

INVESTIGATION OF INFERTILE COUPLE.

* Please check out [this link](#) to know if there are any changes or additions.

Revised by

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Color index: **Important** | **Doctors notes** | Further explanation.

OBJECTIVES:

- ✓ Identify the causes of infertility in men and women.
- ✓ Understand the diagnostic approaches to infertility in men and women.
- ✓ Interpret the results of investigation of infertility in men and women.

INFERTILITY / SUBFERTILITY

❖ What is “infertility”?

- Failure of a couple to conceive after **one year** of regular, **UN**protected intercourse. (not on any kind of contraception or having a protected intercourse).

❖ Causes?

- ⇒ **Endocrine problems: Common in females** (1/3rd patients). & Rare in males
- ⇒ **Hormone dysfunction** is a **rare** cause of male infertility.
- ⇒ **Idiopathic**: In some couples no cause can be identified.

❖ Endocrine causes of female infertility:

Excessive secretion of ovarian androgens:	Primary ovarian failure:	Hypogonadotropic hypogonadism
<ul style="list-style-type: none"> ▪ Obesity ▪ Insulin resistance 	<p>✓ High gonadotrophins, low oestradiol (postmenopausal hormonal pattern).</p> <p>برايمري = المشكلة من المبايض نفسها = ماتكون الاستروجين ولا تستجيب لأوامر القونادوتروفنز.. فتصير كميات الاستروجين منخفضة والقونادوتروفنز عالية.</p> <p>Hormone replacement therapy can be given (will not treat infertility).</p> <p>So it may improve libido for example but it will have no effect on fertility</p>	<p>✓ Low gonadotrophin/oestradiol.</p> <p>هنا المشكلة من فوق "ميب من المبايض".. فماتوصلها أوامر علشان تقدر تصنع استروجين.. "نفس فكرة سؤال الميد"</p> <ul style="list-style-type: none"> • Rare • Due to hypothalamic-pituitary lesion.
Hyperprolactinemia	PCOS	Cushing's syndrome

How does Cushing's syndrome affect fertility? High levels of cortisol in the blood affect the ovarian function

the diagnostic approaches to infertility

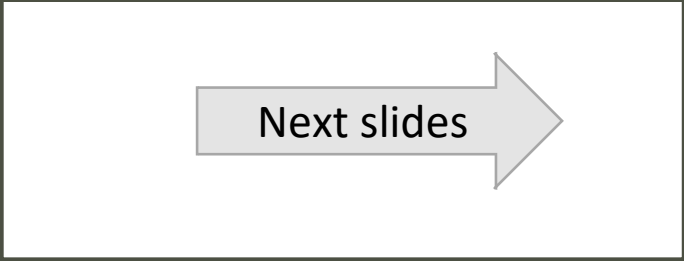
Clinical history taking

- Information on clinical history of the patient should include:
- Serious illness
 - Use of contraceptives
 - Sexually transmitted disease
 - Past Chemo / radiotherapy (DESTROYS FEMALE EGGS)
 - Drug usage such as hormone replacement therapy
 - Frequency of intercourse
 - Congenital abnormalities
 - Previous pregnancy (why? to determine if it is primary or secondary infertility)

Physical examination:

- Information on physical examination should include:
- Hypothalamo-pituitary, thyroid disorders
 - Cushing's syndrome
 - Galactorrhea
 - Lactation in the absence of pregnancy
 - Most common due to hyperprolactinemia
 - Hirsutism (indicates PCOS)

Endocrine investigations



3 خطوات نمشي عليهم بحالة الانفرتلتي:

- الخطوة الأولى: ناخذ الهستوري من المريضة ونسألهم عن الأشياء المذكورة فوق ^.. علشان نعرف السبب ونقلص قائمة الأسباب أو على الأقل نسوي ranking.
- الخطوة الثانية: اقزامنيشين. نشوف اذا فيه أي شي يدلنا على ان المشكلة بالاكسس "مثلا اذا كان فيه bi-temporal hemianopia بنشك بالادينوما" أو اذا كان فيه milky nipple discharge اللي غالبا بيكون سببه hyperprolactinemia.
- الخطوة الثالثة: نطلب تحاليل بناء على الأشياء اللي استنتجناها من الخطوتين السابقت.. ونمشي على بروتوكول معين "يختلف حسب جنس المريض" بنشوفونه السلايدات القادمة.

Some other questions that are included when taking a proper history from an infertile couple:
 1-wether any of them smoke 2-alcohol. 3-history of chronic diseases 4-how long have they been trying to get pregnant,

A. Endocrine investigations in subfertile woman:

After taking History and asking the patient about her menstrual cycle:

If Normal menses: "الدورة منتظمة هل المشكلة بالإباضة؟"

- Investigations are based on the **phase** of menstrual cycle.
- Serum **progesterone** should be measured in the **middle of the luteal phase (day 21)**.

Low progesterone levels (< 10 nmol/L)

No ovulation

Note! if it is between 10 and 30, that means that the cycles are ovulatory cycles but there is a problem in the lute all phase

High progesterone (> 30 nmol/L)

indicates **ovulation**.

If oligomenorrhea or amenorrhea

- ✓ hormone measurement is needed, after knowing she's not pregnant.

FSH:

LH:

Prolactin:

Indicates:

High

Normal.

Ovarian failure.

نفس ماقلنا بسلايد 3.. المشكلة من المبايض نفسها..
ميب قاعدة تستجيب لأوامر للال اتش والاس اف اتش

Low

High

Normal.

Polycystic ovarian syndrome.

Normal

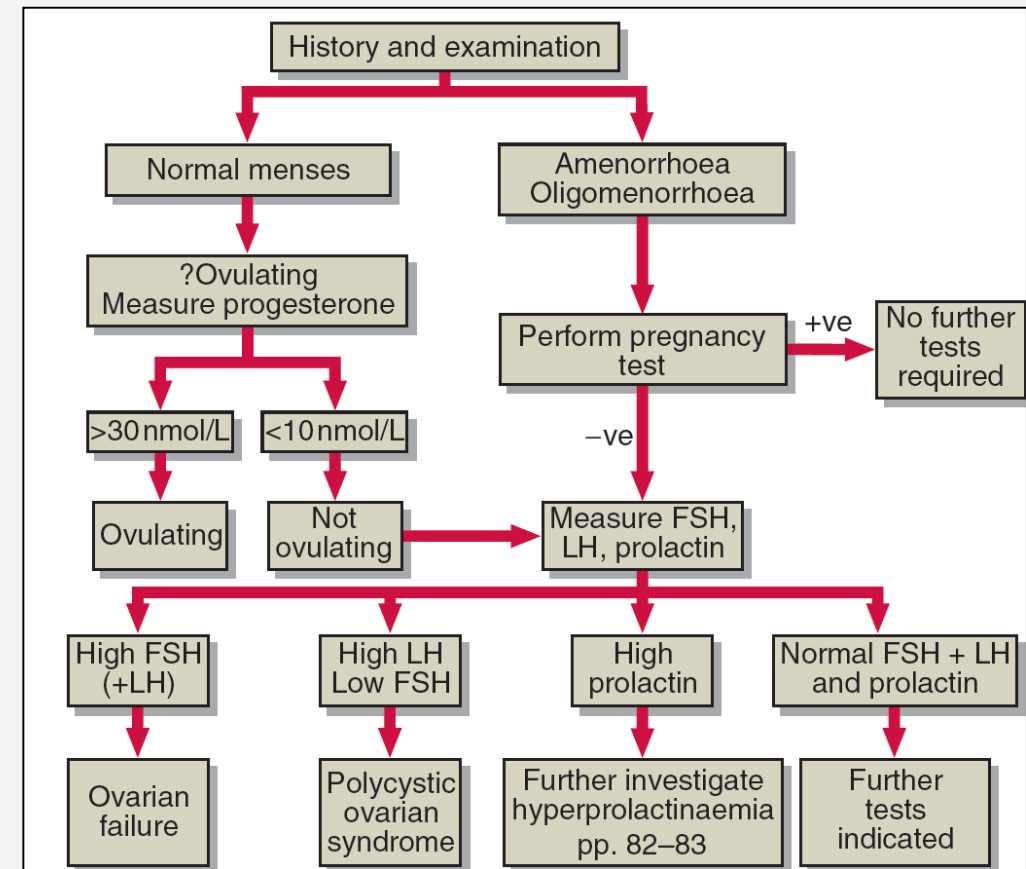
High.

Further investigate hyperprolactinemia.

المشكلة هايبروبرولاكتينيميا.. طيب وش سببها؟ لازم نسوي تستس زيادة

Normal.

Further tests indicated.



In women who are having trouble conceiving the first thing you have to do is check for the regularity of their periods:

1. If they are having regular periods: then you have to check for serum progesterone when she is in the middle of the luteal phase at day 21.
 - Note that YOU DO NOT DO ONE MEASUREMENT ONLY
 - YOU DO MEASUREMENTS FOR THREE CYCLES THEN TAKE THE MEAN VALUE
 - If the serum progesterone is more than 30 nanomoles, then we can say that this woman's menstrual cycles are actually ovulatory cycles!
2. however in a woman with oligomenorrhea or amenorrhea, perform pregnancy test : you have two scenarios, either she is pregnant (amenorrhea is normal in this case) , BUT if she is not pregnant then you must go for hormone measurement.
 - how does one diagnose oligomenorrhea ? there are two ways:
 - when the woman has 8 periods (and not more than 8!) in one year
 - Or when the time between her periods is more than 6 weeks but it has to be less than six months)
 - When do you say that a woman has amenorrhea?
 - It can be primary amenorrhea :absence of menstrual cycle by the age of 16-17 yrs.
 - Or it can be secondary amenorrhea :ABSENCE OF PERIOD FOR MORE THAN 6 MONTHS

B. Endocrine investigations in subfertile man

- ✓ Endocrine causes of infertility in men are **rare**.
- ✓ If your patient is a male, request a semen analysis.

❖ What does it analyze?

Volume	Liquefaction time	Sperm count	Motility
pH 7.2-7.8	WBCs	Presence of abnormal spermatozoa	

- ❖ Note that the time it takes for sperm to turn from gel like to liquid is called the liquefaction time
- ❖ Note that acidity kills sperm
 - When the seminal vesicle is blocked this may lead to acidic semen.
 - Alkaline semen may indicate infection.

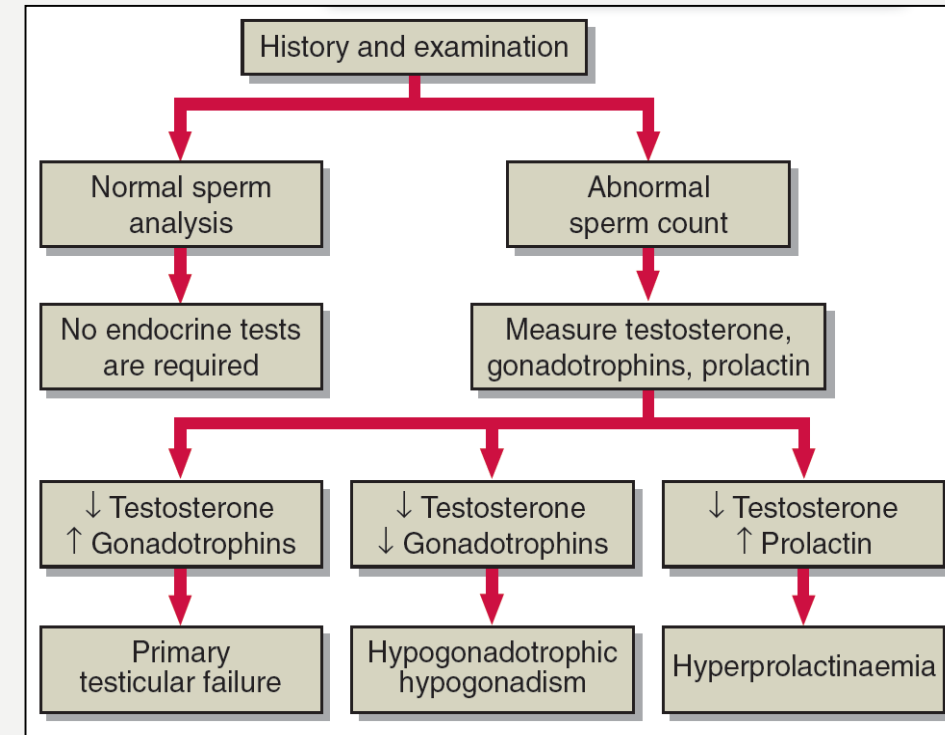
If sperm analysis is normal (Eugonadal)

No endocrine investigations are required!

If sperm analysis is abnormal (Hypogonadal men):

Testosterone:	Low	Decreased	Low
Gonadotrophs:	High	Low \ normal	Low \ normal
Indicates:	Primary testicular failure	Hypogonadotrophic hypogonadism	Hyperprolactinemia
	Damage in the testes (interstitial, tubular).	Hypothalamic-pituitary disease "تذكرتوا سؤال الميذ؟"	a rare cause in men

Note that if the both LH and FSH are high , this means that damage occurred in both tubular and interstitial part of the testis but if only FSH is high then this indicates that the damage only occurred in the tubular part of the testis

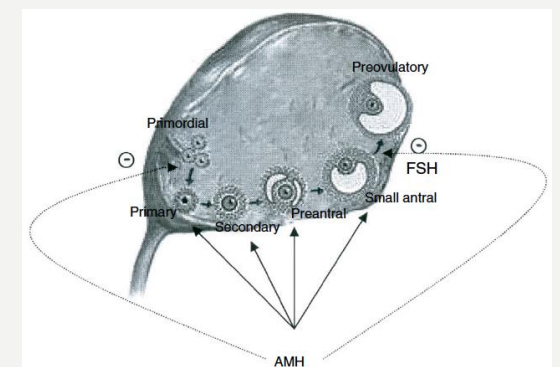


ANTI-MULLERIAN HORMONE (AMH)

Also called:	Mullerian-inhibiting substance
What?	Polypeptide hormone Secreted by: growing ovarian follicles . ✓ Secretion is <u>proportional</u> to follicular development
Action:	<ul style="list-style-type: none"> AMH prevents premature depletion of follicles. prevents early menopause In the ovary it inhibits the: <ul style="list-style-type: none"> Initial recruitment of <u>primary follicles</u> from <u>primordial follicles</u>. Sensitivity of antral follicles to FSH during cyclical recruitment. So when it inhibits this sensitivity, the primordial follicles will not become primary follicles.
Assess?	<ul style="list-style-type: none"> Helps assess ovarian reserve (احتياطي المبايض) and female fertility <ul style="list-style-type: none"> Ovarian reserve: <u>number</u> and <u>quality</u> of oocytes in the ovaries. AMH measures the level of fertility in women, high amount = more ovum in ovaries.
How?	<ul style="list-style-type: none"> The no. of remaining primordial follicles <u>correlate</u> with the no. of growing follicles Since ONLY growing follicles produce AMH, its plasma levels reflect the number of remaining primordial follicles.

AMH prevents depletion of premature follicles so it depletes the follicles when they're mature and active. However, in polycystic ovary syndrome AMH is low and there are a lot of immature follicles with no function giving the ovary a polycystic appearance .

- Low levels **in females** are associated with infertility, while AMH Inhibits formation the female ducts **in males**
- high levels in females are actually normal.
- Primordial follicles transition at puberty into primary follicles.
 - These primary follicles either undergo **atresia** or they are **ovulated**.
- Anti-mullerian hormone is secreted by granulosa cells as they are differentiating.
 - AMH is secreted by growing follicle (mostly **antral follicles**).
- AMH IS PROPORTIONAL TO CHANCES OF GETTING PREGNANT BECAUSE IT IS DIRECTLY PROPRTIONAL TO THE AMOUNT OF FUNCTIONAL FOLLICLES.



Hyperprolactinemia

What is "prolactin"?	An anterior pituitary hormone Note in pregnancy Prolactin leads to milk production but in normal female, high levels will affect the gonads causing infertility, prolactin also decreases LH and FSH and suppresses GNRH		
Targeted gland & action	It acts <u>directly</u> on the mammary glands to control lactation		
Regulation: tightly regulated:	Stimulated by:	Thyroid releasing hormone (TRH)	from hypothalamus
	Inhibited by:	Dopamine	
Hyperprolactinemia: elevated circulating levels of prolactin.			
Result in:	Infertility in both sexes due to gonadal <u>function impairment</u> .		
Early indication	In women	Amenorrhea and galactorrhea (lactating without pregnancy or childbirth due to high prolactin).	أعراض كأنها تقول "ترا يمكن عندك هايبربرولاكتينيما.. روجي شوفي عمرك".. وبالنسبة للرجال ما عندهم أي شيء يدل لأنه اصلا شيء نادر.
	In men	NONE (why?) Because the tumor is only discovered when it becomes so big that it compresses the optic chiasma leading to visual defects	
Causes:	<ol style="list-style-type: none"> Stress Drugs (estrogens, phenothiazines, metoclopramide, α-methyl dopa) Seizures Primary hypothyroidism (prolactin is stimulated by raised TRH). Other pituitary disease Prolactinoma (benign pituitary tumor) Idiopathic hypersecretion (e.g. due to impaired secretion of dopamine that usually inhibits prolactin release) الدوبامين مايفرز بكميات كافية فما فيه شيء يردع البرولاكتن ويقوله ستوب!! 		
Diagnosis:	Exclude:	Stress	Drugs
	Differential diagnosis:	Prolactinoma	Idiopathic hypersecretion

How to differentiate between prolactinoma and idiopathic hypersecretion?

by **TRH** stimulation test. If there is NO increase in prolactin after stimulation with TRH then it is prolactinoma but if there is an increase this indicates idiopathic hypersecretion

Check your understanding!

Q1:Early indication of hyperprolactinemia in men:

- A. Amenorrhea.
- B. Galactorrhea.
- C. Oligomenorrhea .
- D. None.

Q2:Which of the following is cause of hyperprolactinemia:

- A. Stress.
- B. Seizures.
- C. Phenothiazines.
- D. All of the Above.

Q3:Which of the following Stimulates Prolactin secretion:

- A. TRH.
- B. ACTH.
- C. Dopamine.
- D. Both A&C.

Q4:T/F: Eugonadal men with normal sperm analysis do not require endocrine investigations.

- A. T
- B. F

Q5:Which of the following is the site of secretion AMH:

- A. Growing ovarian follicles.
- B. Hypothalamus.
- C. Anterior pituitary.
- D. Testis.

Q6:Which of the following is Endocrine causes of female infertility:

- A. Obesity.
- B. Insulin resistance.
- C. PCOS.
- D. All of the above.

Q7:T/F: The no. of remaining primordial follicles correlate with the no. of growing follicles.

- A. T
- B. F

Done by:

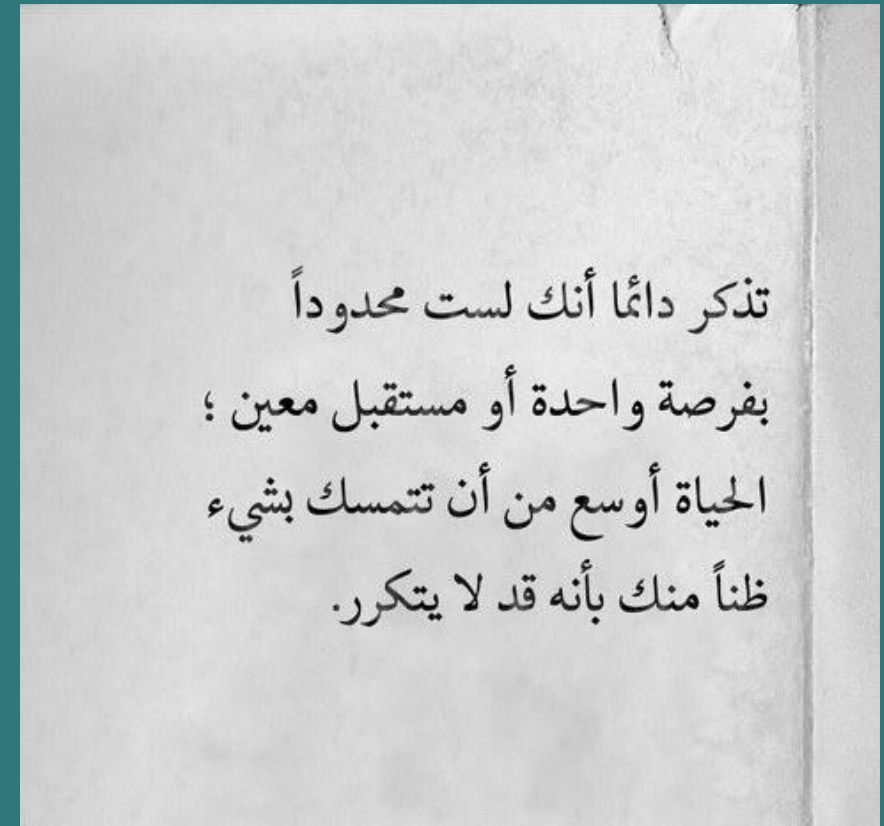
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- 435's slides.



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