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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

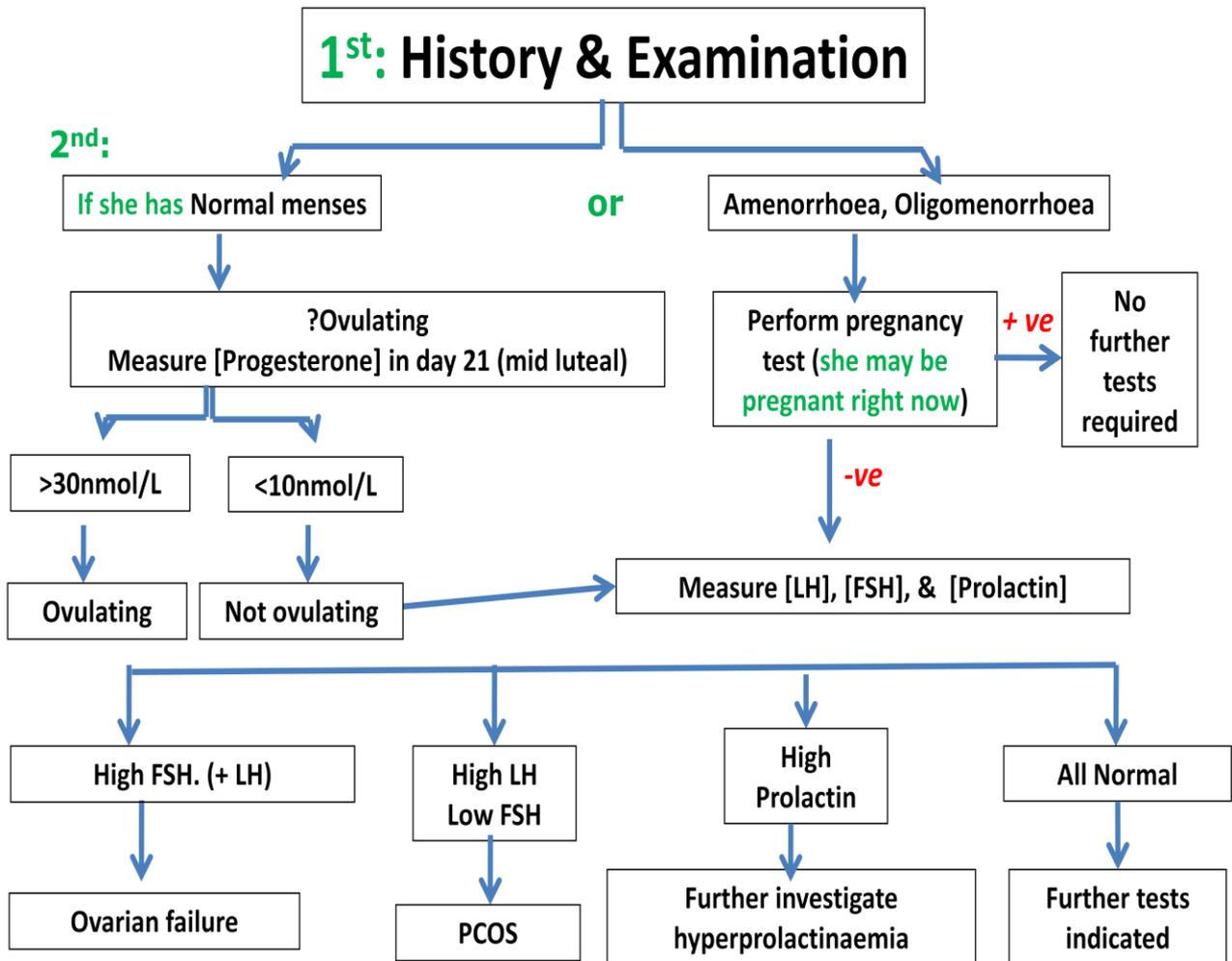
**We will take about :**

- ✓ 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 because 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- )

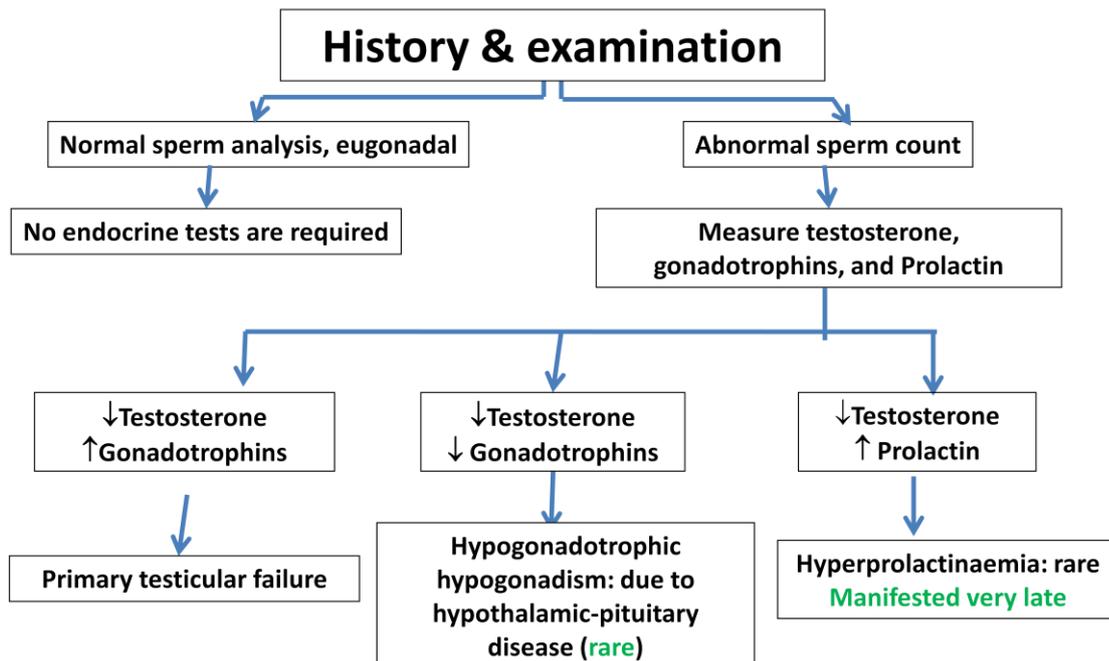
**INVESTIGATION OF MALE INFERTILITY:****Semen Analysis:**

(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

**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

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

**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 & galctorrhoea
  - 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