

2- Investigating Infertile Couple

Infertility / subfertility

Overview	<ul style="list-style-type: none"> Failure of a couple to conceive after one year of regular unprotected intercourse Infertility may be caused by endocrine problems. Hormone dysfunction is common in females (1/3rd patients), but is a rare cause of infertility in males In some couples, no cause can be identified 	
the diagnostic approaches to infertility		
1- Clinical history	Previous pregnancies - Use of contraceptives - Serious illness - Past Chemo / radiotherapy – Congenital abnormalities - Drug usage - Sexually transmitted disease - Frequency of intercourse	
2- Physical examination	Hypothalamopituitary disorders, thyroid disorders - Cushing's syndrome - Hirsutism - Galactorrhea (Lactation in the absence of pregnancy, Most commonly due to hyperprolactinemia)	
3- Endocrine investigations		
Endocrine investigations	Sub-fertile woman	Sub-fertile man
	Investigations are based on the phase of menstrual cycle: <ol style="list-style-type: none"> If menses is normal → Serum progesterone should be measured in the middle of the luteal phase (day 21): <ul style="list-style-type: none"> High progesterone (>30 nmol/L) = ovulation. low progesterone (< 10 nmol/L) = anovulation. In oligomenorrhea or amenorrhea, perform pregnancy test: <ul style="list-style-type: none"> Positive result = no further testing is required Negative result = hormone measurement is needed <p>In these cases, (not ovulating in normal menses or –ve pregnancy test in oligomenorrhea/ amenorrhea), Measure FSH, LH and prolactin:</p> <ul style="list-style-type: none"> ↑ FSH & ↑ LH = ovarian failure ↑ LH & ↓ FSH = PCOS ↑ prolactin = further investigate hyperprolactinemia (coming later) Normal hormones = further testing. 	Based on Semen analysis: <ul style="list-style-type: none"> Volume - Liquefaction time - Sperm count – Motility - Presence of abnormal spermatozoa – pH – WBCs. <ol style="list-style-type: none"> Eugonadal men with normal sperm analysis do not require endocrine investigations, as endocrine cause of infertility in men are rare. In hypogonadal¹ men with abnormal sperm count, Measure Testosterone, Gonadotrophins, and prolactin: <ul style="list-style-type: none"> ↓ Testosterone & ↑ Gonadotrophins = primary testicular failure ↓ Testosterone & ↓ Gonadotrophins = hypogonadotropic hypogonadism ↓ Testosterone & ↑ prolactin = hyperprolactinemia.

¹ **Male hypogonadism** is a condition in which the body doesn't produce enough testosterone or has an impaired ability to produce sperm or both.

Causes	<ul style="list-style-type: none"> • Primary ovarian failure: <ul style="list-style-type: none"> ○ High gonadotrophins, low oestradiol (postmenopausal hormonal pattern) ○ Hormone replacement therapy can be given, but will not treat infertility. • Hypogonadotropic hypogonadism (Rare): <ul style="list-style-type: none"> ○ Low gonadotrophin/oestradiol, ○ Due to hypothalamic-pituitary lesion • Excessive secretion of ovarian androgens: Obesity & Insulin resistance • Hyperprolactinemia, PCOS, and Cushing's syndrome 	<ul style="list-style-type: none"> • Primary testicular failure due to: <ul style="list-style-type: none"> ○ Damage in the testes (interstitial, tubular) ○ Low levels of testosterone • Hypothalamic-pituitary disease: <ul style="list-style-type: none"> ○ Decreased testosterone with low/normal gonadotrophins ○ Suggests hypogonadotropic hypogonadism • Hyperprolactinemia (a rare cause in men)
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Anti-Mullerian hormone (AMH)

- A polypeptide hormone called **Mullerian-inhibiting substance**
- Secreted by **growing ovarian follicles**, increasing in proportion to follicular development.
- AMH prevents premature depletion of follicles in the ovary by inhibiting:
 - Initial recruitment of primary follicles from primordial follicles
 - Sensitivity of antral follicles to FSH during cyclical recruitment
- Helps in assessing **ovarian reserve** and female fertility. (Ovarian reserve: number and quality of oocytes in the ovaries):
The no. of remaining primordial follicles correlate with the no. of growing follicles, and Since only growing follicles produce AMH, its plasma levels reflect the number of remaining primordial follicles

Hyperprolactinemia

Overview	<ul style="list-style-type: none"> • Prolactin is an anterior pituitary hormone. It acts directly on the mammary glands to control lactation • Its secretion is tightly regulated: 1) Stimulated by TRH from the hypothalamus, 2) Inhibited by dopamine from hypothalamus <ul style="list-style-type: none"> ○ Elevated circulating levels of prolactin causes Hyperprolactinemia, which causes infertility in both sexes due to gonadal function impairment ○ Its early indication in women includes amenorrhea and galactorrhea, but no early indication is observed in men.
Causes	<p style="text-align: center;">Stress - Drugs (estrogens, phenothiazines, metoclopramide, α-methyl dopa) – Seizures - Primary hypothyroidism (because 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)</p>
Diagnosis	<p style="text-align: center;">Exclude Stress, Drugs, and Other diseases Differential diagnosis: Prolactinoma, Idiopathic hypersecretion</p>

Done by: لولة الصغير

Revised & edited by: شهد العنزي