Investigating infertile couple

Reproduction System Block

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Objectives

By the end of this lecture, the Second Year students should be able to:

- 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

Overview

- Infertility / subfertility
- Clinical history and physical examination
- Endocrine investigations in subfertile women
- Endocrine causes of female infertility
- Endocrine investigations in subfertile men
- Diagnostic approaches to subfertility in women and men
- Hyperprolactinemia

Infertility / subfertility

- Failure of a couple to conceive after one year of regular, unprotected intercourse

Infertility / subfertility

- Infertility may be caused by endocrine problems:
  - Common in females (1/3rd patients)
  - Rare in males
- Hormone dysfunction is a rare cause of male infertility
- In some couples no cause can be identified

Clinical history taking

Information on clinical history of the patient should include:

- Previous pregnancies
- Use of contraceptives
- Serious illness
- Past Chemo / radiotherapy
- Congenital abnormalities
- Drug usage
- Sexually transmitted disease
- Frequency of intercourse

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

Endocrine investigations in subfertile woman

- Investigations are based on the phase of menstrual cycle
- Serum progesterone should be measured in the middle of the luteal phase (day 21)
- High progesterone (>30 nmol/L) indicates ovulation
- In oligomenorrhea or amenorrhea, hormone measurement is needed

Endocrine causes of female infertility

- Excessive secretion of ovarian androgens:
  - Obesity
  - Insulin resistance
- Primary ovarian failure:
  - High gonadotrophins, low oestradiol (postmenopausal hormonal pattern)
  - Hormone replacement therapy can be given (will not treat infertility)
- Hyperprolactinemia
- PCOS
- Cushing's syndrome
- Hypogonadotrophic hypogonadism
  - Low gonadotrophin/oestradiol
  - Rare
  - Due to hypothalamic-pituitary lesion

Investigation of female infertility

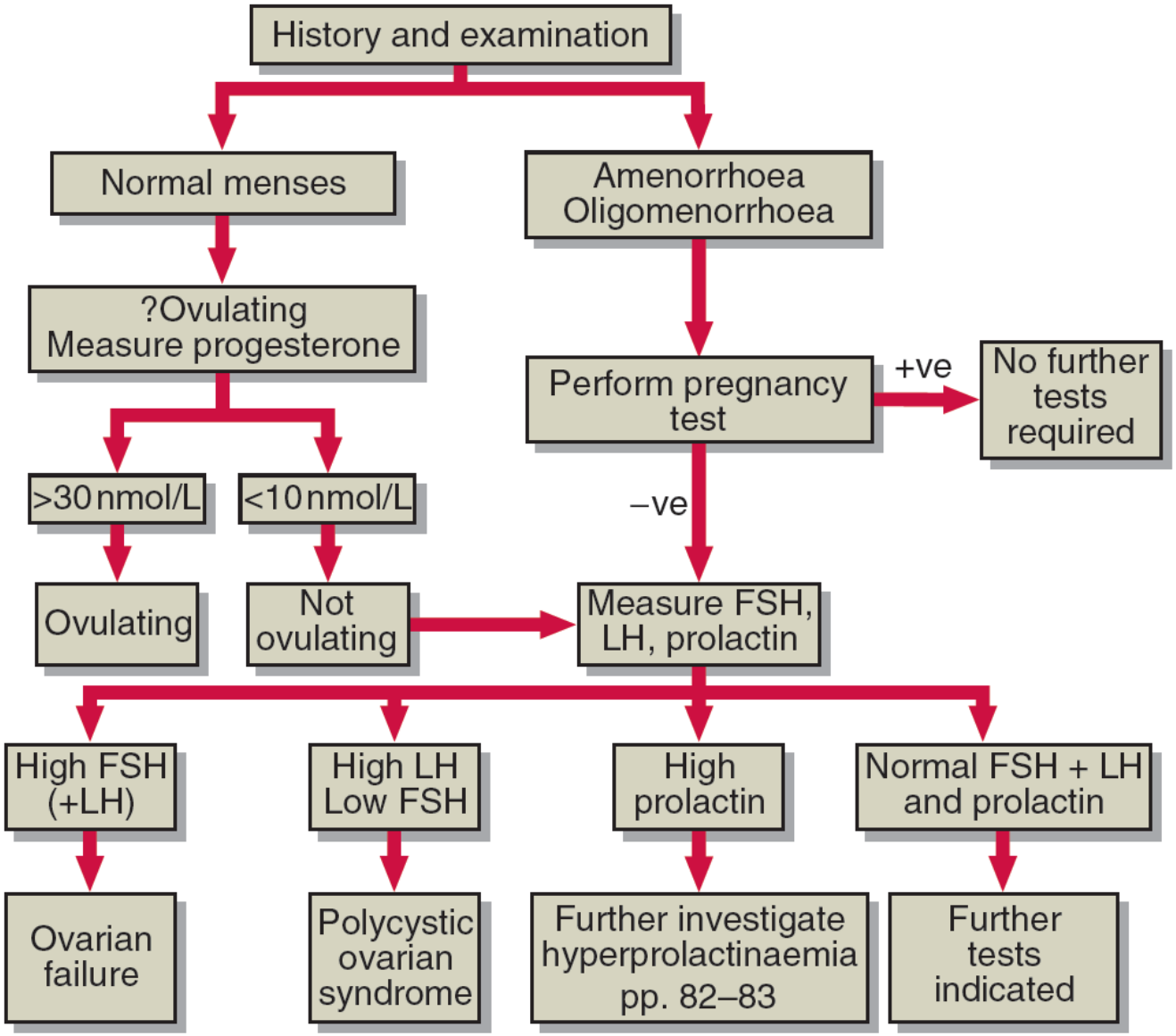


Fig 51.1 **Diagnostic approach to subfertility in the woman.**

Anti-Mullerian hormone (AMH)

- A polypeptide hormone called Mullerian-inhibiting substance
- Secreted by growing ovarian follicles
- Secretion is proportional to follicular development
- Helps assess ovarian reserve and female fertility
- Ovarian reserve: number and quality of oocytes in the ovaries

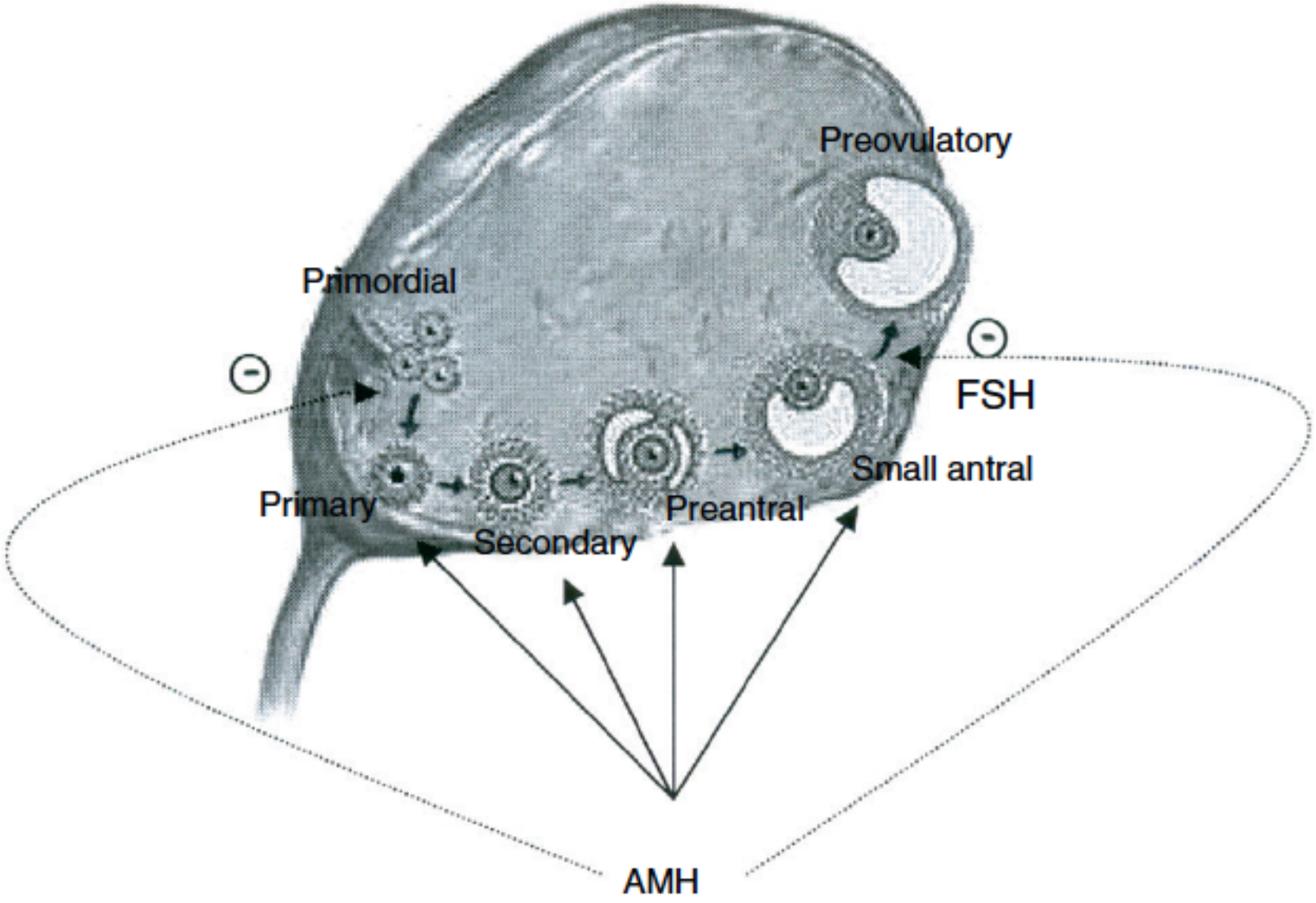
Anti-Mullerian hormone (AMH)

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



Endocrine investigations in subfertile man

- Eugonadal men with normal sperm analysis do not require endocrine investigations
- Endocrine cause of infertility in men are rare
- In hypogonadal men:
  - Testosterone
  - Gonadotrophins should be measured

Semen analysis

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

Endocrine investigations in subfertile men

- Primary testicular failure due to:
  - Damage in the testes (interstitial, tubular)
  - Low levels of testosterone
- Hypothalamic-pituitary disease:
  - Decreased testosterone with low/normal gonadotrophins
  - Suggests hypogonadotrophic hypogonadism
- Hyperprolactinemia (a rare cause in men)

Investigation of male infertility

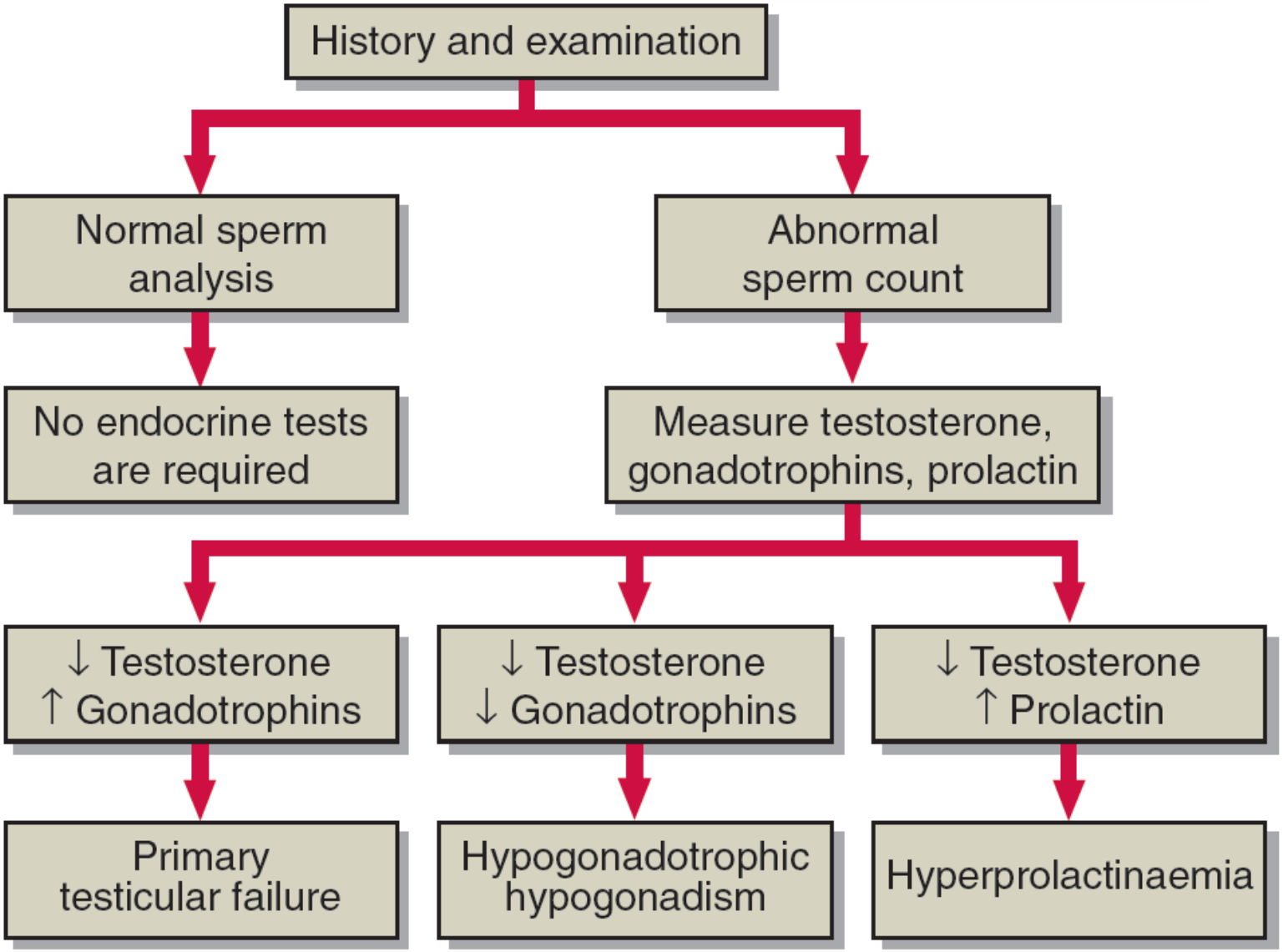


Fig 51.2 **Diagnostic approach to subfertility in the man.**

Hyperprolactinemia

- 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

Hyperprolactinemia

Elevated circulating prolactin

- Causes infertility in both sexes due to gonadal function impairment
- Early indication
  - In women: amenorrhea and galactorrhea
  - In men: none

Causes of hyperprolactinemia

- Stress
- Drugs (estrogens, phenothiazines, metoclopramide, α-methyl dopa)
- Seizures
- Primary hypothyroidism (prolactin is stimulated by raised TRH)
- Other pituitary disease
- Prolactinoma
- Idiopathic hypersecretion (e.g. due to impaired secretion of dopamine that usually inhibits prolactin release)

Diagnosis of hyperprolactinemia

Exclude:

- Stress
- Drugs
- Other disease

Differential diagnosis:

- Prolactinoma
- Idiopathic hypersecretion

Take home message

- Endocrine causes of infertility are more common in women than men
- In women serum progesterone >30nmol/L indicates ovulation
- Hyperprolactinemia is a rare cause of male infertility

References

- Clinical Biochemistry: An Illustrated Colour Text by Allan Gaw, 5th Edition, pp 102 and 84, Churchill Livingstone, UK

- Gasparin, AA et al. Anti-müllerian hormone levels as a predictor of ovarian reserve in systemic lupus erythematosus patients: a review. *Rev. Brasil. Reumatol*. 2015; 55: 363-367