
Investigations of infertility

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OBJECTIVES

- At the end of this lecture, the student should be able to:
 - 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
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Lecture outlines

- Definition of infertility (subfertility)
 - Background
 - Clinical history & physical examinations in infertile cases.
 - Investigations of male infertility
 - Investigations of female infertility
 - Hyperprolactinaemia
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Infertility

□ Definition:

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

Background

- 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
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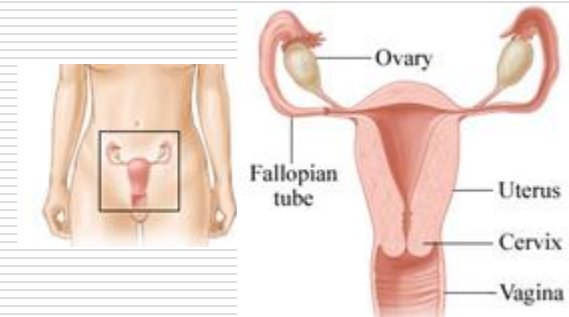
Clinical History taking

- 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
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Physical Examination

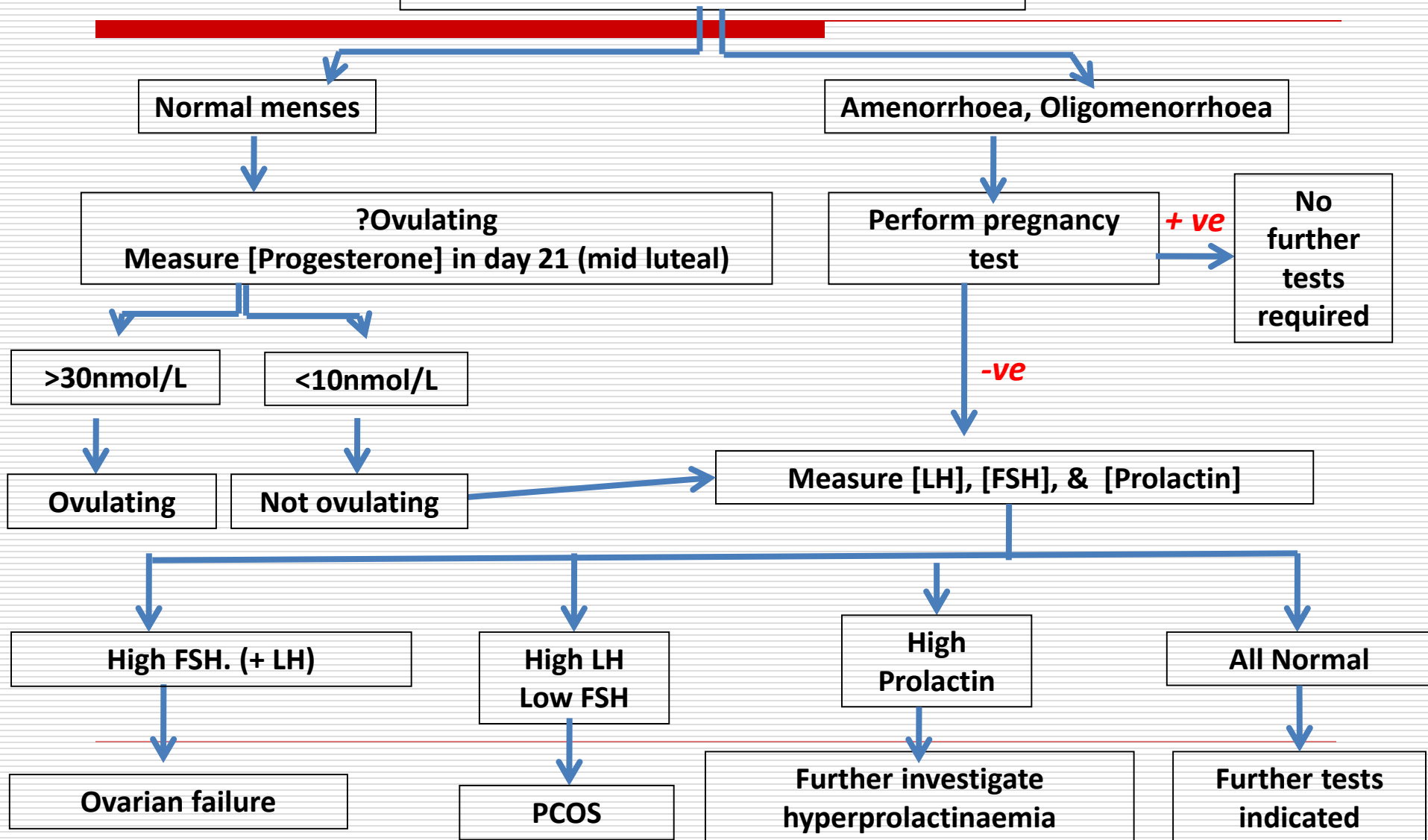
- Should look for indications of:
 - Hypothalamic-pituitary or thyroid disorders
 - Cushing's syndrome
 - Galactorrhoea (*inappropriate breast milk production; i.e. in the absence of pregnancy most commonly caused by hyperprolactinaemia*)
 - Hirsutism (*an increase in body hair with male pattern distribution*)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



Diagnostic approach to infertility in the woman

History & Examination



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)
- Hormone replacement therapy can be given (this will not treat the infertility)

□ Hyperprolactinaemia

□ PCOS:

- ↑ serum [LH]
- Normal (or low) [FSH]

□ Cushing's syndrome

□ Hypogonadotropic hypogonadism:

- Rare
- due to hypothalamic-pituitary lesion

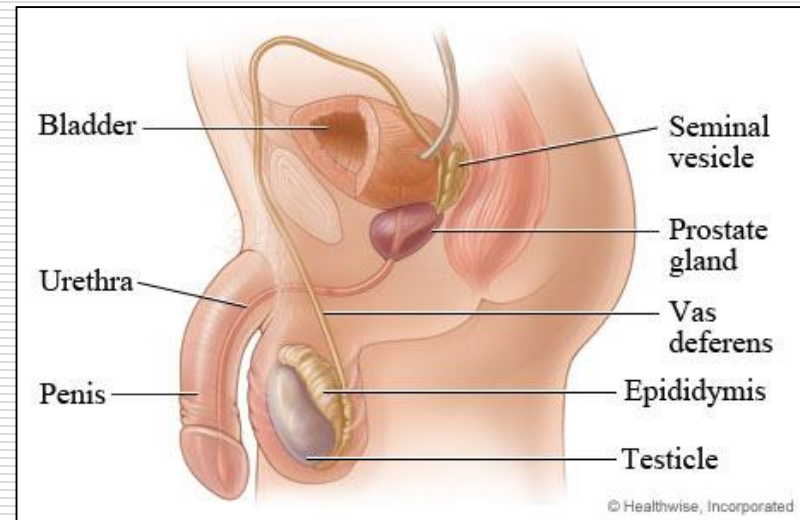
Diagnosis of PCOS*

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)

*PCOS Consensus Workshop Group. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*. Jan 2004;81(1):19-25

INVESTIGATION OF MALE INFERTILITY



Diagnostic approach to subfertility in the man

History & examination

Normal sperm analysis, eugonadal

Abnormal sperm count

No endocrine tests are required

Measure testosterone, gonadotrophins, and Prolactin

↓ Testosterone
↑ Gonadotrophins

↓ Testosterone
↓ Gonadotrophins

↓ Testosterone
↑ Prolactin

Primary testicular failure

Hypogonadotropic hypogonadism: due to hypothalamic-pituitary disease

Hyperprolactinaemia: rare

Semen Analysis

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



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
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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

Prolactin and hyperprolactinaemia, *continued..*

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
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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 impaired secretion of dopamine that usually inhibits prolactin release)
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Causes of hyperprolactinaemia

If these are excluded..

Other pituitary disease

These are the differential diagnosis..

Diagnosis of the cause of hyperprolactinaemia

Exclude:

- Stress
- Drugs
- Other disease

Differential diagnosis:

- prolactinoma or
 - idiopathic hypersecretion
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Diagnosis of the cause of hyperprolactinaemia

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
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AntMullerian hormone (AMH)

- AntMullerian hormone blood levels are often used by fertility specialists as part of the evaluation of **ovarian reserve**
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Anti-Mullerian hormone (AMH)

- ❑ 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
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Ovarian reserve

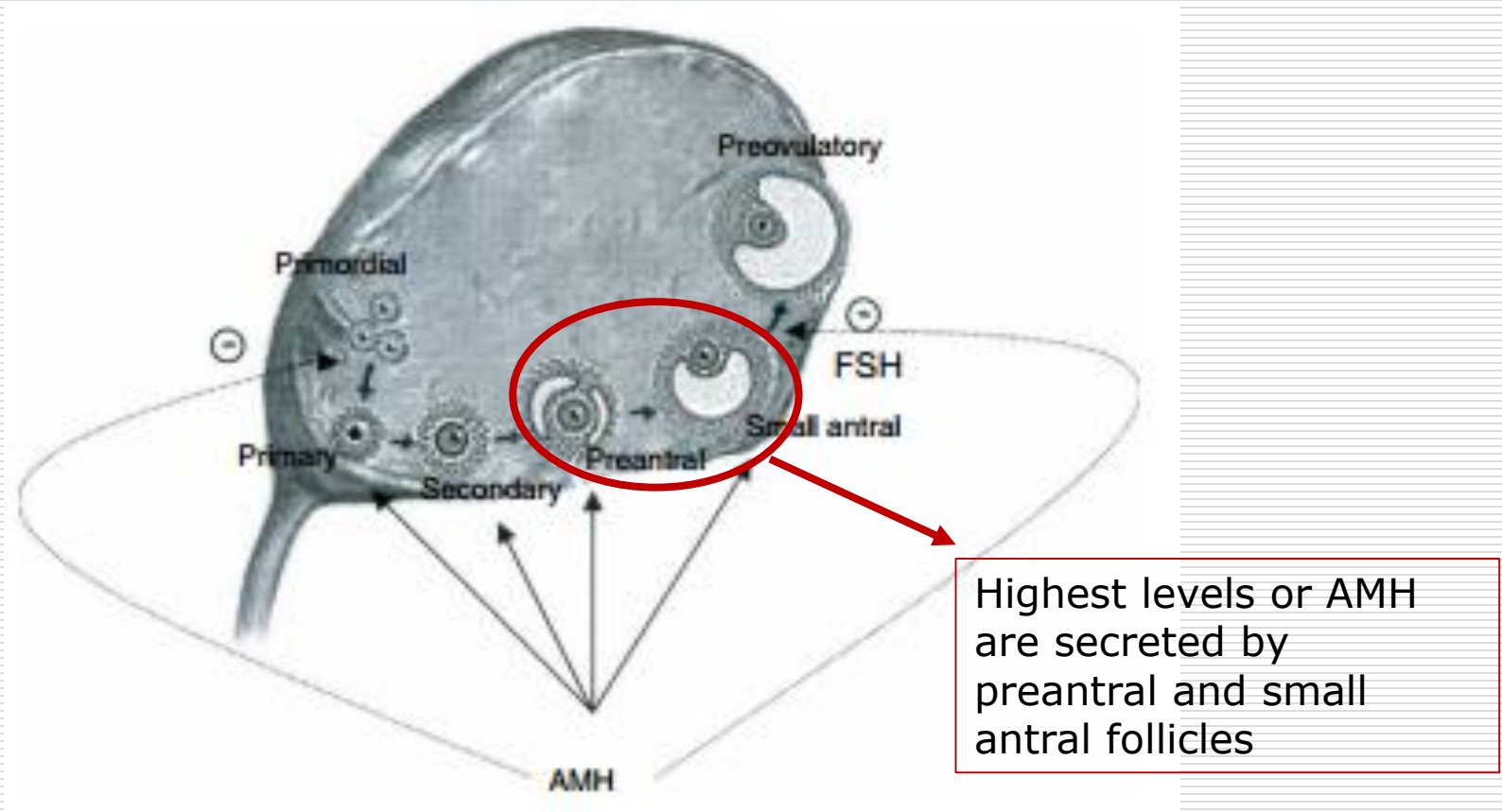
Ovarian reserve: number and quality of oocytes in the ovaries

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
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AMH and Folliculogenesis



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
 - AMH is the best current available measure of ovarian reserve for different clinical conditions.
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Take home message

- Endocrine causes of infertility in the male are rare
 - In both male and female Infertility, a serum [FSH] $>25\text{U/L}$ indicates 1^{ary} gonadal failure
 - Hyperprolactinaemia is a rare cause of male infertility
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References:

- Clinical Biochemistry, An Illustrated Colour Text, Allan Gaw, Churchill Livingstone Elsevier, 2008, pp: 100 & 82
 - Gasparin et al,. Rev Bras Reumatol, 2015. 55:363-367. AMH levels as a predictor of ovarian reserve in SLE patients: a review.
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THANK YOU 😊

