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**Infertility:**

Failure of a couple to conceive after 1 year of regular, unprotected intercourse  
(not using contraceptive)

- ✓ Infertility is very sensitive type of cases.
- ✓ The stress that face the couple when they start investigation for infertility is associated with psychological factors which is a source of sub fertility .

**Background:**

Infertility may be caused by endocrine problems:

- This is common in the female
- But rare in the male
- ✓ In female Elevated serum [progesterone] at day 21 of the menstrual cycle indicates that ovulation has occurred (in the middle of luteal phase)
- ✓ In both men & women infertility a serum [FSH] > 25U/L indicates primary gonadal failure ( primary means the problem in the gonad itself)  
(Very high FSH → means the gonad not responding)

**Investigation**

- First : full clinical history taking
- Second : physical examination

❖ First : **FULL** clinical history:

- Previous pregnancies ( to know if it is secondary infertility or primary )
- Contraceptive practice
- Serious illnesses
- Past chemotherapy or radiotherapy (or exposure to radiation)
- Congenital abnormalities
- Smoking habits
- Drug usage
- STD
- Frequency of intercourse

❖ Second : physical examination.

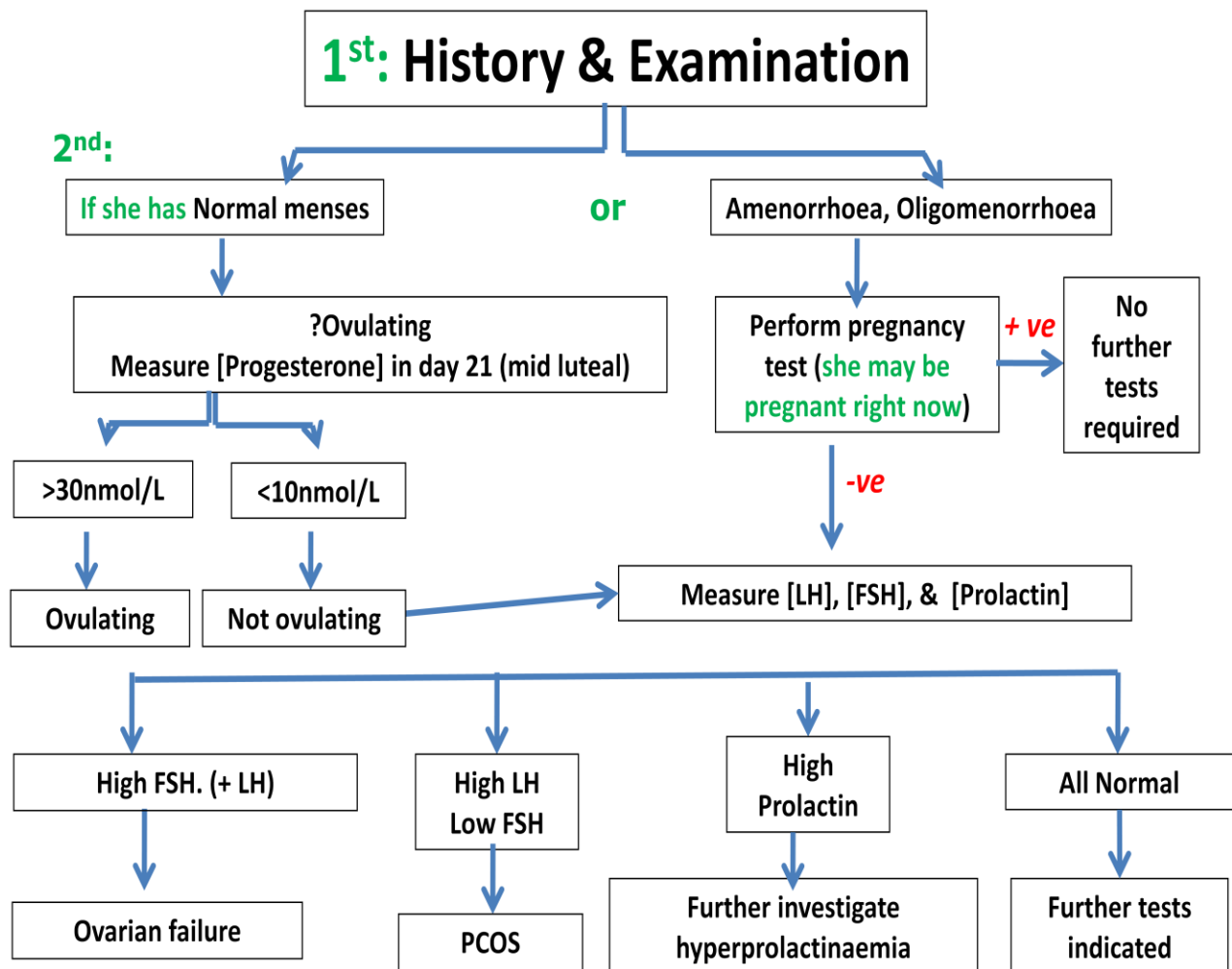
- Hypothalamic-pituitary or thyroid disorders
- Cushing's syndrome (↑ corticosteroid)
- Galactorrhoea (inappropriate breast milk production; i.e. in the absence of pregnancy most commonly caused by hyperprolactinaemia)
- Hirsutism in female (an increase in body hair with male pattern distribution- hyperandrogenic-)

These all are endocrine causes that can lead to subfertility or infertility

We will take about :

- ✓ INVESTIGATION OF FEMALE INFERTILITY
- ✓ INVESTIGATION OF MALE INFERTILITY

- ✓ Channel of investigation in the female is more complicated than male, it is also more costly and invasive in female b/c endocrine causes for infertility more related to women than men.

Investigation of female infertility:**Diagnostic approach to infertility in the woman**

**NOTE :** Present of menstrual cycle (normal menses) doesn't mean that there is an ovulation – (ova coming out from graafian follicle at certain time and go to fallopian tube ready to be fertilized-) so even when she has normal menses we should confirm that ovulation is it normal or not by measuring the **progesterone**.

Endocrine causes of infertility in women:

- **↑ ovarian androgen secretion:**  
e.g.: obesity → Insulin resistance → ↑ ovarian androgen secretion)
- **Primary ovarian failure:**  
postmenopausal hormonal pattern\*: (↑ gonadotrophins & ↓ oestradiol) (no treatment )  
Hormone replacement therapy can be given (this will not treat the infertility).
- **Hyperprolactinaemia**
- **PCOS:**  
↑ serum [LH]  
Normal [FSH]
- **Cushing's syndrome**
- **Hypogonadotrophic hypogonadism:**  
Rare  
due to hypothalamic-pituitary lesion (tumor)

**NOTE :**

- \* She is not postmenopausal but her profile of hormones like postmenopausal women.
- ✓ Hormone replacement therapy only to improve the symptoms due to estrogen deficiency -psychological more than treatment-
- ✓ Hypogonadotrophic hypogonadism: ↓ FSH & LH and ↓ estrogen (not like primary gonadal failure -↑ FSH & LH and ↓ estrogen- )

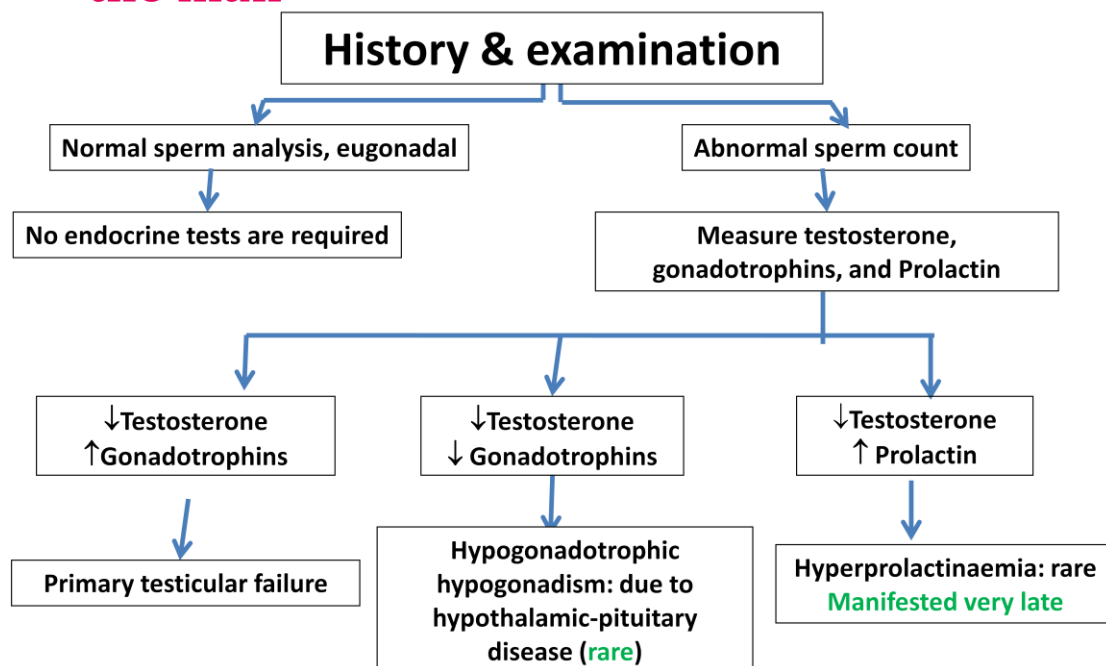
**INVESTIGATION OF MALE INFERTILITY:****Semen Analysis:**

(is very informative we can know the cause without further investigation.)

We see :

- Volume
- Liquefaction time: ( it ↑ when there is bacterial infection b\c bacteria secrete enzymes that make it more liquefied)
- sperm density (count) (40 million and more during ejaculation)
- Motility ( > 60% normally motile)
- the presence of abnormal spermatozoa (abnormal shape, or motility)
- pH
- WBCs? (normally no WBCs. if it was found → indicate for bacterial infection)

## Diagnostic approach to subfertility in the man



- ✓ Eugonadal → means the gonads are normal
- ✓ Hyperprolactinaemia in male is very late manifested : he could have prolactinoma (tumor produce prolactin) and this press the optic nerve so the patient suffer from CNS manifestation.
- ✓ Primary testicular failure (totally or only the tubules)

**Primary testicular failure:****Histological differentiation:**

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

**HYPERPROLACTINAEMIA****Prolactin and hyperprolactinaemia:**

**Prolactin** : is an anterior pituitary hormone

**NOTE:** TRH & dopamine are the main regulator for prolactin secretion.

**Its secretion is tightly regulated:**

- ✓ stimulated by TRH (Thyrotropin-releasing hormone) from the hypothalamus
- ✓ inhibited by dopamine from hypothalamus .

It acts directly on the mammary glands to control lactation

**HYPERPROLACTINAEMIA**

- ✓ It is elevated circulating [Prolactin]
- ✓ It is a common condition
- ✓ It causes infertility in both sexes due to gonadal function impairment.
- ✓ Early indication of hyperprolactinaemia:
  - In women: amenorrhoea & galactorrhoea
  - In men: none

**NOTE:** No early indication for hyperprolactinemia in male clinically ( ask for blood sample of prolactin)

Causes of hyperprolactinaemia:

- ✓ Stress
- ✓ Drugs  
(e.g. oestrogens, phenothiazines, metoclopramide,  $\alpha$ -methyl dopa )
- ✓ Seizures ( convulsion  $\rightarrow$  stress  $\rightarrow$   $\uparrow$  prolactin)
- ✓ 1<sup>ary</sup> hypothyroidism (prolactin is stimulated by the raised TRH)
- ✓ Other pituitary disease
- ✓ Prolactinoma ( a tumor produces prolactin ) (commonly microadenoma) –in pituitary-
- ✓ Idiopathic hypersecretion (e.g. due to impaired secretion of dopamine that usually inhibits prolactin release.

Diagnosis of the cause of hyperprolactinaemia:

- Exclude:
  1. Stress
  2. Drugs
  3. Other disease
- Differential diagnosis:
  1. prolactinoma or
  2. idiopathic hypersecretion:
- Detailed pituitary imaging (MRI)
- Dynamic tests of Prolactin secretion:
- Administration of TRH, then measure serum [prolactin]:
  1. if  $\uparrow$ : idiopathic hyperprolactinaemia,
  2. If no rise: pituitary tumor



**Take home message:**

- Abnormal menstruation & infertility in women can arise from disease of the hypothalamus, pituitary, ovary, adrenal or thyroid.
- In female, if there is a regular ovulating menstrual cycle, serum [progesterone] measured in the middle of the luteal phase (day 21) should be  $>30\text{nmol/L}$
- If serum [progesterone] measured in the middle of the luteal phase (day 21)  $<10\text{nmol/L}$ : ovulation has not occurred
- Endocrine causes of infertility in the male are rare
- In both male and female a serum [FSH]  $>25\text{U/L}$  indicates 1ary gonadal failure
- Hyperprolactinaemia is a rare cause of male infertility (common in female)

**Small revision :**

1. What are the methods you can perform to check for infertility
  - a. Clinical history
  - b. Physical examination
  - c. Endocrine investigations in male and female
2. What is infertility?
  - a. Failure of a couple to conceive after one year of regular, unprotected intercourse
  - b. Diagnoses must be established after waiting for a year
3. Most common cause of infertility in females
  - a. Hormonal or endocrine
4. Hormonal or endocrine are more common cause of infertility in males or females
  - a. Females
5. What is the most important test to check for male infertility?
  - a. Sperm analysis (volume, sperm density, motility, presence of abnormal spermatozoa)
  - b. Because hormonal is rare in men
6. What is the most important test to check for female infertility
  - a. Endocrine or hormonal investigations
7. What is the hormone that is measured to indicate ovulation?
  - a. progesterone
8. How do you confirm ovulation?
  - a. Progesterone levels of  $>30$  nmol/L (indicates ovulation)
  - b.  $<10$  nmol/L (no ovulation)
9. How can obesity contribute to female infertility?
  - a. By causing excessive androgen secretion from the ovaries
10. What can cause gonadal failure?
  - a. Post menopausal pattern ( high gonadotropins , low estradiol ) ; this means the patient has extra levels of LH/FSH and low levels of estrogen but is she hasn't menopause ( like when giving hormone replacement therapy)
  - b. Elevated levels of prolactin. How? prolactin inhibits the release of gonadotropins thus lowering gonadal function
11. What is the first step in checking for male infertility?
  - a. Sperm analysis
    - i. If normal , no need for endocrine investigation

Serum FSH level of  $>25$  U/L indicates primary gonadal failure in both men and women