Disorders of Menstrual Regularity

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The information included in this presentation are not the only source for this topic and you should explore other valuable references in order to satisfy the ILOs of this topic.

LEARNING OBJECTIVES

- Describe the causes and investigation of primary and secondary amenorrhea and oligomenorrhea.
- Understand the epidemiology and effects of polycystic ovary syndrome (PCOS), its diagnosis and management.
- Describe the common effects and management of premenstrual syndrome (PMS).
- Describe premature cessation of periods.

INTRODUCTION

Normal menstrual cycle

- The average age of menarch *(first menstruation in the female life)* is 12.5 year.
- Normal frequency: from 24-38 days.
- Normal duration : 8days or less
- Normal Regularity (regular; shortest to longest 7-9 days)
- Normal flow volume : patient determined.
- No intermenstrual discharge in normal cycle

Parameter	Normal	Abnormal	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
	Infrequent (>38 days)		☐
	Normal (≥24 to ≤38 days)		☐
	Frequent (<24 days)		☐
Duration	Normal (≤8 days)		☐
	Prolonged (>8 days)		☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		☐
	Irregular (shortest to longest cycle variation: ≥8-10 days)*		☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
	Heavy		☐

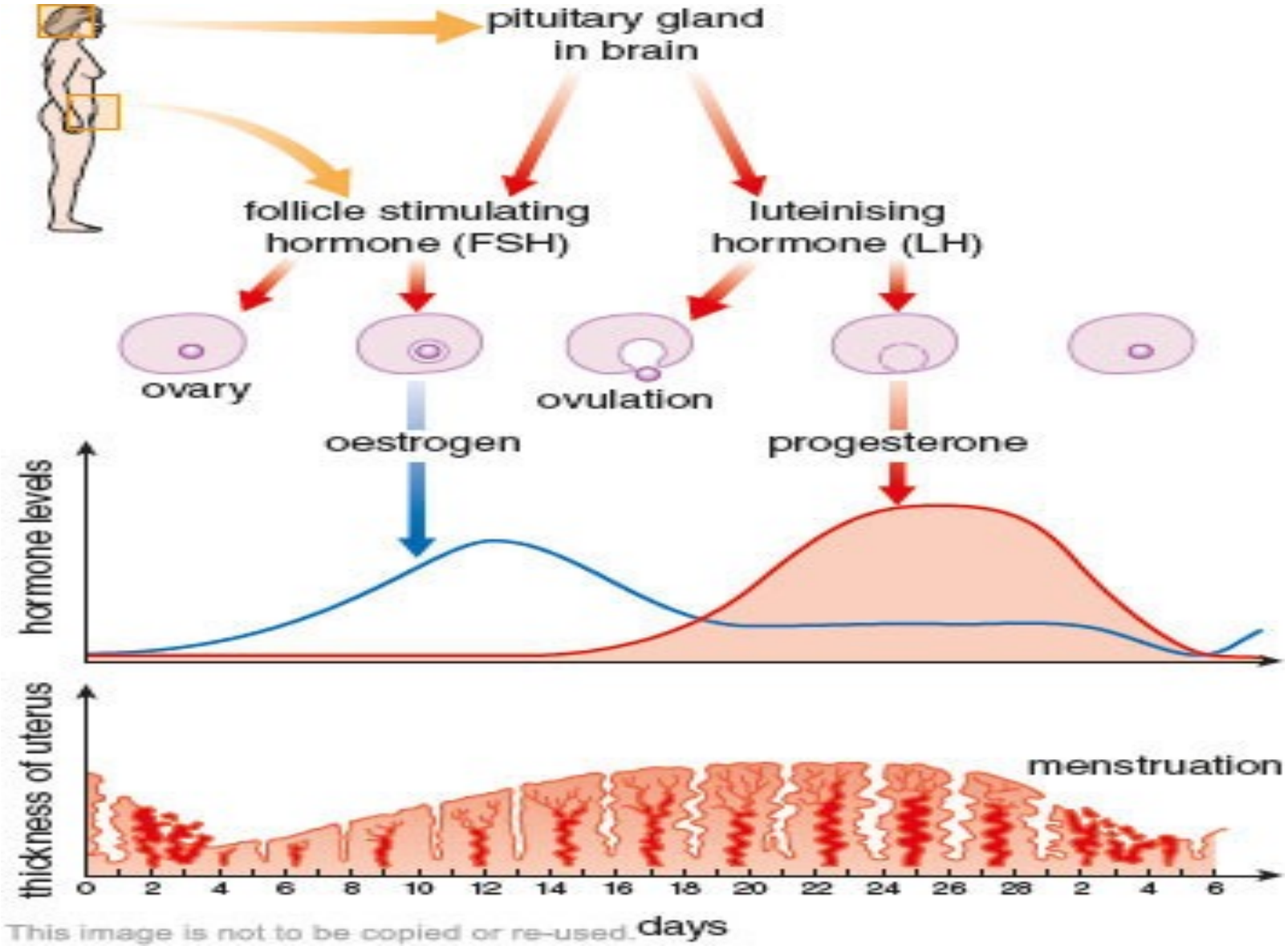
Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		☐
	Random		☐
	Cyclic (Predictable)	Early Cycle	☐
		Mid Cycle	☐
		Late Cycle	☐

Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)	☐
	None (on gonadal steroid medication)	☐
	Present	☐

Amenorrhea and oligomenorrhea

- Amenorrhea is defined as the absence of menstruation for more than 6 months in the absence of pregnancy in a woman of fertile age.
- Oligomenorrhea is defined as irregular periods at intervals of more than 38 days, with only 4–9 periods a year.
- The causes may be *hypothalamic*, pituitary, ovarian or endometrial, and both amenorrhea and oligomenorrhoea may be primary or secondary

Hypothalamo-pituitary-ovarian-uterine axis



ETIOLOGY OF AMENORRHEA/OLIGOMENORRHEA

	Etiology	Defect	result
1	HYPOTHALAMIC	Primary defective production of GnRH	Dcreased FSH/ LH (HYPOGONADOTROPIC HYPOGONADISM)
2	PITUITARY	Primary defective production of gonadotropins (FSH/LH) by pituitary	HYPOGONADOTROPIC HYPOGONADISM)
3	OVARIAN	Primary defect of estrogen production by the ovary	Negative feedback to pituitary resulting in increased production of FSH/LH→ HYPERGONADOTROPIC HYPOGONADISM
4	UTERINE	Primary defect in the ENDOMETRIUM	EUGONADOTROPIC

Osama Warda

Amenorrhea

- *Primary amenorrhea* is when girls fail to menstruate by 16 years of age.
- *Secondary amenorrhea* is absence of menstruation for more than 6 months in a normal female of reproductive age that is not due to pregnancy, lactation or the menopause.

Hypothalamic disorders

Hypothalamic disorders will give rise to hypo-gonadotrophic hypogonadism, with the following causes:

1. **Excessive exercise**, weight loss and stress.

2.**Hypothalamic lesions** (cranio-pharyngioma, glioma), which can compress hypothalamic tissue or block dopamine. 3. **Head injuries.**

4. **Kallman's syndrome** (X-linked recessive condition resulting in *deficiency in GnRH causing underdeveloped genitalia).*

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

6. **Drugs**: progestogens, HRT or dopamine antagonists.

Pituitary disorders

- *Pituitary disorders will also give rise to hypogonadotrophic hypogonadism, with the following causes:*

1. Adenomas, of which prolactinoma is most common.
2. Pituitary necrosis (e.g. Sheehan's syndrome, due to prolonged hypotension following major obstetric hemorrhage).
3. Iatrogenic damage (surgery or radiotherapy).
4. Congenital failure of pituitary development.

Ovarian disorders

- Anovulation is often due to polycystic ovary syndrome (PCOS), described below.
- Ovarian failure is the cause of *hypergonadotrophic hypogonadism*. Premature ovarian failure (POF) is defined as cessation of periods before 40 years of age.

Endometrial disorders

- Primary amenorrhea may result from *Müllerian defects* in the genital tract including an absent uterus, or outflow tract abnormalities, leading to a hematocolpos.
- Secondary amenorrhea may result from scarring of the endometrium called Asherman syndrome.

Clinical Diagnosis

- HISTORY TAKING: Findings from the history should guide the examination. A general inspection of the patient should be carried out to assess:

1. body mass index (BMI),
2. secondary sexual characteristics (hair growth, breast development using Tanner scores)
3. signs of endocrine abnormalities (hirsutism, acne, abdominal striae, moon face, skin changes).
4. If the history is suggestive of a pituitary lesion, an assessment of visual fields is indicated.
5. External genitalia and a vaginal examination should be performed to detect structural outflow abnormalities or demonstrate atrophic changes consistent with hypo-estrogenism.

Investigation of amenorrhea/oligomenorrhea (lab. studies)

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

1- A pregnancy test should be carried out if the patient is sexually active.

2-Blood can be taken for[LH, FSH and testosterone, TSH & PRL];

a) - raised LH or raised testosterone could be suggestive of PCOS;

b)-raised FSH may be suggestive of POF.

c)- raised prolactin level may indicate a prolactinoma.

3- Thyroid function should be checked if clinically indicated.

4. Karyotyping is diagnostic of Turner's and other sex chromosome abnormalities.

Investigation of amenorrhea/oligomenorrhea (imaging)

1. An ultrasound scan can be useful in detecting the classical appearances of polycystic ovaries. Also to confirm presence of the uterus.
2. MRI of the brain should be carried out if symptoms are consistent with a pituitary adenoma.
3. Hysteroscopy is not routine, but is a suitable investigation where Asherman or cervical stenosis is suspected.

Management of amenorrhea/oligomenorrhea

CAUSE	MANAGEMENT
1. LOW BODY MASS INDEX	Dietary advice & support
2. HYPOTHALAMIC LESIONS (e.g glioma)	Surgery
3. HYPER-PROLACTINEMIA/ PROLACTINOMA	Dopamine agonists (cabergoline, bromocryptin) or surgery if medications fail.
4. PREMATURE OVARIAN FAILURE (POF)	COCP , HRT
5. POLYCYSTIC OVARIAN SYNDROME (PCOS)	COCP, Clomiphene
6. ASHERMAN'S SYNDROME	ADHYSIOLYSIS & IUD insertion at time of hysteroscopy
7. CERVICAL STENOSIS	HYSTEROSCOPY & CERVICAL DILATION

Polycystic ovary syndrome

- PCOS is a syndrome of ovarian dysfunction along with the cardinal features of hyper-androgenism and polycystic ovary morphology .
- The prevalence of polycystic ovaries seen on ultrasound is around 25% of all women but is not always associated with the full syndrome.
- Clinical manifestations include *menstrual irregularities*, *signs of androgen excess* (e.g. hirsutism and acne) and *obesity*.
- Elevated serum LH levels, biochemical evidence of hyper-androgenism and raised insulin resistance are also common features.

Polycystic ovary syndrome

- PCOS is associated with an increased risk of type 2 diabetes and cardiovascular events.
- It affects around 5–10% of women of reproductive age.
- The etiology of PCOS is not completely clear, although the frequent familial trend points to a genetic cause.

Polycystic ovary syndrome: Clinical features

1. **Oligomenorrhea/amenorrhea in up to 75% of patients, predominantly related to chronic anovulation.**
2. **Hirsutism.**
3. **Subfertility in up to 75% of women.**
4. **Obesity in at least 40% of patients.**
5. **Acanthosis nigricans (areas of increased velvety skin pigmentation occur in the axillae and other flexures).**
6. **May be asymptomatic.**

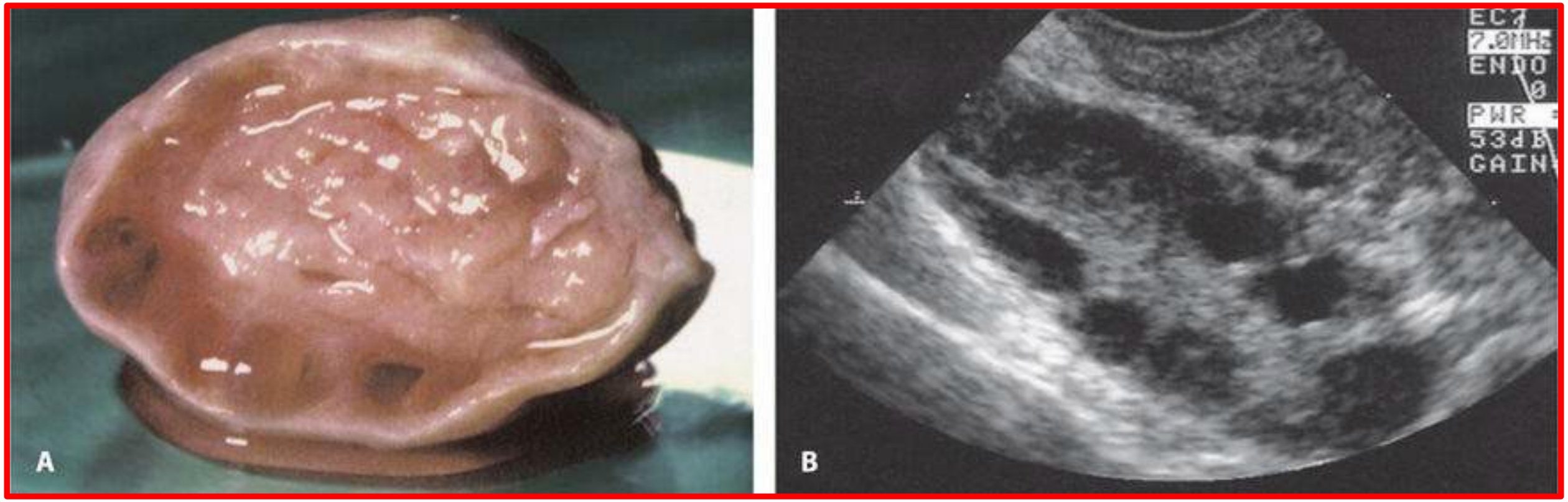

PCOS SYMPTOMS:
HAIR LOSS
HIRSUTISM
PELVIC PAIN
OVERWEIGHT
ACNE
MONTH
IRREGULAR PERIODS
INFERTILITY
OH
HIGH TESTOSTERONE LEVELS
POLYCYSTIC OVARY SYNDROMS (PCOS)

Polycystic ovary syndrome: Diagnosis

Patients must have two out of the three features below:

1. Amenorrhea/oligomenorrhea.
2. Clinical or biochemical hyper-androgenism.
3. Polycystic ovaries on ultrasound. The ultrasound criteria for the diagnosis of a polycystic ovary are[≧ 8 sub-capsular follicular cysts <10 mm in diameter and increased ovarian stroma. While these findings support a diagnosis of PCOS, they are not by themselves sufficient to identify the syndrome.

Polycystic ovary syndrome (PCOS)



Gross appearance of a polycystic ovary (**A**) and transvaginal ultrasound scan image (**B**).

Polycystic ovary syndrome: Management

- *Management of PCOS involves the following:*

1. COCP to regulate menstruation. This also increases sex hormone- binding globulin, which will help reduce androgenic symptoms.
2. Cyclical oral progesterone: used to regulate a withdrawal bleed.
3. Clomiphene: this can be used to induce ovulation where subfertility is a factor.
4. Lifestyle advice: dietary modification and exercise is appropriate in these patients as they are at an increased risk of developing diabetes and cardiovascular disease later in life. Aerobic exercise has been shown to improve insulin resistance.
5. Weight reduction.
6. Ovarian drilling, a laparoscopic procedure to destroy some of the ovarian stroma that may prompt ovulatory cycles.

Polycystic ovary syndrome: Management

7. Treatment of hirsutism/androgenic symptoms:

a) eflornithine cream (Vaniqua™) applied topically;

b) cyproterone acetate (an antiandrogen contained in the Dianette™ contraceptive pill, sometimes used alone);

c) metformin: this is beneficial in a subset of patients with PCOS, those with hyperinsulinaemia and cardiovascular risk factors. It improves parameters of insulin resistance, hyperandrogenaemia, anovulation and acne in PCOS, and may aid weight loss. It is less effective than clomiphene for ovulation induction and does not improve pregnancy outcome;

d) GnRH analogues with low-dose HRT: this regime should be reserved for women intolerant of other therapies;

e) surgical treatments (e.g. laser or electrolysis).

Premenstrual syndrome

- *Premenstrual syndrome (PMS)* is the occurrence of cyclical somatic, psychological and emotional symptoms that occur in the luteal (premenstrual) phase of the menstrual cycle and resolve by the time menstruation ceases.
- Premenstrual symptoms occur *in almost all women of reproductive age*.
- In 3–60% symptoms are severe, causing disruption to everyday life, in particular interpersonal relationships.

Premenstrual syndrome: Etiology

- The precise etiology of PMS is unknown, but cyclical ovarian activity and the effects of estradiol and progesterone on certain neurotransmitters, including serotonin, appear to play a role.

Premenstrual syndrome: Clinical diagnosis

- The patient is likely to complain of *some or all* of the following:

1- bloating, 2- cyclical weight gain, 3- mastalgia, 4-abdominal cramps,

5-fatigue, 6-headache, 7-depression, 8-irritability.

- *The cyclical nature of PMS is the cornerstone of the diagnosis*. A symptom chart, to be filled in by the patient prospectively, may help.

Premenstrual syndrome: Management

A. Simple therapies: include stress reduction, alcohol and caffeine limitation and exercise.

B. Medical treatments:

1. **COCP:** the most effective regime appears to be bicycling or tricycling pill packets (i.e. taking two or three packets in a row without a scheduled break);
2. **Transdermal estrogen**: this has been shown to significantly reduce PMS symptoms, by overcoming the fluctuations of the normal cycle;
3. **GnRH analogues** are a very effective treatment for PMS as they turn off ovarian activity. To reduce the risk of osteoporosis it is recommended that a continuous combined form of hormone replacement therapy is administered concurrently;
4. **Selective serotonin-reuptake inhibitors (SSRIs):** there is good evidence that this group of drugs significantly improves PMS.

Premenstrual syndrome: Management

C. Hysterectomy with bilateral salpingo-oopherectomy: this procedure obviously completely removes the ovarian cycle. *It should only be performed if all other treatments have failed.* It is essential for such patients to have a preoperative trial of GnRH analogue as a 'test' to ensure that switching off ovarian function (by removing the ovaries at hysterectomy) will indeed cure the problem.

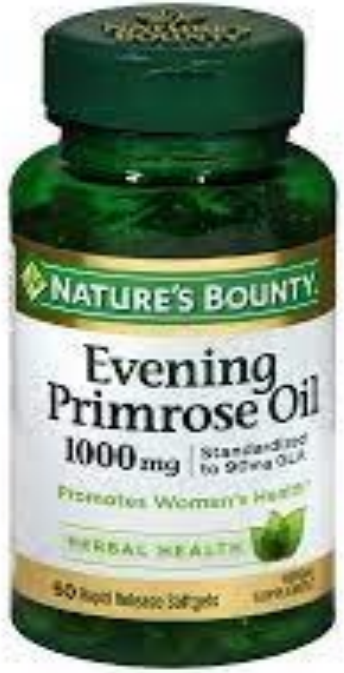
Premenstrual syndrome: Management

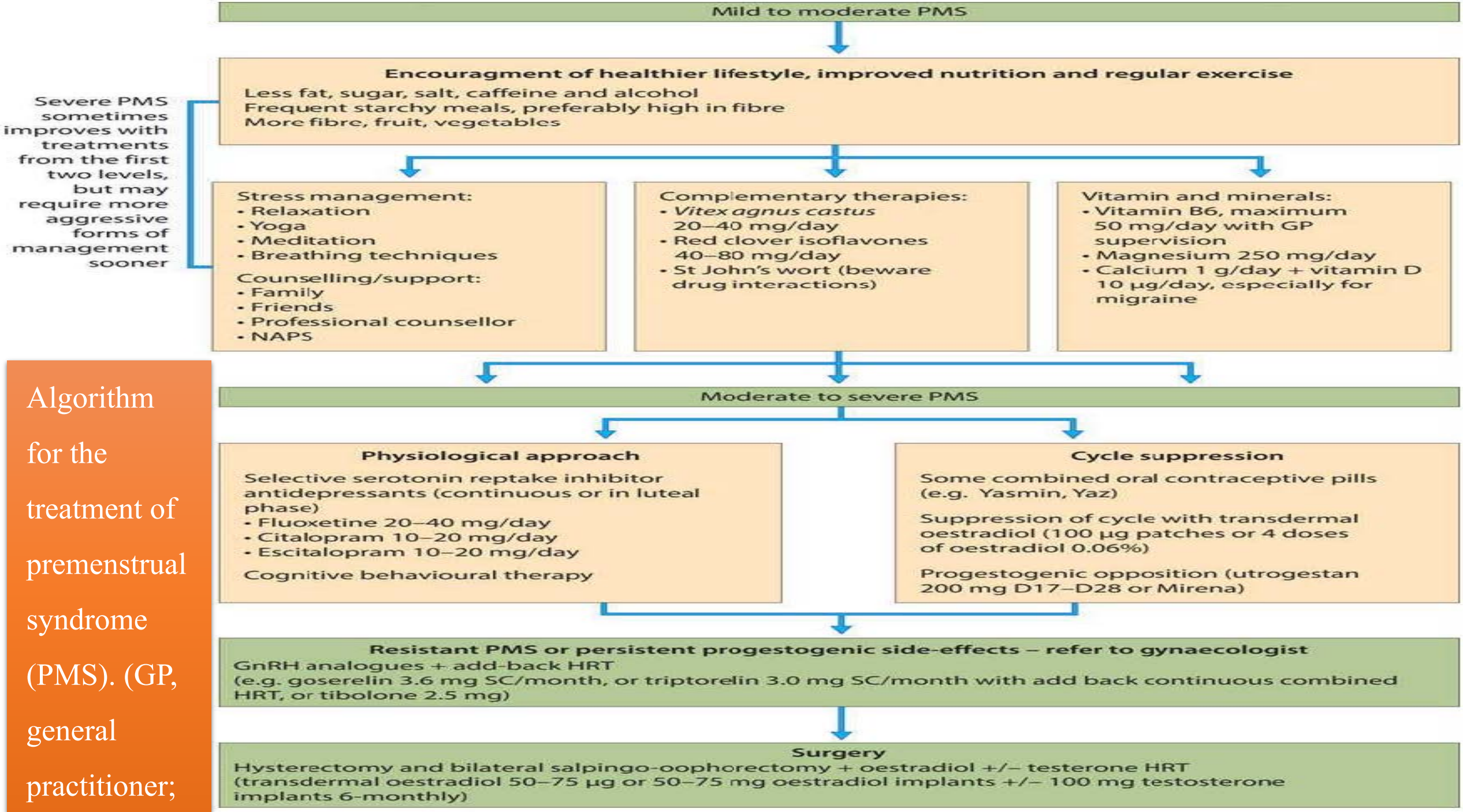
D. Vitamins: initial studies suggest that magnesium, calcium and isoflavones and vitamin B6 may be useful in treating PMS.

E. Alternative therapies:

- initial results of St John's Wort are promising, particularly in improving mood. Although Evening Primrose oil is commonly used, there is no evidence to support this treatment for PMS;
- cognitive-behavioural therapy (CBT): CBT appears to be particularly effective when combined with SSRIs.


BIOVEA
st. john's wort
guaranteed premium quality
450mg
dietary supplement
240
vegetarian capsules


NATURE'S BOUNTY
Evening Primrose Oil
1000 mg



Algorithm for the treatment of premenstrual syndrome (PMS). (GP, general practitioner;

KEY LEARNING POINTS

- Oligomenorrhea and amenorrhea may be primary or secondary and may be caused by hypothalamic, pituitary, ovarian or other hormonal disorders. They can also be caused by endometrial problems.
- PCOS is a common disorder associated with oligomenorrhea.
- PMS is common and can be treated with simple remedies as well as medical remedies.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谢谢
dakujem vám
ありがとう
ngiyabonga
dziękuję
merci
suksema
danke
thank
you
baie dankie
धन्यवाद
molte grazie
gracias
obrigada
takk
obrigado
teşekkür ederim
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dank u
teşekkür ederim
mahalo
tack så mycket