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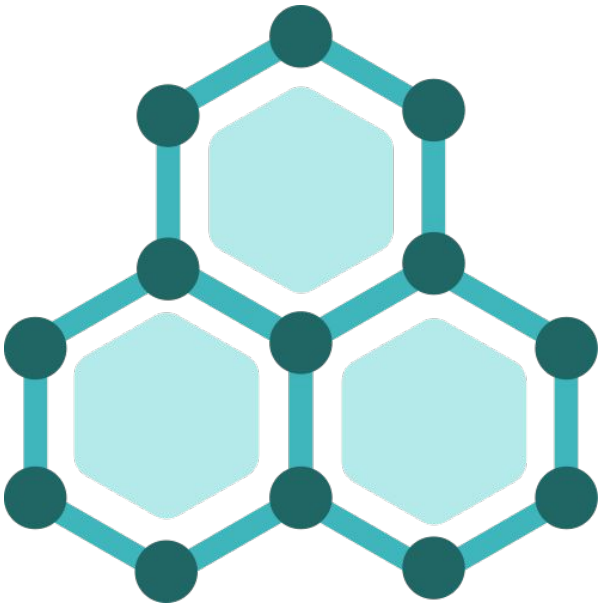
Investigation of infertile couples

Reproductive Block



Objectives

- ***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***

This Lecture was presented by:
Dr.Usman Ghani / Dr.Sumbul

Editing File

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Infertility / Subfertility

Definition

failure of a couple to conceive (get pregnant) after one year of regular, unprotected intercourse (without oral contraceptives).

Female < 35 years → investigations after 1 year
> 35 years → after six months
> 35 + risk factors (family history..) → start investigations right away

Causes:

- May be caused by **endocrine problems**:
  - ➔ **Females**: common (1/3rd of patients).
  - ➔ **Males**: rare, rarely caused by hormone dysfunction.
- In some couples **no cause** can be identified.

Clinical History Taking	Physical Examination
Previous pregnancies - 1ry or 2ry infertility?	Hypothalamo-pituitary disorders
Use of contraceptives - Fertility ↓ for several months after stopping them	Cushing syndrome - Check BMI & central obesity - Related more to women infertility
Serious illness	Thyroid disorders
Past chemo / radiotherapy - Affect number of oocytes	Hirsutism, acne (PCOS)
Congenital abnormalities	**Galactorrhea** - Lactation in the absence of pregnancy - Most common due to hyperprolactinemia
Drug usage - Affect hormone levels	
Sexually transmitted disease	
Frequency of intercourse	

Endocrine Investigations in subfertile Women

1. Investigations are based on the phase of menstrual cycle.

2. Serum **progesterone** should be measured in the **middle of luteal** phase (**day 21**). 7 days before the end of the cycle, if cycle is 30 days → measure on day 23 for at least 3 cycles then avg. is taken.

3. High **progesterone** (>30 nmol/L) → indicates ovulation. No. 1 investigation If low, then do more investigations

4. When do we need hormone measurement? **oligomenorrhea** or **amenorrhea**. Progesterone will be much lower

5. Endocrine **causes** of female infertility:

➔ ↑ secretion of **ovarian androgens:**
- Obesity
- insulin resistance (diabetes)

➔ **PCOS** (major cause)

➔ **Primary ovarian failure:**
- **Postmenopausal hormonal pattern:** ↑ gonadotropins +↓oestradiol
- Hormone replacement therapy can be given (doesn't treat infertility).

➔ **Hyperprolactinemia**

➔ **Cushing syndrome**

➔ **Hypogonadotropic hypogonadism:**
- **Due to:** hypothalamic- pituitary lesion, Rare
- ↓ gonadotropin / oestradiol. Malnourished female

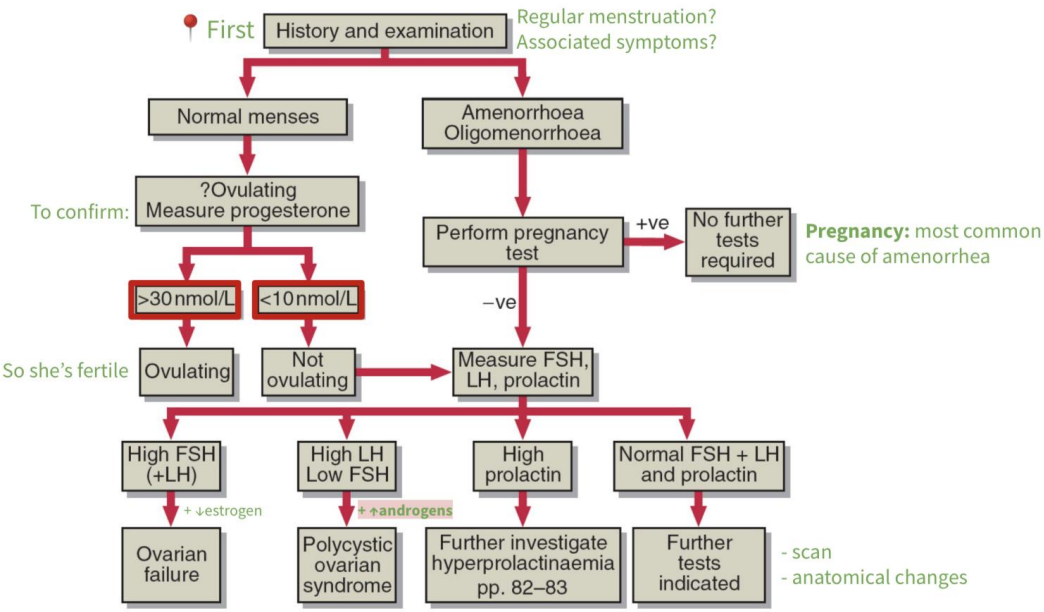


Fig 51.1 **Diagnostic approach to subfertility in the woman.**

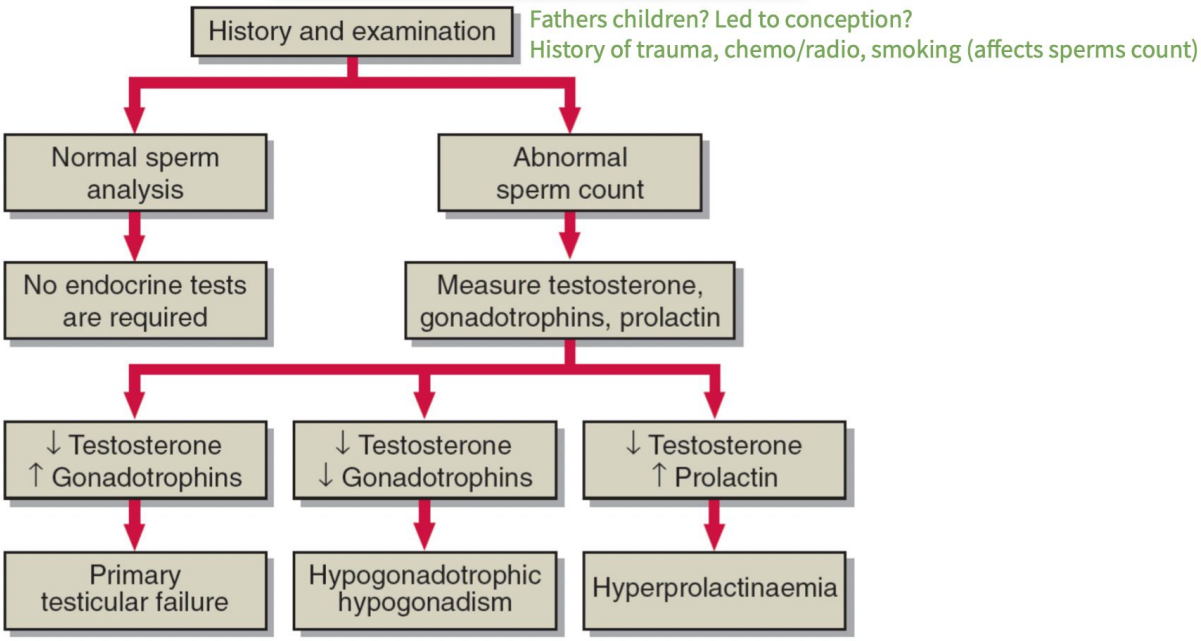
Endocrine Investigations in subfertile Man

1. **Eugonadal** men + **normal sperm analysis** → **no** endocrine investigations.
2. Endocrine causes of infertility in men are rare.
3. In **hypogonadal** men, we should **measure**: **- Testosterone - Gonadotropins**
4. Semen analysis : Volume - liquefaction time - sperm count - motility - presence of abnormal spermatozoa, PH - WBCs .
5. Endocrine investigations in **subfertile** men:

➔ **Primary testicular Failure:**
- Due to damage in the testes (Interstitial ,tubular)
- **low testosterone + high gonadotropins**

➔ **Hyperprolactinemia** (a **rare** cause in men)

➔ **Hypothalamic-pituitary Disease:**
- **Decreased testosterone** with **low/normal gonadotropins**
- suggests **hypogonadotropic hypogonadism**



Anti Mullerian Hormone (AMH)

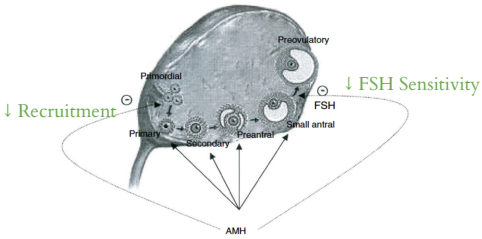
Definition	Secreted by	Asses
◎ A polypeptide hormone called **Mullerian- inhibiting substance.**	◎ **growing** ovarian **follicles,** Secretion is proportional to **follicular development.**	◎ **ovarian reserve** and female **fertility.** ◎ **Ovarian reserve:** number and quality of oocytes in the ovaries.

In the ovary, it inhibits the:

1. Initial recruitment of primary follicles from primordial follicles.
2. Sensitivity of antral follicles to FSH during cyclical recruitment.
3. premature depletion of follicles. (So it delays menopause)

The number of **remaining primordial follicles** correlate with the number of **growing follicles.**

Since only growing follicles produce AMH → **AMH** plasma levels reflect the number of **remaining primordial follicles.**



AMH and folliculogenesis

Hyperprolactinemia

Hormone affected	**Prolactin,** an anterior pituitary hormone.
Regulation of Prolactin	**Stimulated** by **TRH** from hypothalamus. **Inhibited** by **dopamine** from hypothalamus.
Target	Acts directly on the mammary glands to **control lactation.**
Abnormal secretion	↑ **prolactin** → gonadal function impairment → **infertility** in both sexes.
Early indication	**Women:** amenorrhea and galactorrhea. **Men:** none
Diagnosis	**Diagnosis: exclude** stress, drugs, other diseases, **Differential diagnosis: Prolactinoma , Idiopathic hypersecretion**
Causes	1. Stress 2. Prolactinoma 3. Other **pituitary disease** **4. Seizures** **5. Primary hypothyroidism:** prolactin is stimulated by TRH 6. **Drugs** : Estrogens, Phenothiazines, Metoclopramide, α-methyl dopa 7. **Idiopathic hypersecretion:** impaired secretion of dopamine (usually inhibits prolactin release).

Take Home Messages

Endocrine causes of infertility are more common in women than men

In women serum progesterone >30 nmol/L indicates ovulation

Hyperprolactinemia is a rare cause of male infertility

MCQs

Q1. Which one of the following would you measure first in a 27 year old woman with regular menses and is unable to conceive for a year?			
A. Prolactin	B. FSH	C. LH	D. Progesterone
Q2. Which one of the following indicates primary ovarian failure?			
A. Low FSH, LH & Estradiol	B. Elevated FSH, LH & Estradiol	C. Low FSH, LH & Elevated Estradiol	D. Elevated FSH,LH & Low Estradiol
Q3. Which one of the following hormones is most appropriate in determining female infertility in terms of ovarian follicle quality and reserve?			
A. FSH	B. Anti-Mullerian hormone	C. LH	D. CA-125
Q4. Which one of the following indicates ovulation in females with regular menstruation?			
A. High Progesterone levels on day 21 >30 nmol/l	B. High Progesterone levels on day 2 >30 nmol/l	C. Low Progesterone levels on day 21 >30 nmol/l	D. Low Progesterone levels on day 2 >30 nmol/l
Q5. Which one of the following does not cause women infertility?			
A. Hypogonadotropic Hypogonadism	B. Hypoprolactinemia	C. Cushing's Syndrome	D. Polycystic Ovary Syndrome
Q6. Which of the following drugs could cause Hyperprolactinemia?			
A.Bromocriptine	B. Cabergoline	C. Metoclopramide	D. Cycloset

A1. D A2. D A3. B A4. A A5. B A6. C

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