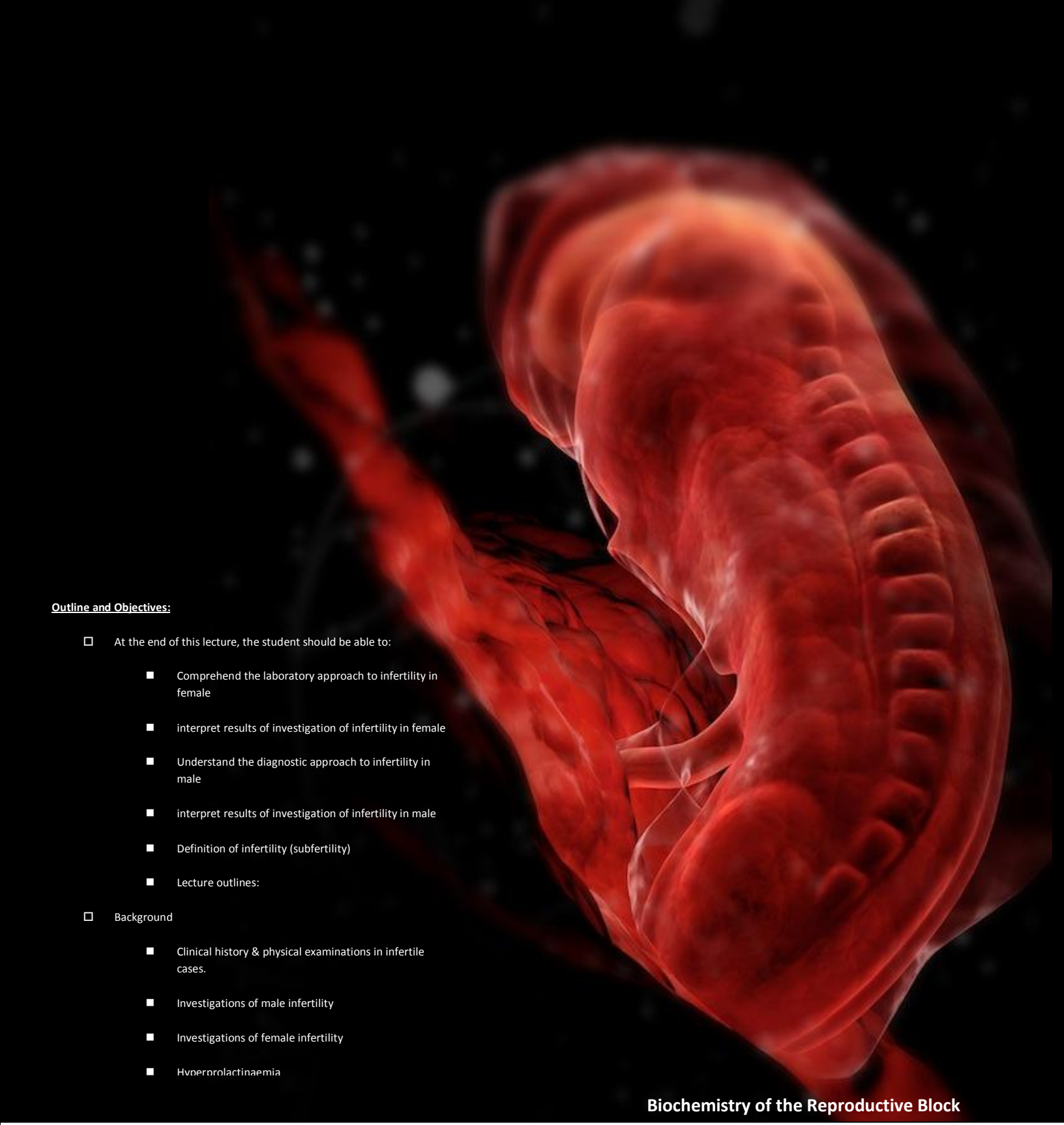

Outline and Objectives:

- At the end of this lecture, the student should be able to:
  - Comprehend the laboratory approach to infertility in female
  - interpret results of investigation of infertility in female
  - Understand the diagnostic approach to infertility in male
  - interpret results of investigation of infertility in male
  - Definition of infertility (subfertility)
  - Lecture outlines:
- Background
  - Clinical history & physical examinations in infertile cases.
  - Investigations of male infertility
  - Investigations of female infertility
  - Hyperprolactinaemia

Biochemistry of the Reproductive Block

Investigations of infertility

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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***

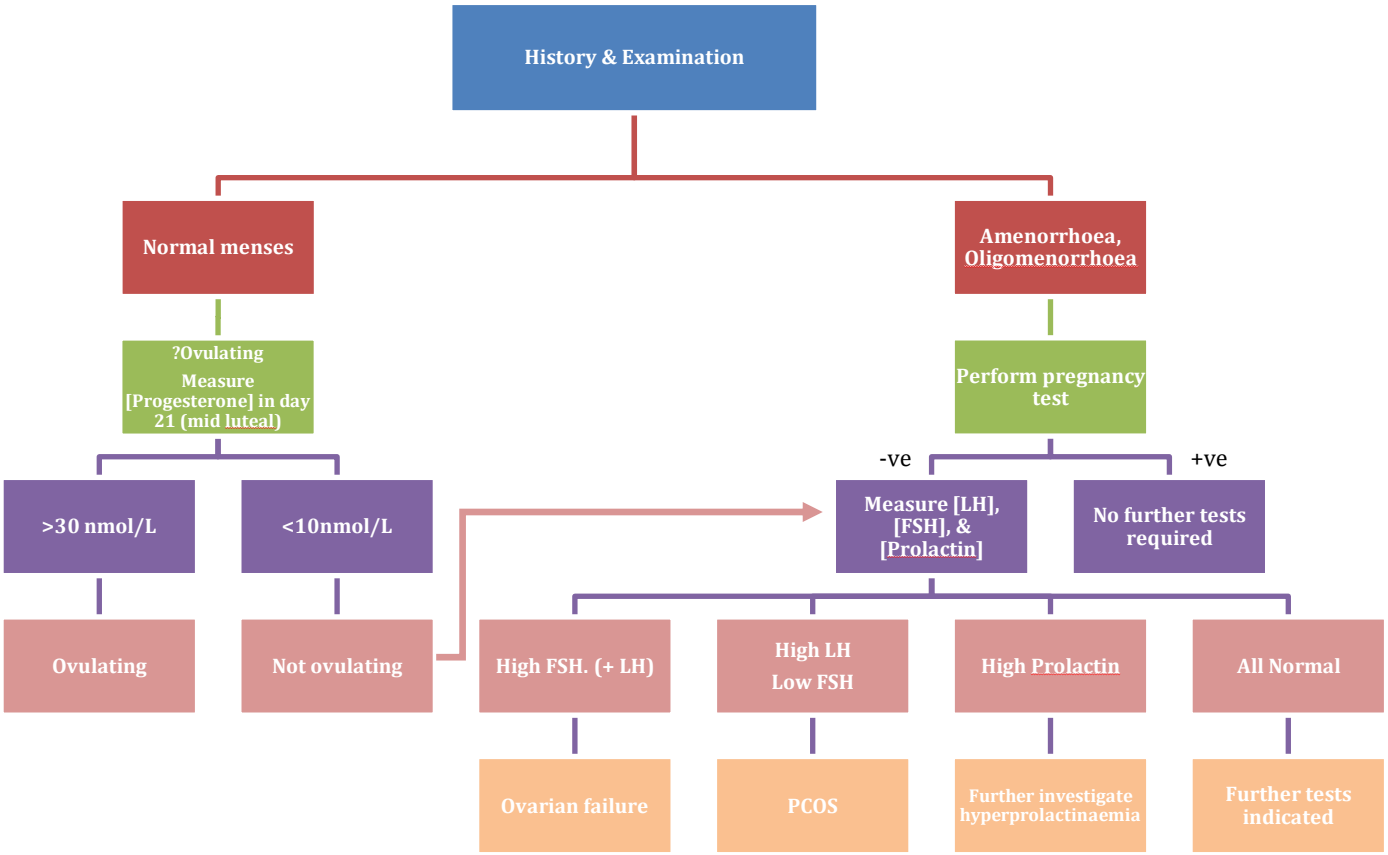
Clinical History taking:

- Should be **full** clinical history
- **Before** physical examinations
- Information about:
  - Previous pregnancies
  - Contraceptive practice
  - Serious illnesses
  - Past chemotherapy or radiotherapy
  - Congenital abnormalities
  - Smoking habits
  - Drug usage
  - STD
  - Frequency of intercourse

Physical Examination

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

INVESTIGATION OF FEMALE INFERTILITY - Diagnostic approach to infertility in the woman



Presence of menstrual cycle (normal menses) doesn't mean that there is ovulation – (ova comes out from graafian follicle at certain time , goes to fallopian tube & gets ready to be fertilized-) However, even when the woman has normal menses we should confirm if the ovulation is normal or not by measuring the progesterone.

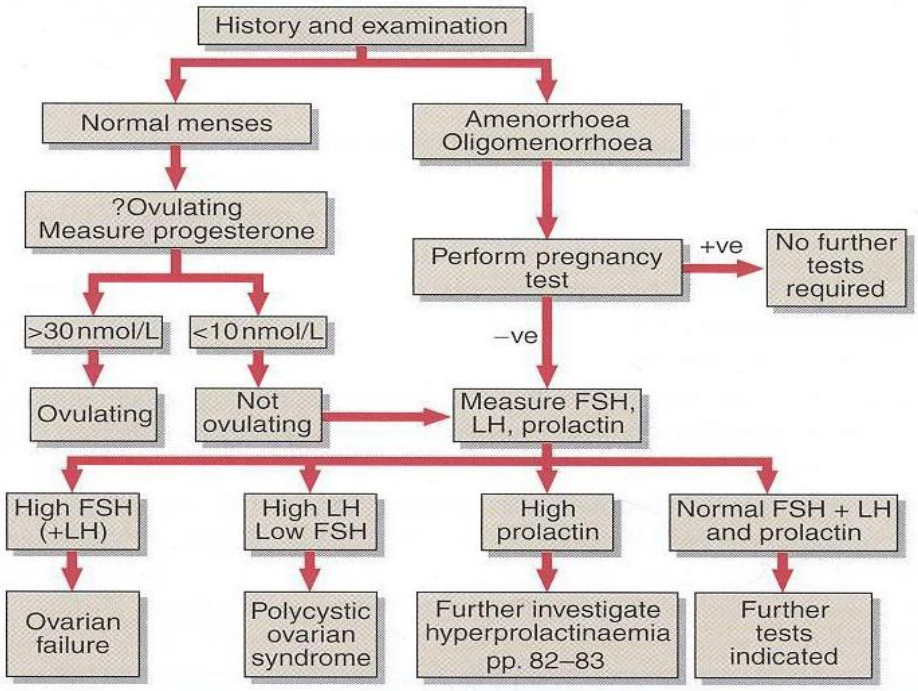


Fig. 1 **Diagnostic approach to subfertility in the woman.**

Endocrine causes of infertility in women

- ☐ **↑ ovarian androgen secretion:**
    - e.g.: obesity → Insulin resistance → ↑ ovarian androgen secretion)

  Obesity and Insulin resistance have a risk factor of sub-fertility, due to the increased production of androgen as Cushing's syndrome.

- ☐ **Primary ovarian failure**:
    - Postmenoposal hormonal pattern: (↑ gonadotrophins & ↓ oestradiol)

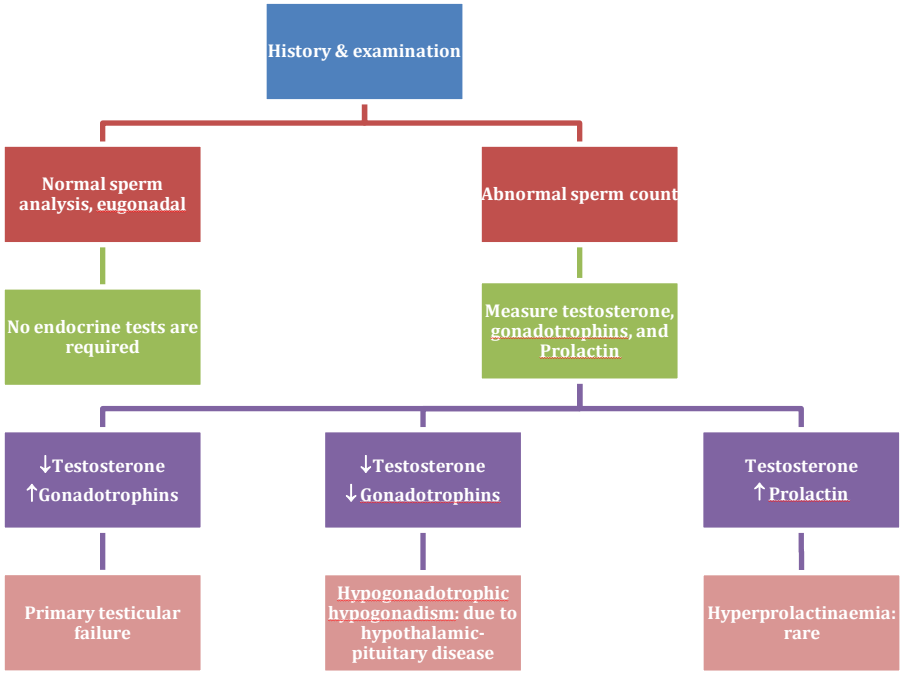
  She is not postmenopausal lady but her profile of hormones resembles post-menopausal women.
    - Hormone replacement therapy can be given (this will not treat the infertility
- ❑ **Hyperprolactinaemia**
- ❑ **PCOS:**
    - ↑ serum [LH]
    - Normal (or low) [FSH]
- ❑ **Cushing's syndrome**
- ❑ **Hypogonadotrophic hypogonadism:**
    - 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)

INVESTIGATION OF MALE INFERTILITY - Diagnostic approach to subfertility in the man



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

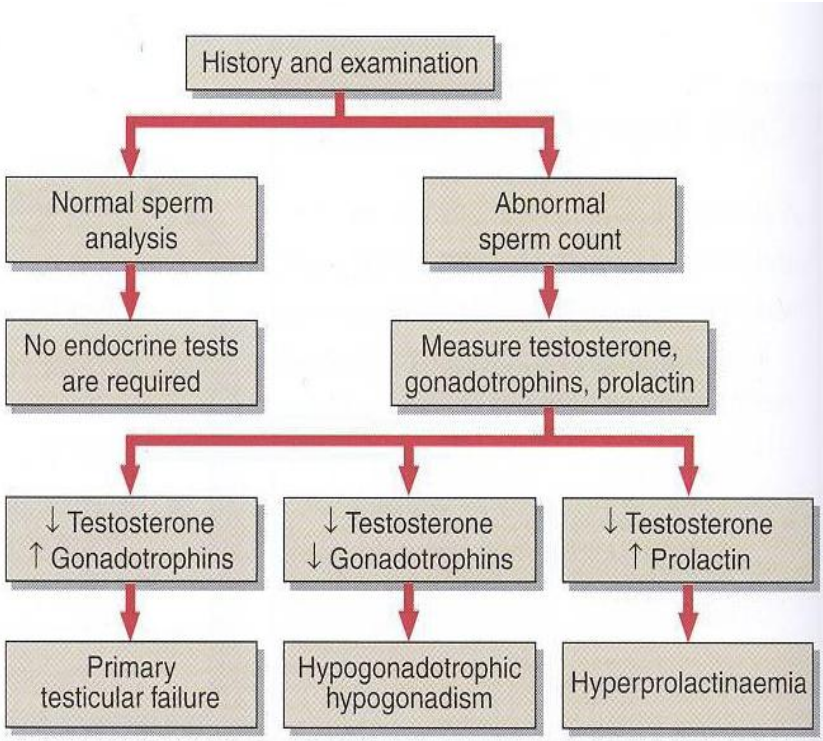


Fig. 2 **Diagnostic approach to subfertility in the man.**

- **Semen Analysis**
    - Comment on:
        - Volume
        - Liquefaction time
        - sperm density (count)
        - Motility
        - the presence of abnormal spermatozoa (abnormal shape, or motility)
        - pH
        - WBCs?

    Normally WBCs are absent. If WBCs were found → bacterial infection.

- **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

HYPERPROLACTINAEMIA: Prolactin and hyperprolactinaemia

Prolactin is an anterior pituitary hormone

Its secretion is tightly regulated:

- Stimulated by TRH from the hypothalamus

- Inhibited by dopamine from hypothalamus

It acts directly on the mammary glands to control lactation

Hyperprolactinaemia is elevated circulating [Prolactin]

- A common condition
- It causes infertility in both sexes due to gonadal function impairment.

What is the early indication of hyperprolactinaemia?

- In women: amenorrhoea & galactorrhoea

- In men: none

Causes of hyperprolactinaemia

- Stress
- Drugs
- e.g. oestrogens, phenothiazines, metoclopramide, α-methyl dopa
- Seizures
- 1^{ary} hypothyroidism (prolactin is stimulated by the raised TRH)

- Other pituitary disease
- Prolactinoma (commonly microadenoma)
- Idiopathic hypersecretion (e.g. due to imparied secretion of dopamine that usually inhibits prolactin release)

If these are excluded, These are the differential diagnosis..

Diagnosis of the cause of hyperprolactinaemia

- ☐ Exclude:
  - Stress
  - Drugs
  - Other disease
- ☐ Differential diagnosis:
  - prolactinoma or
  - 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 hyperprolactinaemia
    - If no rise: pituitary tumor.

Summary

- 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 >30nmol/L
- If serum [progesterone] measured in the middle of the luteal phase (day 21) <10nmol/L: ovulation has not occurred
- Endocrine causes of infertility in the male are rare
- In both male and female Infertility, a serum [FSH] >25U/L indicates 1^{ary} gonadal failure
- Hyperprolactinaemia is a rare cause of male infertility