruation which either temporary or permanent. Amenorrhoea is divided into primary and secondary.

**Primary amenorrhoea:** menstruation has not occurred by the age of 14 in the absence of secondary sexual characters or by the age of 16, even if secondary sexual characters are present.

**Secondary amenorrhoea:** is absence of menstruation for more than 6 months (or a time equivalent to the length of three previous cycles) in a normal female of reproductive age that is not due to pregnancy, lactation or the menopause.

**Oligomenorrhoea:** in frequent menstruation, where the duration between periods is more than 35 days.

**Causes of amenorrhoea:**

It is important to remember that amenorrhoea and Oligomenorrhoea are symptoms and not a final diagnosis. The occurrence of regular menses requires a co-ordinated interaction between the hypothalamus, pituitary, ovaries and the outflow tract (uterus and vagina). A disturbance at any of these levels can lead to amenorrhoea.

**Anatomical disorders:**

-Genital tract abnormality: like Mullerian agenesis which include absence of uterus, cervix or only upper vagina. Absence of uterus, cervix and also upper vagina and only lower third of vagina present like in Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome. Imperforated hymen which lead to collection of menstrual blood and lead to haematocolpos. Transverse vaginal septum in this condition the vagina failure to cannulate, the upper and lower parts of the vagina are separate.

-Trauma: like Asherman's syndrome where intrauterine adhesions prevent menstruation, the most common cause being over-vigorous uterine curettage, or surgical removal (hysterectomy). The patient usually present with secondary amenorrhoea.

-Inflammation: like post-partum or post-abortive infection. The patient present with secondary amenorrhoea.

**Ovarian disorders:**

-Congenital:

\*Complete androgen insensitivity in an XY female in which the patients have XY karyotype and a female phenotype.

\*Gonadal dysgenesis which mean abnormal formation of gonad like Turner syndrome or true hermaphrodite.

Usually these patients present with primary amenorrhoea, but some cases of mosaic Turner (XX/X0) and some cases of gonadal dysgenesis present with secondary amenorrhoea but also present with early menopause.

-Anovulation like poly cystic ovary syndrome (PCOS), and usually present with secondary amenorrhoea.

-Premature ovarian failure (POF) is define as cessation of periods before 40 years of age. It is usually unexplained, but may be due to chemotherapy, radiotherapy, autoimmune disease or chromosomal disorder like mosaic Turner's. These patients present with secondary amenorrhoea.

-Trauma like radiotherapy, chemotherapy and surgical removal.

-Inflammation like severe genital tuberculosis causing ovarian damage.

-Neoplastic like variety of benign or malignant ovarian tumours.

Trauma, inflammation and neoplastic conditions if occurs before puberty the patient present with primary amenorrhoea, but if occur later causing secondary amenorrhoea.

**Pituitary disorders:**

-Adenomas of which prolactinoma is the most common, or extra pituitary tumour compressing the pituitary and hence leading to hyperprolactinoma due to interference with dopamine (prolactin inhibitory). Surgical removal of pituitary tumour could also destroy pituitary tissue.

-pituitary necrosis e.g. Sheehan's syndrome is a condition of hypopituitarism due to ischemic necrosis of pituitary after prolong hypotension following massive postpartum haemorrhage. The first hormones to be affected are gonadotrophins and growth hormone followed by ACTH and finally TSH.

Both those conditions cause the patient present with secondary amenorrhoea.

**Hypothalamic disorders:**

-Excessive exercise, weight loss like in patient with anorexia nervosa and stress can switch off hypothalamic stimulation of the pituitary.

-Hypothalamic lesions like (craniopharyngioma, glioma) can compress hypothalamic tissue or block dopamine.

-Head injuries.

-Inflammation like encephalitis and meningitis.

-Kallman's syndrome (X-linked recessive) is a condition associated with congenital absence of GnRH causing underdeveloped genitalia.

-Systemic disorders including sarcoidosis, tuberculosis resulting in an infiltrative process in the hypothalamo-hypophyseal region.

-Drugs like progesterone, HRT or dopamine antagonists.

All those condition present with secondary amenorrhoea and treat underlying cause result in returning of menstruation.

**Constitutional causes:**

A number of girls have constitutional delay and normal secondary sexual characteristic, but there is no anatomical anomaly and endocrine investigations are all normal. Those patient present with primary amenorrhoea and usually finally menstruate and need no interference.

**Investigations:**

History should guide the examination

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| --- | --- | --- |
| **Possible diagnosis** | **Relevant factors** | **Information required** |
| Congenital malformation or chromosomal abnormality | Delayed/ incomplete | Developmental history including menarche |
| PCOS  POF | Oligomenorrhoea  Secondary amenorrhoea | Menstrual history |
| PCOS  Congenital malformation | infertility | Reproductive history |
| Congenital malformation  Imperforated hymen | Cyclical pain without menstruation | Cyclical symptoms |
| PCOS | Hirsutism | Hair growth |
| Hypothalamic malfunction  PCOS | Dramatic weight loss  Difficulty losing weight | Weight |
| Hypothalamic | Exercise, stress | Lifestyle |
| Hypothalamic malfunction | Systemic disease e.g. sarcoidosis | Past medical history |
| Asherman's | Evacuation of uterus | Past surgical history |
| Hypothalamic malfunction | Dopamine agonists, HRT | Drug history |
| Pituitary adenoma |  | Headache |
| Prolactinoma |  | Galactorrhoea |
| Pituitary adenoma |  | Visual disturbance |

A general inspection of the patient should be carried out to access BMI, secondary sexual characteristic and signs of endocrine abnormalities. If the history is suggestive of a pituitary lesion, an assessment of visual fields is indicated. External genitalia and a vaginal examination should be performed to detect structural outflow abnormalities or demonstrate atrophic changes due to hypo-oestrogenism.

Findings from the history and examination should guide the choice and order of investigations.

A **pregnancy test** should be carried out if the patient is sexually active. Blood can be taken for LH, FSH and testosterone, raised LH or raised testosterone could be due to PCOS, raised FSH may be POF.

A raised prolactin level may indicate a prolactinoma. Thyroid function should be checked if clinically indicated.

An U/S can be useful in detecting the classical appearance of PCO, MRI should be carried out if symptoms are consistent with pituitary adenoma. Hysteroscopy is not routine, but is a suitable investigation where Asherman's or cervical stenosis is suspected.

Karyotyping is diagnostic of Turner's.

**Treatment:**

This should be directed to the cause and depends on patient's current desire for fertility. Specific pathologies that will require intervention include:

-treatment of feeding disorders and normalization of body weight by dietary advice and support

-removal of space occupying lesion either in hypothalamus, pituitary or brain tumours by surgery. Prolactinoma can be managed conservatively with dopamine agonist (e.g. cabergoline or bromocriptine) or surgery if medications failed.

-hysteroscopic resection of intrauterine adhesion in cases with Asherman's syndrome. Adhesiolysis and IUD insertion at time of hysteroscopy to prevent recurrence of adhesions and cervical dilatation in case of cervical stenosis

-surgical correction of outflow tract obstruction e.g. incision of an imperforated hymen

-correction of thyroid disorders

Where fertility is not required, regular withdrawal bleeds may be induced using cyclic oestrogen/progesterone therapy (COCP). The COCP or another form of combined HRT should also be used for women with POF to protect the bone mineral density.

Where fertility is required in anovulatory women, the primary method of ovulation induction is the treatment of choice like in patients with PCOS. Oocyte donation and IVF for the patients with POF for best chance of pregnancy although spontaneous pregnancy could happen. Women with pituitary or hypothalamic causes of amenorrhoea (hypogonadotrophic hypogonadism) are treated with gonadotrophin or less commonly with pulsatile GnRH.