Biochemistry Bandits 434

Investigations Of Infertile Couple

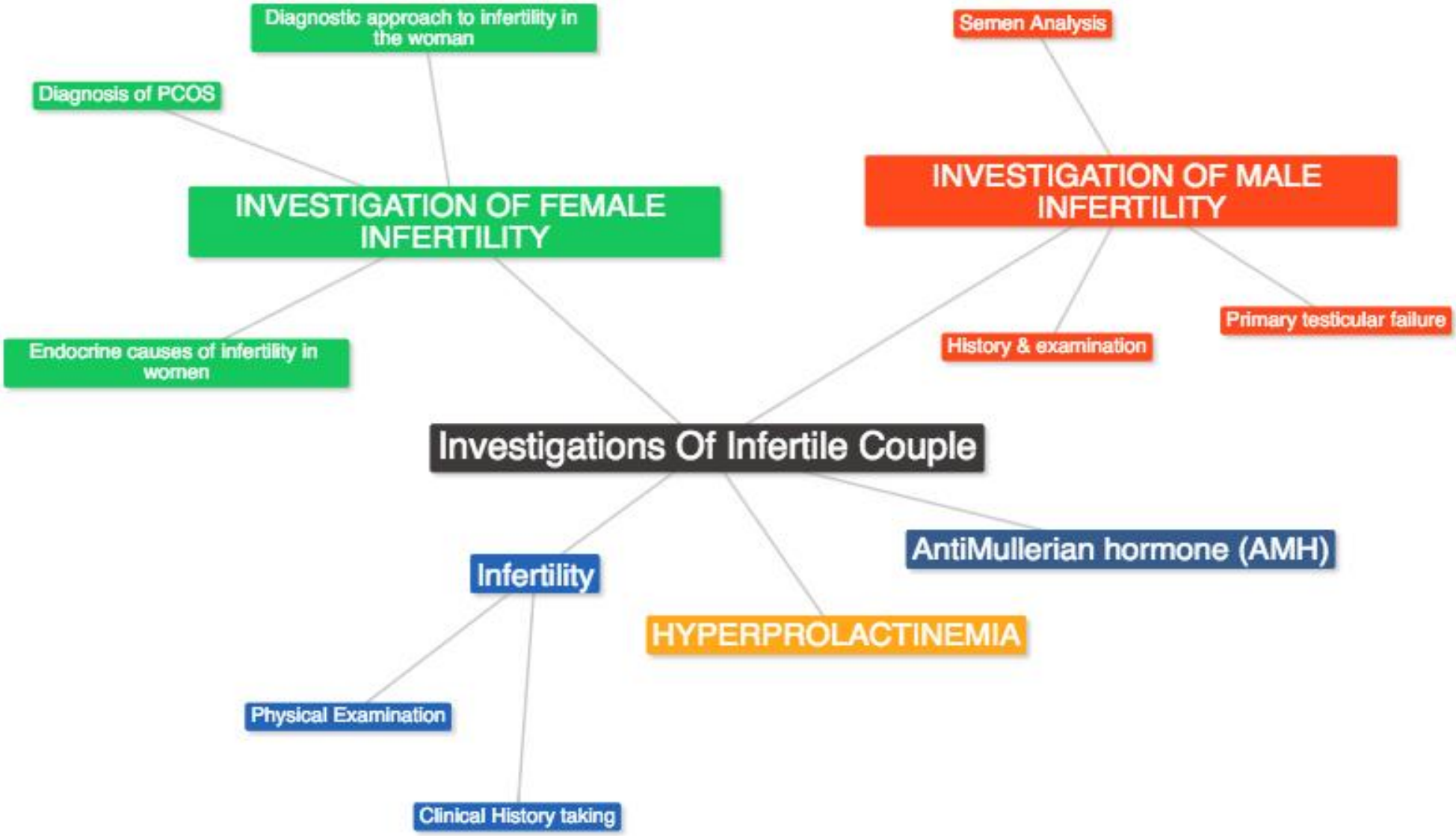
OBJECTIVES:

- ❑ Determine the laboratory approach to infertility in female.
- ❑ interpret results of investigation of infertility in female.
- ❑ Determine the diagnostic approach to infertility in male.
- ❑ interpret results of investigation of infertility in male

❖ **Important** ❖ Extra ❖ Biochemistry Edit

Reproductive Block

MIND MAP


Diagnostic approach to infertility in the woman
Diagnosis of PCOS
INVESTIGATION OF FEMALE INFERTILITY
Endocrine causes of infertility in women
Semen Analysis
INVESTIGATION OF MALE INFERTILITY
Primary testicular failure
History & examination
Investigations Of Infertile Couple
AntiMullerian hormone (AMH)
Infertility
HYPERPROLACTINEMIA
Physical Examination
Clinical History taking

Infertility:

Failure of a couple to conceive **after 1 year** of regular , unprotected intercourse.

Infertility may be caused by endocrine problems:

- This is **common** in the female
- But **rare** in the male.

- Elevated serum [**progesterone**] at **day 21** of the menstrual cycle indicates that **ovulation has occurred**

- In both men & women infertility, a serum **[FSH] > 25U/L** indicates **primary gonadal failure**

?What information should be obtained from patient

Clinical History taking:

Should be **full** clinical history
Before physical examinations

- Previous pregnancies[1]
- Contraceptive practice
- Serious illnesses
- Past chemotherapy or radiotherapy
- Congenital abnormalities
- Smoking habits
- Drug usage
- STD Sexual transmitted disease
- Frequency of intercourse

Physical Examination:

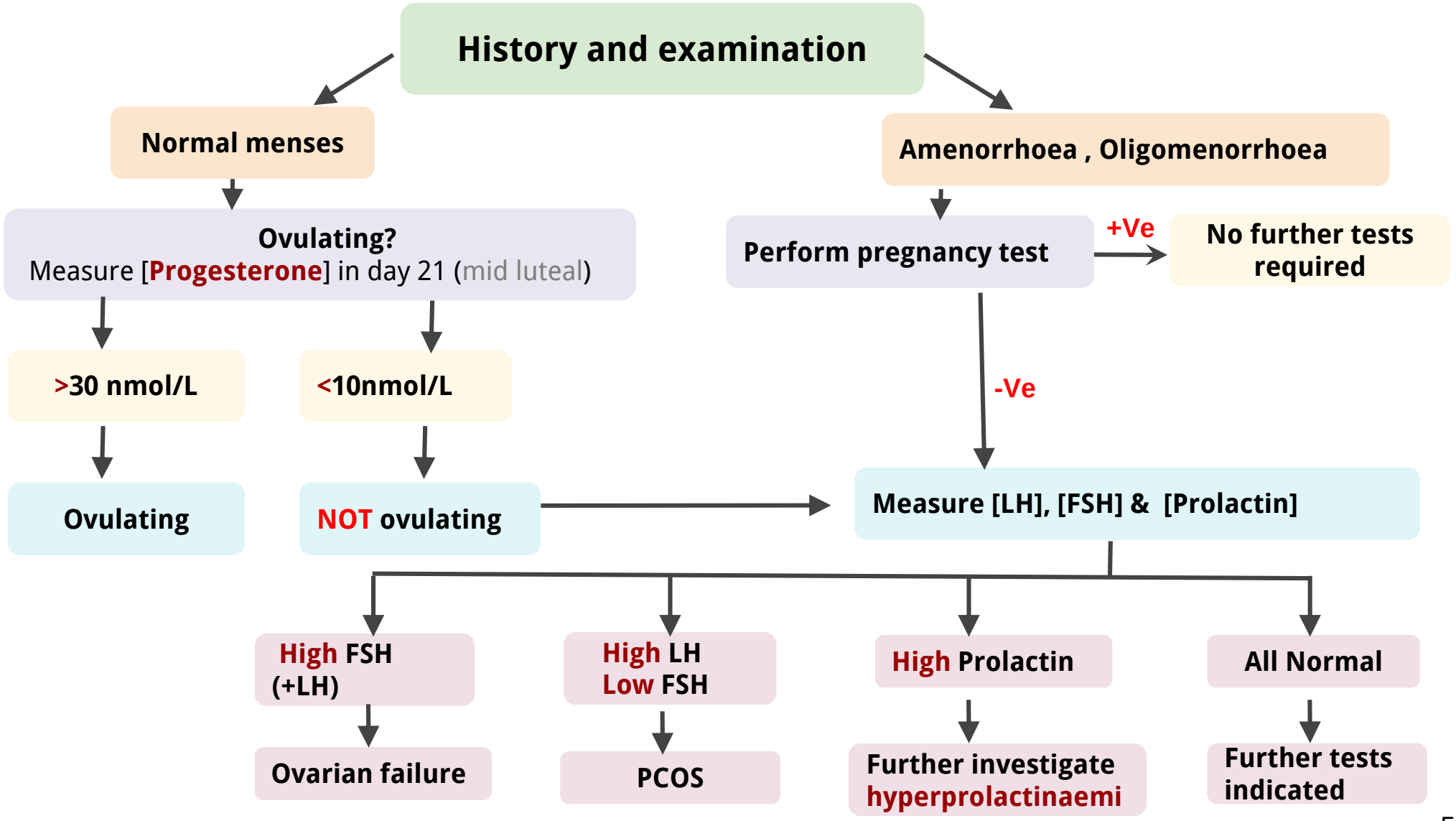
Should look for indications of:

- Hypothalamic-pituitary
- thyroid disorders
- Cushing's syndrome[2]
- Galactorrhoea (inappropriate breast milk production); i.e. in the absence of pregnancy most commonly caused by **hyperprolactinemia**.
- Hirsutism (increase in body hair with male pattern distribution)

1.to know if it is secondary infertility or Primary.
2. The high levels of cortisol and androgens in Cushing's syndrome disrupt a woman's ovaries. Her menstrual periods may stop completely or become irregular. As a result, women with Cushing's syndrome almost always have difficulty becoming pregnant. For those who do become pregnant, the risk of miscarriage is high. In men, Cushing's syndrome may effect may spermtic function.

INVESTIGATION OF FEMALE INFERTILITY

Diagnostic approach to infertility in the woman



Endocrine causes of infertility in women

↑ ovarian androgen secretion	Primary ovarian failure	PCOS	Cushing's syndrome	Hyperprolactinemia	Hypogonadotropic hypogonadism
e.g.: obesity → Insulin resistance → ↑ovarian androgen secretion.	Postmenopausal hormonal pattern: (↑ gonadotrophins & ↓ oestradiol) ❑ Hormone replacement therapy can be given (this will not treat the infertility)	↑ **serum [LH]** **Normal (or low) [FSH]**			❖ Rare ❖ due to hypothalamic-pituitary lesion

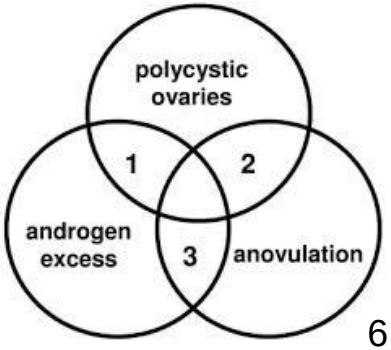
Diagnosis of PCOS*:

In 2003, the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM) recommended that **at least 2 of the following 3 features are required for PCOS to be diagnosed:**

1. **Oligo-ovulation or anovulation manifested** as oligomenorrhea or amenorrhea

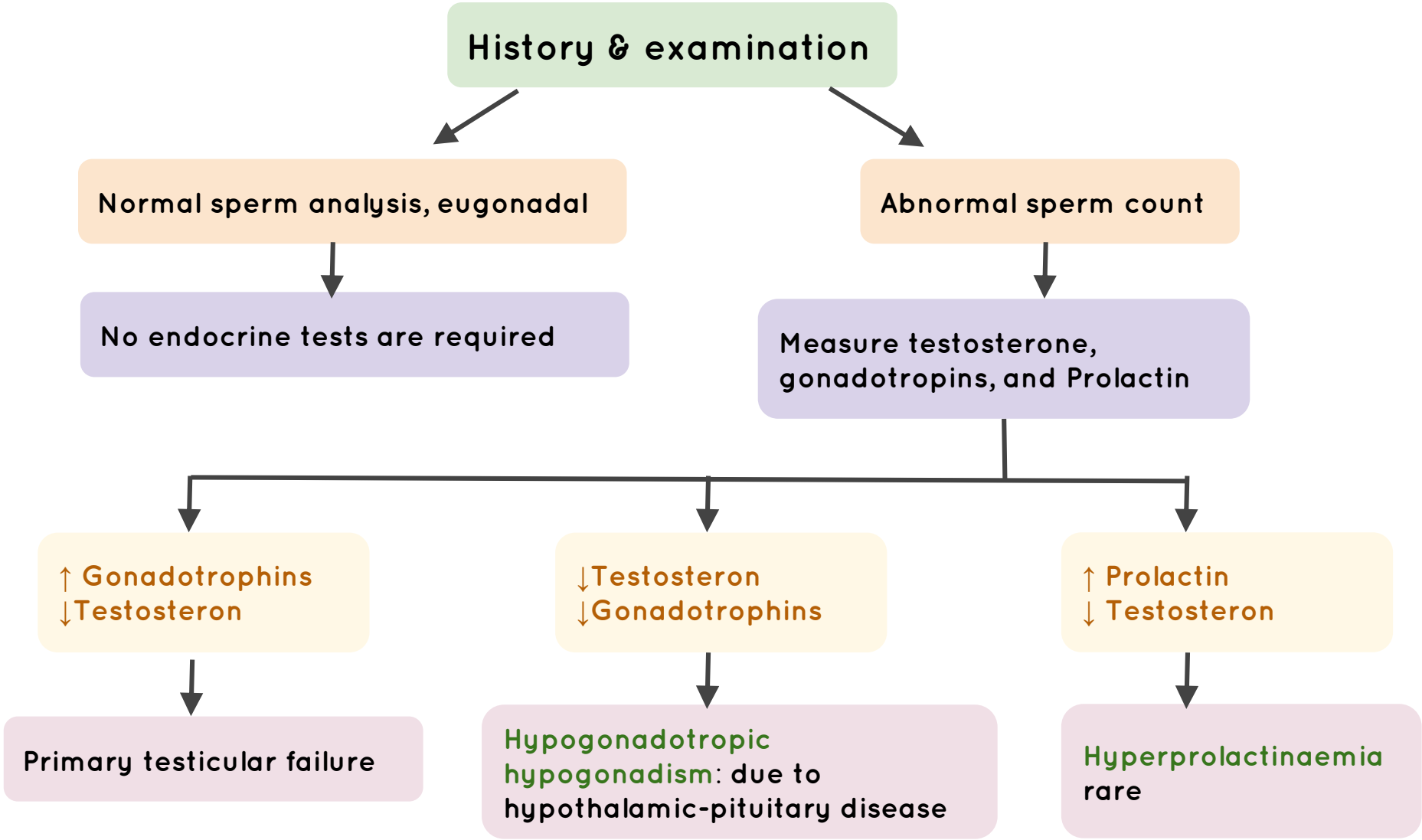
2. **Hyperandrogenism** (clinical evidence of androgen excess) **or hyperandrogenemia** (biochemical evidence of androgen excess)

3. **Polycystic ovaries** (as defined on ultrasonography)



* polycystic ovarian syndrome

INVESTIGATION OF MALE INFERTILITY



INVESTIGATION OF MALE INFERTILITY

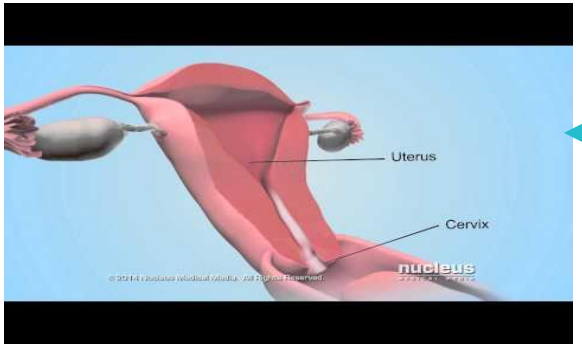
Semen Analysis

Comment on:

- Volume
- Liquefaction time[1]
- sperm density (count)
- Motility
- the presence of abnormal spermatozoa (abnormal shape, or motility)
- pH
- WBCs infection or inflammatory process

Primary testicular failure

- Damage to both the **interstitial cells** and **tubules**
  ↓Testosterone & ↑ Gonadotrophins (LH & FSH)
- **Only tubular** impairment selective↑ in FSH, while androgen may be normal



The animation explains the reasons for a semen analysis and describes the main tests it includes.

1.Liquefaction time: is the time it takes for the semen to turn to liquid after being a thick gel at the time of ejaculation.

HYPERPROLACTINEMIA

What is Prolactin? It is an anterior pituitary hormone that acts directly on the mammary glands to control lactation. Prolactin secretion is tightly regulated:	**Stimulated** by TRH from the hypothalamus. **Inhibited** by dopamine from hypothalamus
Hyperprolactinemia: It is elevated circulating **[Prolactin]** A common condition. It causes infertility in both sexes due to gonadal function impairment.	Early indication of hyperprolactinemia: • In women: amenorrhoea & galactorrhoea • In men: none

Causes of hyperprolactinemia	Diagnosis of the cause of hyperprolactinemia
• Stress • Drugs : e.g. oestrogens, phenothiazines, metoclopramide, α-methyldopa. • Seizures[1]. • 1ary hypothyroidism (prolactin is stimulated by the raised TRH). • Other pituitary disease. • Prolactinoma (commonly microadenoma). • Idiopathic hypersecretion (e.g. due to impaired secretion of dopamine that usually inhibits prolactin release).	Exclude: ❖ Stress ❖ Drugs ❖ Other disease Differential diagnosis: ❖ prolactinoma. ❖ Idiopathic hypersecretion.

How to differentiate between prolactinoma & idiopathic hypersecretion?

- ❖ **Detailed pituitary imaging.**
- ❖ **Dynamic tests of Prolactin secretion:**
  - ➢ administration of TRH, then measure serum [prolactin]:

-If ↑ : Idiopathic hyperprolactinemia.

-If **NO** rise : Pituitary tumor

AntiMullerian hormone (AMH)

Ovarian reserve:
number and quality of oocytes in the ovaries.

- A polypeptide hormone.
- Also called Mullerian-inhibiting substance.
- Secreted by growing ovarian follicles.
- Secretion is proportional to follicular development.
- Helps assess ovarian reserve and female fertility.
- Anti Mullerian hormone blood levels are often used by fertility specialists as part of the evaluation of **ovarian reserve.**
- In the ovary it inhibits the:

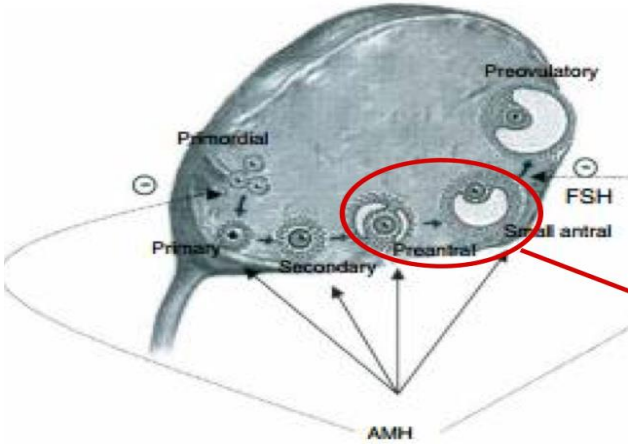
- -Initial recruitment of primary follicles from primordial follicles.
- -Sensitivity of antral follicles to FSH during cyclical recruitment.

- AMH prevents premature depletion of follicles.
- The No. of remaining primordial follicles correlate with the No. of growing follicles.
- Since only growing follicles produce AMH, its plasma levels reflect the number of remaining primordial follicles.

AMH and Folliculogenesis:
Highest levels of AMH are secreted by preantral and small antral follicles.

SUMMARY

- Infertility (subfertility) is defined as the failure of a couple to conceive after one year of regular, unprotected intercourse
- Endocrine problems are common cause of Infertility in the female but rare in the males
- Presence of ovulation is confirmed by measuring progesterone levels at day 21:
  IF progesterone levels >30 nmol/L => Indicates ovulation
  IF progesterone levels <10 nmol/L => NO ovulation
- Hyperprolactinemia is a rare cause of male infertility.
- We differentiate between prolactinoma & idiopathic hypersecretion by:
  - Detailed pituitary imaging.
  - Dynamic tests of Prolactin secretion.
- AMH is the best current available measure of ovarian reserve for different clinical conditions.
- Highest levels of AMH are secreted by preantral and small antral follicles.



MCQS

1) In female, if there is a regular ovulatory menstrual cycle, serum [Progesterone] measured in the middle of the luteal phase should be ?

A) >30nmol/L B) <5nmol/L C) <10nmol/L

2) In both men and women infertility, a serum [FSH] > ..... indicates primary gonadal failure:

A) 50U/L B) 25U/L C) 75U/L

3) High LH, low FSH indicates which of the following?

A) PCOS
B) Ovarian failure
C) Hyperprolactinemia

4) Prolactin hormone is inhibited by which one of the following?

A) TRH B) Dopamine C) ACTH

5) If there is no rise in the dynamic tests of prolactin secretion this indicates:

A) Pituitary tumor
B) Idiopathic hyperprolactinaemia
C) Stress

6) AMH is secreted by which one of the following:

A) growing ovarian follicles
B) primordial follicles
C) Theca cells

ANSWER :
1- A 2-B 3-A 4-B 5-A 6-A

SAQs

1) How to differentiate between prolactinoma & idiopathic hypersecretion?

by detailed pituitary imaging and dynamic tests of Prolactin secretion if the test is elevated this indicates Idiopathic hyperprolactinaemia and if there is no rise in the level of prolactin this indicates pituitary tumor.

2) What are the functions of AMH in the ovary?

it inhibits the: - Initial recruitment of primary follicles from primordial follicles.

- Sensitivity of antral follicles to FSH during cyclical recruitment.

3) what are the Endocrine causes of infertility in women ?

PCOS - ↑ ovarian androgen secretion- Primary ovarian failure-Hyperprolactinaemia-Cushing's syndrome -Hypogonadotropic hypogonadism

4)What are the features are required for PCOS to be diagnosed?

1. Oligo-ovulation or anovulation .
2. Hyperandrogenism or hyperandrogenemia.
3. Polycystic ovaries.

Biochemistry Bandits 434

Thank you

DONE BY:

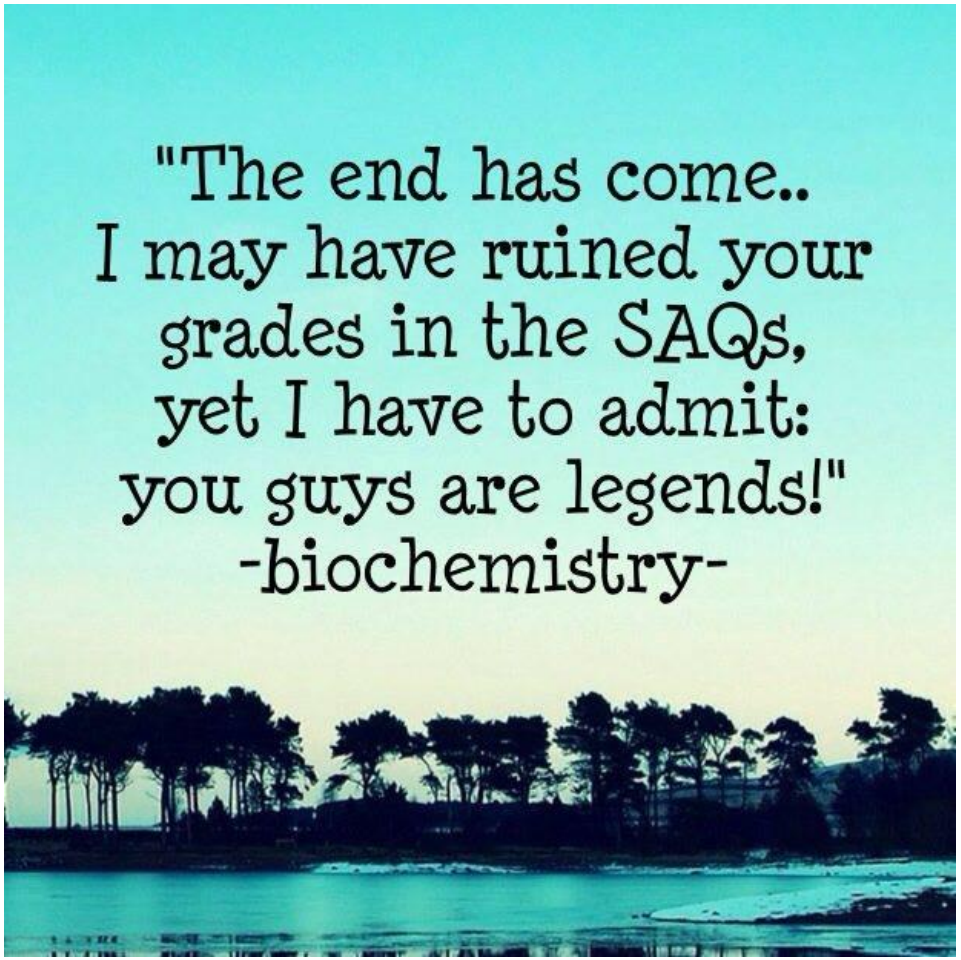
Nourah Almofarej
Jawaher AlEmran

REVIEWED & EDITED BY:

Sarah Alsalman
Elham Alghamdi
Mohammad Alotaibi

Special thanks to:

Lina Aljurf



For questions and comments contact us: Biochemistry434@gmail.com