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15/MHS06/020

**MLS 514**

**ANSWERS**

**QUESTION 1**A

A major [organ](https://en.wikipedia.org/wiki/Organ_%28anatomy%29) of the [endocrine system](https://en.wikipedia.org/wiki/Endocrine_system), the **anterior pituitary** (also called the **adenohypophysis** or **pars anterior**) is the [glandular](https://en.wikipedia.org/wiki/Glandular), [anterior](https://en.wikipedia.org/wiki/Anatomical_terms_of_location#Usage_in_human_anatomy) lobe that together with the [posterior](https://en.wikipedia.org/wiki/Anatomical_terms_of_location#Usage_in_human_anatomy) lobe ([posterior pituitary](https://en.wikipedia.org/wiki/Posterior_pituitary), or the neurohypophysis) makes up the [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland) (hypophysis). The anterior pituitary regulates several [physiological](https://en.wikipedia.org/wiki/Physiological) processes, including [stress](https://en.wikipedia.org/wiki/Stress_%28medicine%29), [growth](https://en.wikipedia.org/wiki/Human_development_%28biology%29), [reproduction](https://en.wikipedia.org/wiki/Reproduction), and [lactation](https://en.wikipedia.org/wiki/Lactation). Proper functioning of the anterior pituitary and of the organs it regulates can often be ascertained via [blood tests](https://en.wikipedia.org/wiki/Blood_test) that measure [hormone](https://en.wikipedia.org/wiki/Hormone) levels.

Hormones secreted by the anterior pituitary are [trophic hormones](https://en.wikipedia.org/wiki/Trophic_hormone) Trophic hormones directly affect growth either as hyperplasia or hypertrophy on the tissue it is stimulating. Tropic hormones are named for their ability to act directly on target tissues or other [endocrine glands](https://en.wikipedia.org/wiki/Endocrine_gland) to release hormones, causing numerous cascading physiological responses.

These tropic hormones include:

[Adrenocorticotropic hormone](https://en.wikipedia.org/wiki/Adrenocorticotropic_hormone), [Thyroid-stimulating hormone](https://en.wikipedia.org/wiki/Thyroid-stimulating_hormone), [Follicle-stimulating hormone](https://en.wikipedia.org/wiki/Follicle-stimulating_hormone), [Luteinizing hormone](https://en.wikipedia.org/wiki/Luteinizing_hormone), [Growth hormone](https://en.wikipedia.org/wiki/Growth_hormone), Melanocyte stimulating hormone and [Prolactin](https://en.wikipedia.org/wiki/Prolactin)

1. **Adrenocorticotropic hormone** (**ACTH**; also **adrenocorticotropin**, **corticotropin**) is a [polypeptide](https://en.wikipedia.org/wiki/Peptide) [tropic hormone](https://en.wikipedia.org/wiki/Tropic_hormone) produced by and secreted by the [anterior pituitary gland](https://en.wikipedia.org/wiki/Anterior_pituitary).[[1]](https://en.wikipedia.org/wiki/Adrenocorticotropic_hormone#cite_note-MortonHall2012-1) It is also used as a [medication and diagnostic agent](https://en.wikipedia.org/wiki/Adrenocorticotropic_hormone_%28medication%29). ACTH is an important component of the [hypothalamic-pituitary-adrenal axis](https://en.wikipedia.org/wiki/Hypothalamic-pituitary-adrenal_axis) and is often produced in response to biological stress (along with its precursor [corticotropin-releasing hormone](https://en.wikipedia.org/wiki/Corticotropin-releasing_hormone) from the [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus)). Its principal effects are increased production and release of [cortisol](https://en.wikipedia.org/wiki/Cortisol) by the [cortex](https://en.wikipedia.org/wiki/Adrenal_cortex) of the [adrenal gland](https://en.wikipedia.org/wiki/Adrenal_gland). ACTH is also related to the [circadian rhythm](https://en.wikipedia.org/wiki/Circadian_rhythm) in many organisms.

**Associated conditions include:** Deficiency of ACTH is a sign of secondary [adrenal insufficiency](https://en.wikipedia.org/wiki/Adrenal_insufficiency) (suppressed production of ACTH due to an impairment of the [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland) or [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus), cf. [hypopituitarism](https://en.wikipedia.org/wiki/Hypopituitarism)) or tertiary adrenal insufficiency (disease of the hypothalamus, with a decrease in the release of [corticotropin releasing hormone (CRH)](https://en.wikipedia.org/wiki/Corticotropin_releasing_hormone)). Conversely, chronically elevated ACTH levels occur in primary adrenal insufficiency (e.g. [Addison's disease](https://en.wikipedia.org/wiki/Addison%27s_disease)) when adrenal gland production of [cortisol](https://en.wikipedia.org/wiki/Cortisol) is chronically deficient. In Cushing's disease a pituitary tumor is the cause of elevated ACTH (from the anterior pituitary) and an excess of cortisol (hypercortisolism) – this constellation of signs and symptoms is known as [Cushing's syndrome](https://en.wikipedia.org/wiki/Cushing%27s_syndrome).

1. **Thyroid-stimulating hormone** (also known as **thyrotropin**, **thyrotropic hormone**, or abbreviated **TSH**) is a [pituitary hormone](https://en.wikipedia.org/wiki/Pituitary_hormone) that stimulates the [thyroid](https://en.wikipedia.org/wiki/Thyroid) gland to produce [thyroxine](https://en.wikipedia.org/wiki/Thyroxine) (T4), and then [triiodothyronine](https://en.wikipedia.org/wiki/Triiodothyronine) (T3) which stimulates the metabolism of almost every tissue in the body. It is a [glycoprotein](https://en.wikipedia.org/wiki/Glycoprotein) hormone produced by [thyrotrope](https://en.wikipedia.org/wiki/Thyrotrope) cells in the [anterior pituitary gland](https://en.wikipedia.org/wiki/Anterior_pituitary_gland), which regulates the endocrine function of the [thyroid](https://en.wikipedia.org/wiki/Thyroid). TSH is secreted throughout life but particularly reaches high levels during the periods of rapid growth and development, as well as in response to stress. The [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus), in the base of the brain, produces [thyrotropin-releasing hormone](https://en.wikipedia.org/wiki/Thyrotropin-releasing_hormone) (TRH). TRH stimulates the anterior [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland) to produce TSH.

#### Diagnosis of disease

TSH concentrations are measured as part of a thyroid function test in patients suspected of having an excess ([hyperthyroidism](https://en.wikipedia.org/wiki/Hyperthyroidism)) or deficiency ([hypothyroidism](https://en.wikipedia.org/wiki/Hypothyroidism)) of thyroid hormones. Interpretation of the results depends on both the TSH and T4 concentrations. In some situations measurement of T3 may also be useful.

A TSH assay is now also the recommended screening tool for thyroid disease. Recent advances in increasing the sensitivity of the TSH assay make it a better screening tool than free T4.

1. **Follicle stimulating hormone:** Follicle-stimulating hormone (FSH) is a [gonadotropin](https://en.wikipedia.org/wiki/Gonadotropin), a [glycoprotein](https://en.wikipedia.org/wiki/Glycoprotein) [polypeptide](https://en.wikipedia.org/wiki/Polypeptide) [hormone](https://en.wikipedia.org/wiki/Hormone). FSH is synthesized and secreted by the [gonadotropic cells](https://en.wikipedia.org/wiki/Gonadotropic_cell) of the [anterior pituitary gland](https://en.wikipedia.org/wiki/Anterior_pituitary_gland),and regulates the development, growth, [pubertal maturation](https://en.wikipedia.org/wiki/Puberty), and reproductive processes of the body. FSH and [luteinizing hormone](https://en.wikipedia.org/wiki/Luteinizing_hormone) (LH) work together in the [reproductive system](https://en.wikipedia.org/wiki/Reproductive_system). FSH is used commonly in infertility therapy, mainly for [ovarian hyperstimulation](https://en.wikipedia.org/wiki/Controlled_ovarian_hyperstimulation) as part of [IVF](https://en.wikipedia.org/wiki/IVF). In some cases, it is used in [ovulation induction](https://en.wikipedia.org/wiki/Ovulation_induction) for reversal of [anovulation](https://en.wikipedia.org/wiki/Anovulation) as well. FSH is available mixed with LH activity in various [menotropins](https://en.wikipedia.org/wiki/Menotropins) including more purified forms of urinary [gonadotropins](https://en.wikipedia.org/wiki/Gonadotropins) such as [Menopur](https://en.wikipedia.org/wiki/Menopur), as well as without LH activity as recombinant FSH (Gonapure, Gonal F, Follistim, Follitropin alpha).

### High FSH levels: The most common reason for high serum FSH concentration is in a female who is undergoing or has recently undergone [menopause](https://en.wikipedia.org/wiki/Menopause).. If high FSH levels occur during the reproductive years, it is abnormal. Conditions with high FSH levels include: [Premature menopause](https://en.wikipedia.org/wiki/Premature_menopause) also known as Premature Ovarian Failure, [Poor ovarian reserve](https://en.wikipedia.org/wiki/Poor_ovarian_reserve) also known as Premature Ovarian Aging, [Gonadal dysgenesis](https://en.wikipedia.org/wiki/Gonadal_dysgenesis), [Turner syndrome](https://en.wikipedia.org/wiki/Turner_syndrome), [Castration](https://en.wikipedia.org/wiki/Castration), [Swyer syndrome](https://en.wikipedia.org/wiki/Swyer_syndrome), Certain forms of [CAH](https://en.wikipedia.org/wiki/Congenital_adrenal_hyperplasia), Testicular failure, [Klinefelter syndrome](https://en.wikipedia.org/wiki/Klinefelter_syndrome), [Systemic Lupus Erythematosus](https://en.wikipedia.org/wiki/Systemic_Lupus_Erythematosus) also known as Lupus

### Low FSH levels: Diminished secretion of FSH can result in failure of gonadal function (hypogonadism). This condition is typically manifested in males as failure in production of normal numbers of sperm. In females, cessation of reproductive cycles is commonly observed. Conditions with very low FSH secretions are: [Polycystic Ovarian Syndrome](https://en.wikipedia.org/wiki/Polycystic_Ovarian_Syndrome), [Polycystic Ovarian Syndrome](https://en.wikipedia.org/wiki/Polycystic_Ovarian_Syndrome) + Obesity + Hirsutism + Infertility, [Kallmann syndrome](https://en.wikipedia.org/wiki/Kallmann_syndrome), [Hypothalamic suppression](https://en.wikipedia.org/wiki/Hypothalamic_suppression), [Hypopituitarism](https://en.wikipedia.org/wiki/Hypopituitarism), [Hyperprolactinemia](https://en.wikipedia.org/wiki/Hyperprolactinemia), [Gonadotropin deficiency](https://en.wikipedia.org/wiki/Gonadotropin_deficiency), Gonadal suppression therapy.

### Luteinizing hormone

**Luteinizing hormone** (**LH**, also known as **lutropin** and sometimes **lutrophin**) is a [hormone](https://en.wikipedia.org/wiki/Hormone) produced by [gonadotropic cells](https://en.wikipedia.org/wiki/Gonadotropic_cell) in the [anterior pituitary gland](https://en.wikipedia.org/wiki/Anterior_pituitary_gland). In females, an acute rise of LH ("**LH surge**") triggers [ovulation](https://en.wikipedia.org/wiki/Ovulation)and development of the [corpus luteum](https://en.wikipedia.org/wiki/Corpus_luteum). In males, where LH had also been called **interstitial cell–stimulating hormone** (**ICSH**), it stimulates [Leydig cell](https://en.wikipedia.org/wiki/Leydig_cell) production of [testosterone](https://en.wikipedia.org/wiki/Testosterone). It acts synergistically with follicle-stimulating hormone ([FSH](https://en.wikipedia.org/wiki/Follicle-stimulating_hormone)).

**Excess:** Persistently high LH levels are indicative of situations where the normal restricting feedback from the gonad is absent, leading to a pituitary production of both LH and FSH. While this is typical in menopause, it is abnormal in the reproductive years. There it may be a sign of: [Premature menopause](https://en.wikipedia.org/wiki/Premature_menopause), [Gonadal dysgenesis](https://en.wikipedia.org/wiki/Gonadal_dysgenesis), [Turner syndrome](https://en.wikipedia.org/wiki/Turner_syndrome), [Castration](https://en.wikipedia.org/wiki/Castration), [Swyer syndrome](https://en.wikipedia.org/wiki/Swyer_syndrome), [Polycystic ovary syndrome](https://en.wikipedia.org/wiki/Polycystic_ovary_syndrome), Certain forms of [congenital adrenal hyperplasia](https://en.wikipedia.org/wiki/Congenital_adrenal_hyperplasia), [Testicular failure](https://en.wikipedia.org/wiki/Hypergonadotropic_hypogonadism), Pregnancy - BetaHCG can mimic LH so tests may show elevated LH

Note: A medical drug for inhibiting luteinizing hormone secretion is [Butinazocine](https://en.wikipedia.org/wiki/Butinazocine).

### Deficiency: Diminished secretion of LH can result in failure of gonadal function (hypogonadism). This condition is typically manifest in males as failure in production of normal numbers of sperm. In females, [amenorrhea](https://en.wikipedia.org/wiki/Amenorrhea) is commonly observed. Conditions with very low LH secretions include: [Pasqualini syndrome](https://en.wikipedia.org/wiki/Fertile_eunuch_syndrome), [Kallmann syndrome](https://en.wikipedia.org/wiki/Kallmann_syndrome), [Hypothalamic suppression](https://en.wikipedia.org/wiki/Hypothalamic_suppression), [Hypopituitarism](https://en.wikipedia.org/wiki/Hypopituitarism), [Eating disorder](https://en.wikipedia.org/wiki/Eating_disorder), [Female athlete triad](https://en.wikipedia.org/wiki/Female_athlete_triad), [Hyperprolactinemia](https://en.wikipedia.org/wiki/Hyperprolactinemia), [Hypogonadism](https://en.wikipedia.org/wiki/Hypogonadism), Gonadal suppression therapy [GnRH antagonist](https://en.wikipedia.org/wiki/GnRH_antagonist)

1. **Growth hormone** (**GH**) or **somatotropin**, also known as **human growth hormones** (**hGH** or **HGH**) in its human form, is a [peptide hormone](https://en.wikipedia.org/wiki/Peptide_hormone) that stimulates growth, [cell](https://en.wikipedia.org/wiki/Cell_%28biology%29) reproduction, and cell regeneration in humans and other animals. It is thus important in [human development](https://en.wikipedia.org/wiki/Human_development_%28biology%29). GH also stimulates production of [IGF-1](https://en.wikipedia.org/wiki/IGF-1) and increases the concentration of [glucose](https://en.wikipedia.org/wiki/Glucose) and [free fatty acids](https://en.wikipedia.org/wiki/Free_fatty_acid). It is a type of [mitogen](https://en.wikipedia.org/wiki/Mitogen) which is specific only to the [receptors](https://en.wikipedia.org/wiki/Receptor_%28biochemistry%29) on certain types of cells. GH is a 191-[amino acid](https://en.wikipedia.org/wiki/Amino_acid), single-chain [polypeptide](https://en.wikipedia.org/wiki/Polypeptide) that is synthesized, stored and secreted by [somatotropic cells](https://en.wikipedia.org/wiki/Somatotropic_cell) within the lateral wings of the [anterior pituitary](https://en.wikipedia.org/wiki/Anterior_pituitary) gland.

**Excess:** Prolonged GH excess thickens the bones of the jaw, fingers and toes, resulting heaviness of the jaw and increased size of digits, referred to as [acromegaly](https://en.wikipedia.org/wiki/Acromegaly). Accompanying problems can include sweating, pressure on nerves (e.g. [carpal tunnel syndrome](https://en.wikipedia.org/wiki/Carpal_tunnel_syndrome)), muscle weakness, excess [sex hormone-binding globulin](https://en.wikipedia.org/wiki/Sex_hormone-binding_globulin) (SHBG), insulin resistance or even a rare form of [type 2 diabetes](https://en.wikipedia.org/wiki/Diabetes_mellitus_type_2), and reduced sexual function.

**Deficiency:** Major manifestations of GH deficiency in children are [growth failure](https://en.wikipedia.org/wiki/Growth_failure), the development of a [short stature](https://en.wikipedia.org/wiki/Short_stature), and delayed sexual maturity. In adults, somatomedin alteration contributes to increased [osteoclast](https://en.wikipedia.org/wiki/Osteoclast) activity, resulting in weaker bones that are more prone to [pathologic fracture](https://en.wikipedia.org/wiki/Pathologic_fracture) and [osteoporosis](https://en.wikipedia.org/wiki/Osteoporosis). However, deficiency is rare in adults, with the most common cause being a [pituitary adenoma](https://en.wikipedia.org/wiki/Pituitary_adenoma). Other adult causes include a continuation of a childhood problem, other structural lesions or [trauma](https://en.wikipedia.org/wiki/Injury), and very rarely idiopathic GHD.

1. **Prolactin** (**PRL**), also known as **luteotropic hormone** or **luteotropin**, is a [protein](https://en.wikipedia.org/wiki/Protein) best known for its role in enabling mammals (and birds), usually females, to [produce milk](https://en.wikipedia.org/wiki/Lactation). It is influential in over 300 separate processes in various vertebrates, including humans. Prolactin is secreted from the [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland) in response to eating, mating, estrogen treatment, ovulation and nursing. It is secreted heavily in pulses in between these events. Prolactin plays an essential role in metabolism, regulation of the [immune system](https://en.wikipedia.org/wiki/Immune_system) and pancreatic development.

In mammals, prolactin is associated with milk production; in fish it is thought to be related to the control of water and salt balance. Prolactin also acts in a [cytokine](https://en.wikipedia.org/wiki/Cytokine)-like manner and as an important regulator of the immune system. It has important cell cycle-related functions as a growth-, differentiating- and anti-[apoptotic](https://en.wikipedia.org/wiki/Apoptotic) factor. As a growth factor, binding to cytokine-like receptors, it influences [hematopoiesis](https://en.wikipedia.org/wiki/Hematopoiesis) and [angiogenesis](https://en.wikipedia.org/wiki/Angiogenesis), and is involved in the regulation of blood clotting through several pathways. The hormone acts in [endocrine](https://en.wikipedia.org/wiki/Endocrine), [autocrine](https://en.wikipedia.org/wiki/Autocrine_signalling) and [paracrine](https://en.wikipedia.org/wiki/Paracrine_signalling) manner through the [prolactin receptor](https://en.wikipedia.org/wiki/Prolactin_receptor) and numerous [cytokine receptors](https://en.wikipedia.org/wiki/Cytokine_receptor).

Elevated levels: [Hyperprolactinaemia](https://en.wikipedia.org/wiki/Hyperprolactinaemia), or excess serum prolactin, is associated with [hypoestrogenism](https://en.wikipedia.org/wiki/Hypoestrogenism), [anovulatory](https://en.wikipedia.org/wiki/Anovulatory) [infertility](https://en.wikipedia.org/wiki/Infertility), [oligomenorrhoea](https://en.wikipedia.org/wiki/Oligomenorrhoea), [amenorrhoea](https://en.wikipedia.org/wiki/Amenorrhoea), unexpected [lactation](https://en.wikipedia.org/wiki/Lactation) and loss of [libido](https://en.wikipedia.org/wiki/Libido) in women and [erectile dysfunction](https://en.wikipedia.org/wiki/Erectile_dysfunction) and loss of libido in men.

Decreased levels:[Hypoprolactinemia](https://en.wikipedia.org/wiki/Hypoprolactinemia), or serum prolactin deficiency, is associated with ovarian dysfunction in women, and [arteriogenic](https://en.wikipedia.org/wiki/Arteriogenesis) [erectile dysfunction](https://en.wikipedia.org/wiki/Erectile_dysfunction), [premature ejaculation](https://en.wikipedia.org/wiki/Premature_ejaculation), [oligozoospermia](https://en.wikipedia.org/wiki/Oligozoospermia), [asthenospermia](https://en.wikipedia.org/wiki/Asthenospermia), hypofunction of [seminal vesicles](https://en.wikipedia.org/wiki/Seminal_vesicles) and [hypoandrogenism](https://en.wikipedia.org/wiki/Hypoandrogenism) in men. In one study, normal sperm characteristics were restored when prolactin levels were raised to normal values in hypoprolactinemic men. Hypoprolactinemia can result from [hypopituitarism](https://en.wikipedia.org/wiki/Hypopituitarism), excessive [dopaminergic](https://en.wikipedia.org/wiki/Dopaminergic) action in the [tuberoinfundibular pathway](https://en.wikipedia.org/wiki/Tuberoinfundibular_pathway) and ingestion of [D2 receptor](https://en.wikipedia.org/wiki/D2_receptor) [agonists](https://en.wikipedia.org/wiki/Agonist) such as [bromocriptine](https://en.wikipedia.org/wiki/Bromocriptine).

 **QUESTION 1B**.

**Letrozole**, sold under the brand name **Femara** among others, is an [aromatase inhibitor](https://en.wikipedia.org/wiki/Aromatase_inhibitor) which is used in the treatment of hormonally-responsive [breast cancer](https://en.wikipedia.org/wiki/Breast_cancer) after surgery.

**Clomifene**, also known as **clomiphene**, is a medication used to treat [infertility](https://en.wikipedia.org/wiki/Infertility) in women who [do not ovulate](https://en.wikipedia.org/wiki/Anovulation). This includes those who have [polycystic ovary syndrome](https://en.wikipedia.org/wiki/Polycystic_ovary_syndrome). Use results in a greater chance of [twins](https://en.wikipedia.org/wiki/Twins). It is taken by mouth once a day with a course of treatment generally lasting five days. Common side effects include [pelvic pain](https://en.wikipedia.org/wiki/Pelvic_pain) and [hot flashes](https://en.wikipedia.org/wiki/Hot_flashes).Other side effects can include changes in vision, vomiting, trouble sleeping, [ovarian cancer](https://en.wikipedia.org/wiki/Ovarian_cancer), and [seizures](https://en.wikipedia.org/wiki/Seizures). It is not recommended in people with [liver disease](https://en.wikipedia.org/wiki/Liver_disease), [abnormal vaginal bleeding](https://en.wikipedia.org/wiki/Abnormal_vaginal_bleeding) of unknown cause, or who are [pregnant](https://en.wikipedia.org/wiki/Pregnant). Clomifene is in the [selective estrogen receptor modulator](https://en.wikipedia.org/wiki/Selective_estrogen_receptor_modulator) (SERM) family of medication and is a nonsteroidal medication. It works by causing the release of [GnRH](https://en.wikipedia.org/wiki/GnRH) by the [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus), and subsequently [gonadotropin](https://en.wikipedia.org/wiki/Gonadotropin) from the [anterior pituitary](https://en.wikipedia.org/wiki/Anterior_pituitary).

**Menotropin** (also called **human menopausal gonadotropin** or **hMG**) is a [hormonally](https://en.wikipedia.org/wiki/Hormone) active medication for the treatment of [fertility disturbances](https://en.wikipedia.org/wiki/Fertility_disturbances). Menotropins ar\ extracted from the urine of [postmenopausal](https://en.wikipedia.org/wiki/Postmenopause) women.

Letrozole in combination with HMG is an effective protocol for reducing the risks of hyperstimulation for ovarian induction in CC-resistant women with PCOS. This combination may be more appropriate in patients who are particularly sensitive to gonadotropin.

Gonadotropin has been used to stimulate ovulation in clomiphene-resistant infertile women with polycystic ovary syndrome (PCOS), but it is associated with overstimulated cycles with the development of many follicles. The aim of the study was to evaluate the effectiveness and efficacy of letrozole and clomiphene citrate (CC) combined with human menopausal gonadotropin (HMG) in CC-resistant infertile women with PCOS.

The principle behind the use of letrozole, clomiphene and menotropin/ gonadotrophins is ovulation induction. Ovulation induction is the stimulation of ovulation by medication. It is usually used in the sense of stimulation of the development of ovarian follicles to reverse anovulation or oligoovulation as in cases of women with Polycystic Ovarian cycle.

**QUESTION NUMBER 2**

If a young woman of about 24 years misses her period for 3 months consecutively, the condition may be described as Amenorrhea, more specifically secondary Amenorrhea.

**Amenorrhea** is the absence of a [menstrual period](https://en.wikipedia.org/wiki/Menstrual_cycle) in a woman of reproductive age. Physiological states of amenorrhoea are seen, most commonly, during [pregnancy](https://en.wikipedia.org/wiki/Pregnancy) and [lactation](https://en.wikipedia.org/wiki/Lactation) ([breastfeeding](https://en.wikipedia.org/wiki/Breastfeeding)), the latter also forming the basis of a form of contraception known as the [lactational amenorrhoea method](https://en.wikipedia.org/wiki/Lactational_amenorrhea_method). Outside the reproductive years, there is absence of menses during childhood and after [menopause](https://en.wikipedia.org/wiki/Menopause).

Amenorrhoea is a symptom with many potential causes.

 Primary amenorrhoea is defined as an absence of [secondary sexual characteristics](https://en.wikipedia.org/wiki/Secondary_sex_characteristic) by age 14 with no [menarche](https://en.wikipedia.org/wiki/Menarche) or normal secondary sexual characteristics but no menarche by 16 years of age. It may be caused by developmental problems, such as the congenital absence of the uterus, failure of the [ovary](https://en.wikipedia.org/wiki/Ovary) to receive or maintain [egg cells](https://en.wikipedia.org/wiki/Egg_cells), or delay in pubertal development.

 Secondary amenorrhoea (menstrual cycles ceasing) is often caused by hormonal disturbances from the [hypothalamus](https://en.wikipedia.org/wiki/Hypothalamus) and the [pituitary gland](https://en.wikipedia.org/wiki/Pituitary_gland), from premature [menopause](https://en.wikipedia.org/wiki/Menopause) or intrauterine scar formation. It is defined as the absence of menses for three months in a woman with previously normal menstruation, or six months for women with a history of [oligomenorrhoea](https://en.wikipedia.org/wiki/Oligomenorrhea).

**Causes includes;** Low body weight, Drug-induced, Breastfeeding, Celiac disease, Physical, Stress etc.

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 **DIAGNOSIS OF AMENORRHEA:**

### Primary amenorrhoea

Primary amenorrhoea can be diagnosed in female children by age 14 if no [secondary sex characteristics](https://en.wikipedia.org/wiki/Secondary_sex_characteristics), such as enlarged breasts and body hair, are present. In the absence of secondary sex characteristics, the most common cause of amenorrhoea is low levels of FSH and LH caused by a delay in puberty. Gonadal dysgenesis, often associated with [Turner's Syndrome](https://en.wikipedia.org/wiki/Turner%27s_Syndrome), or premature ovarian failure may also be to blame. If secondary sex characteristics are present, but menstruation is not, primary amenorrhoea can be diagnosed by age 16. A reason for this occurrence may be that a person phenotypically female but genetically male, a situation known as [androgen insensitivity syndrome](https://en.wikipedia.org/wiki/Androgen_insensitivity_syndrome). If undescended testes are present, they are often removed after puberty (~21 years of age) due to the increased risk of testicular cancer. In the absence of undescended testes, an MRI can be used to determine whether or not a uterus is present. [Müllerian agenesis](https://en.wikipedia.org/wiki/M%C3%BCllerian_agenesis) causes around 15% of primary amenorrhoea cases. If a uterus is present, outflow track obstruction may be to blame for primary amenorrhoea.

**Secondary amenorrhea**

Secondary amenorrhea's most common and most easily diagnosable. Initial [laboratory](https://www.wikidoc.org/index.php/Laboratory) tests for evaluating amenorrhea include [pregnancy test](https://www.wikidoc.org/index.php/Pregnancy_test), [thyroid stimulating hormone (TSH)](https://www.wikidoc.org/index.php/Thyroid_stimulating_hormone), [follicle stimulating hormone (FSH)](https://www.wikidoc.org/index.php/Follicle_stimulating_hormone), and [prolactin (PRL)](https://www.wikidoc.org/index.php/Prolactin). Second line [laboratory](https://www.wikidoc.org/index.php/Laboratory) tests include free and total [testosterone](https://www.wikidoc.org/index.php/Testosterone), [dehydroepiandrosterone sulfate (DHEAS)](https://www.wikidoc.org/index.php/Dehydroepiandrosterone-sulfate), and also [progesterone](https://www.wikidoc.org/index.php/Progesterone) challenge.

Below are some biochemical tests and its laboratory findings

Urine or serum pregnancy test

* Some patients with amenorrhea may have positive urine or serum [pregnancy test](https://www.wikidoc.org/index.php/Pregnancy_test), which is usually suggestive of [pregnancy](https://www.wikidoc.org/index.php/Pregnancy)-induced amenorrhea.

Thyroid function tests

* Thyroid function tests in patients of amenorrhea include:
	+ Elevated [TSH](https://www.wikidoc.org/index.php/TSH) and reduced free [thyroxine (T4)](https://www.wikidoc.org/index.php/Thyroxine), suggestive of [hypothyroidism](https://www.wikidoc.org/index.php/Hypothyroidism).
	+ Reduced [TSH](https://www.wikidoc.org/index.php/TSH) and elevated [T4](https://www.wikidoc.org/index.php/Thyroxine), suggestive of [hyperthyroidism](https://www.wikidoc.org/index.php/Hyperthyroidism).
	+ Elevated [anti-thyroglobulin antibodies](https://www.wikidoc.org/index.php/Antithyroglobulin_antibody) and anti-[thyroid peroxidase](https://www.wikidoc.org/index.php/Thyroid_peroxidase) [antibodies](https://www.wikidoc.org/index.php/Antibodies), suggestive of [thyroiditis](https://www.wikidoc.org/index.php/Thyroiditis).
	+ Elevated anti-[thyrotropin receptor](https://www.wikidoc.org/index.php/Thyrotropin_receptor%22%20%5Co%20%22Thyrotropin%20receptor) [antibodies](https://www.wikidoc.org/index.php/Antibodies), suggestive of [Graves' disease](https://www.wikidoc.org/index.php/Graves%27_disease).

Prolactin (PRL)

* Some patients with amenorrhea may have elevated concentration of [prolactin](https://www.wikidoc.org/index.php/Prolactin), which is usually suggestive of amenorrhea due to [hyperprolactinemia](https://www.wikidoc.org/index.php/Hyperprolactinemia) (may be due to [pituitary](https://www.wikidoc.org/index.php/Pituitary) causes, such as [prolactinoma](https://www.wikidoc.org/index.php/Prolactinoma)).

Basal plasma gonadotropins

* Basal plasma [gonadotropins](https://www.wikidoc.org/index.php/Gonadotropins) in patients of amenorrhea include:
	+ Reduced [luteinizing hormone (LH)](https://www.wikidoc.org/index.php/Luteinizing_hormone) and [FSH](https://www.wikidoc.org/index.php/FSH), suggestive of [hypothalamic](https://www.wikidoc.org/index.php/Hypothalamic) and [pituitary](https://www.wikidoc.org/index.php/Pituitary) diseases or [premature ovarian failure](https://www.wikidoc.org/index.php/Premature_ovarian_failure).
	+ Reduced [LH](https://www.wikidoc.org/index.php/LH), suggestive of complete [androgen insensitivity syndrome](https://www.wikidoc.org/index.php/Androgen_insensitivity_syndrome).

Estradiol

* Estradiol interpretation in patients of amenorrhea include:
	+ Reduced [estradiol](https://www.wikidoc.org/index.php/Estradiol), suggestive of [ovarian failure](https://www.wikidoc.org/index.php/Ovarian_failure) or [pituitary](https://www.wikidoc.org/index.php/Pituitary) causes.
	+ Elevated [estradiol](https://www.wikidoc.org/index.php/Estradiol), suggestive of [androgen insensitivity syndrome](https://www.wikidoc.org/index.php/Androgen_insensitivity_syndrome).

Progesterone

* Some patients with amenorrhea may have reduced concentration of [progesterone](https://www.wikidoc.org/index.php/Progesterone), which is usually suggestive of [ovarian failure](https://www.wikidoc.org/index.php/Ovarian_failure).

Free and total testosterone

* Some patients with amenorrhea may have elevated concentration of [testosterone](https://www.wikidoc.org/index.php/Testosterone), which is usually suggestive of amenorrhea due to complete [androgen insensitivity syndrome](https://www.wikidoc.org/index.php/Androgen_insensitivity_syndrome).

Dehydroepiandrosterone sulfate (DHEAS)

* Some patients with amenorrhea may have elevated concentration of [dehydroepiandrosterone sulfate (DHEAS)](https://www.wikidoc.org/index.php/Dehydroepiandrosterone_sulfate), which is usually suggestive of amenorrhea due to [polycystic ovary syndrome (PCOS)](https://www.wikidoc.org/index.php/Polycystic_ovary_syndrome).

Delta 4-androstenedione

* Some patients with amenorrhea may have elevated concentration of [delta 4-androstenedione](https://www.wikidoc.org/index.php/Androstenedione), which is usually suggestive of amenorrhea due to [polycystic ovary syndrome (PCOS)](https://www.wikidoc.org/index.php/Polycystic_ovary_syndrome).

17-hydroxyprogesterone

* Some patients with amenorrhea may have elevated concentration of [17-hydroxyprogesterone](https://www.wikidoc.org/index.php/17-hydroxyprogesterone), which is usually suggestive of amenorrhea due to [congenital adrenal hyperplasia (CAH)](https://www.wikidoc.org/index.php/Congenital_adrenal_hyperplasia_%28CAH%29).

Fasting insulin

* Some patients with amenorrhea may have elevated concentration of fasting [insulin](https://www.wikidoc.org/index.php/Insulin), which is usually suggestive of amenorrhea due to [polycystic ovary syndrome (PCOS)](https://www.wikidoc.org/index.php/Polycystic_ovary_syndrome).

Fasting glucose (FBS)

* Some patients with amenorrhea may have elevated concentration of [fasting glucose (FBS)](https://www.wikidoc.org/index.php/Fasting_plasma_glucose), which is usually suggestive of amenorrhea due to [polycystic ovary syndrome (PCOS)](https://www.wikidoc.org/index.php/Polycystic_ovary_syndrome).

Insulin resistance indexes

* Some patients with amenorrhea may have elevated [insulin resistance](https://www.wikidoc.org/index.php/Insulin_resistance) indexes, which is usually suggestive of amenorrhea due to [polycystic ovary syndrome (PCOS)](https://www.wikidoc.org/index.php/Polycystic_ovary_syndrome).

Adrenocorticotropic hormone (ACTH)

* Some patients with amenorrhea may have elevated concentration of [adrenocorticotropic hormone (ACTH)](https://www.wikidoc.org/index.php/Adrenocorticotropic_hormone), which is usually suggestive of amenorrhea due to [pituitary](https://www.wikidoc.org/index.php/Pituitary) causes ([ACTH-secreting adenoma](https://www.wikidoc.org/index.php/Adreno-corticotrophic_adenoma)).

Cortisol

* Some patients with amenorrhea may have elevated concentration of [cortisol](https://www.wikidoc.org/index.php/Cortisol), which is usually suggestive of amenorrhea due to [pituitary](https://www.wikidoc.org/index.php/Pituitary) causes ([ACTH-secreting adenoma](https://www.wikidoc.org/index.php/Adreno-corticotrophic_adenoma)).

Markers of ovarian tumors

* Some patients with amenorrhea may have elevated concentration of markers of [ovarian tumors](https://www.wikidoc.org/index.php/Ovarian_cancer), which is usually suggestive of [ovarian failure](https://www.wikidoc.org/index.php/Ovarian_failure) (due to [adenocarcinoma](https://www.wikidoc.org/index.php/Adenocarcinoma)).

Progesterone challenge test

* [Progesterone](https://www.wikidoc.org/index.php/Progesterone) challenge test is used in secondary amenorrhea with normal female [androgen](https://www.wikidoc.org/index.php/Androgen) in order to measure circulating [estrogen](https://www.wikidoc.org/index.php/Estrogen). It reveals the insufficient [endometrial](https://www.wikidoc.org/index.php/Endometrial) estrogenization.
* It is consisted of [Provera](https://www.wikidoc.org/index.php/Provera) 10 mg PO for 7 days and then following for [bleeding](https://www.wikidoc.org/index.php/Menstrual_bleeding). If patient bleed it means that [estrogen](https://www.wikidoc.org/index.php/Estrogen) is repleted, [hypothalamic-pituitary-ovarian (HPO) axis](https://www.wikidoc.org/index.php/Hypothalamic-pituitary-gonadal_axis) immaturity or [PCOS](https://www.wikidoc.org/index.php/PCOS).

Leptin

* Some patients with amenorrhea may have reduced concentration of [leptin](https://www.wikidoc.org/index.php/Leptin), which is usually suggestive of amenorrhea due to [hypothalamic](https://www.wikidoc.org/index.php/Hypothalamic) disorders.

Inhibin

* Some patients with amenorrhea may have reduced concentration of [inhibin](https://www.wikidoc.org/index.php/Inhibin), which is usually suggestive of amenorrhea due to [ovarian failure](https://www.wikidoc.org/index.php/Ovarian_failure).

**QUESTION 2B**

If the woman was 60 years of age, I would have described the condition as Menopause

**Menopause**, also known as the **climacteric**, is the time in most women's lives when [menstrual periods](https://en.wikipedia.org/wiki/Menstrual_cycle) stop permanently, and they are no longer [able to bear children](https://en.wikipedia.org/wiki/Fertility). Menopause typically occurs between 49 and 52 years of age. Medical professionals often define menopause as having occurred when a woman has not had any menstrual bleeding for a year. It may also be defined by a decrease in [hormone](https://en.wikipedia.org/wiki/Hormone) production by the [ovaries](https://en.wikipedia.org/wiki/Ovary). In those who have had surgery to remove their [uterus](https://en.wikipedia.org/wiki/Uterus) but still have ovaries, menopause may be considered to have occurred at the time of the surgery or when their hormone levels fell. Following the removal of the uterus, symptoms typically occur earlier, at an average of 45 years of age.

In the years before menopause, a woman's periods typically become irregular, which means that periods may be longer or shorter in duration or be lighter or heavier in the amount of flow. During this time, women often experience [hot flashes](https://en.wikipedia.org/wiki/Hot_flash); these typically last from 30 seconds to ten minutes and may be associated with shivering, [sweating](https://en.wikipedia.org/wiki/Sweating), and reddening of the skin. Hot flashes often stop occurring after a year or two. Other symptoms may include [vaginal dryness](https://en.wikipedia.org/wiki/Vaginal_dryness), trouble sleeping, and mood changes. The severity of symptoms varies between women. While menopause is often thought to be linked to an increase in [heart disease](https://en.wikipedia.org/wiki/Heart_disease), this primarily occurs due to increasing age and does not have a direct relationship with menopause. In some women, problems that were present like [endometriosis](https://en.wikipedia.org/wiki/Endometriosis) or [painful periods](https://en.wikipedia.org/wiki/Painful_periods) will improve after menopause.

Specific treatment is not usually needed. Some symptoms, however, may be improved with treatment. With respect to hot flashes, avoiding smoking, caffeine, and alcohol is often recommended. Sleeping in a cool room and using a fan may help. The following medications may help: [menopausal hormone therapy](https://en.wikipedia.org/wiki/Menopausal_hormone_therapy) (MHT), [clonidine](https://en.wikipedia.org/wiki/Clonidine), [gabapentin](https://en.wikipedia.org/wiki/Gabapentin), or [selective serotonin reuptake inhibitors](https://en.wikipedia.org/wiki/Selective_serotonin_reuptake_inhibitors). Exercise may help with sleeping problems.

**QUESTION 3A**

 Fertility in men and women is regulated by a series of tightly coordinated and synchronized interactions within the hypothalamic-pituitary-gonadal axis. The operational characteristics of the reproductive axis leave little room for error. Reproductive tract structures are also at risk for the development of diseases that render them unfit or compromised in their primary role of reproduction. Disorders at any level of the system may lead to involuntary infertility, which affects approximately 15% to 20% of couples or approximately 11 million reproductive-age people in the United States. Infertility therapy has been evaluated carefully in the last decade as new medical and assisted reproductive techniques have gained widespread approval. Advancements in the basic science of gamete physiology, conception, and implantation have also added greatly to our knowledge base, while at the same time have introducing a number of controversies in the treatment of infertile couples.

Infertility is defined as the inability of a couple practicing frequent intercourse and not using contraception to fail to conceive a child within 1 year.

Primary infertility occurs in couples with no previous history of conception. Secondary infertility exists when a prior conception has been, at a minimum, documented by a positive human chorionic gonadotropin (hCG), histology, or ultrasound. The causes of infertility are equally distributed between males and females and often the physician encounters multiple etiologies during the investigation. Most infertile couples have one or more of three major causes: a male factor, ovulatory dysfunction, or tubal-peritoneal disease.

The infertility evaluation serves to: (1) determine the etiology(ies) of infertility as expediently as possible, (2) provide the couple with recommended treatment protocols, (3) determine expected success rates and approximate costs for recommended therapy, and (4) educate the couple about their specific disorder and available alternatives.

Causes

| Male | Female |
| --- | --- |
| Disturbed spermatogenesis | Congenital anomalies |
|   Acute/chronic illness |  Vaginal |
|  Exposure |  Uterine |
|   Chemicals |  Fallopian tubes |
|   Recreational Drugs | Sexual dysfunction |
|   Heat | Endocrine disorders |
|   Radiation |  Ovary |
|  Genital disorders |  Adrenal |
|  Genital injuries |  Thyroid |
|  Endocrine disorders |  Pituitary |
|  Varicocele |  Hypothalamus |
| Insemination disturbances | Sequelae of pelvic infections and inflammation |
|  Genital anomalies |  Pelvic adhesions |
|  Genital trauma |  Endometriosis |
|  Genital surgery |  Tubal occlusion/phimosis |
|  Pelvic surgery |  IUD complications |
|  Sexual dysfunction |  Postsurgical |
|  Spinal cord injuries |   Oophorectomy/cystectomy |
|  Veneral diseases |   Myomectomy |
| Abnormal seminal fluid/cervical mucus |   Conization of cervix |
|   Interaction |  Pregnancy complications |
|  Infections |   Abortion |
|  Immunologic |   Cesarean section |
|  Intrinsic spermatozoal defects |   Postpartum infections |
|  Unknown |   Ectopic pregnancy |
| Abnormal sperm/egg interaction | Immunologic |
|  Infection |  Serum/cervical mucus antisperm antibodies |
|  Immunologic | Inadequate cervical secretions |
|  Intrinsic spermatozoal defects |  Drug effects |
|  Unknown |  Postsurgical |
| Unexplained (?) | Unexplained (?) |

**EVALUATION OF THE COUPLE AS A UNIT**

Infertility should be regarded as a two-patient disorder. Male and female partners must be thoroughly evaluated, counseled, and included in the therapeutic decision-making processes

The evaluation consists of a detailed history, physical examination, assessment of ovulation, semen evaluation, as well as uterotubal assessment. In addition, follicle-stimulating hormone (FSH), and estradiol levels obtained on the third day of the menstrual cycle maybe useful in women older than 35.

1. **Complete Medical and Gynecologic history:**

**Female**

A thorough workup is based on an extensive history and physical examination. The woman should be asked about the timing of her pubertal development and menarche. Menstrual history should include cycle length, duration, and amount of bleeding, associated dysmenorrhea, or premenstrual symptoms. A history of spontaneous, regular, cyclic predictable menses is, in almost all women, consistent with ovulation, while a history of amenorrhea or abnormal or unpredictable bleeding suggests anovulation or uterine pathology. Previous pregnancies, abortions, and birth control history are also documented. The patient should be asked about dyspareunia or severe dysmenorrhea that may be linked to endometriosis. A history of pelvic inflammatory disease, STD, ruptured appendix or other abdominal surgery, and the past use of an intrauterine device may be associated with tubal disease. A history of galactorrhea may be an indication of elevated prolactin levels, while a history of pubertal onset of progressive hirsutism associated with oligomenorrhea may indicate polycystic ovarian disease or other disorders of androgen excess. Excessive weight loss or weight gain, excessive stress or exercise is often associated with ovulatory disorders. Sexual, social, and psychological issues should be explored. Any prior infertility evaluation, surgery, or medical therapy is essential information and records, films, or surgical photographs should be sought and carefully re-evaluated.

**Male**

The male partner should be questioned about prior fertility, general health, medications, genital surgery, trauma, infection, and impotence. A history of drug or alcohol abuse, frequent hot-tub baths, excess stress, fatigue, or excessive or infrequent coitus should be elicited. Medical conditions that may result in infertility include diabetes (retrograde ejaculation), any serious debilitating disease, adult mumps orchitis, or pituitary hypofunction all may lead to hypogonadism. Herniorrhaphy, varicocele, and bladder neck suspensions are surgical procedures that may potentially be associated with infertility.

1b **. Careful Review of Records**

Many infertile couples have had some prior evaluation for causes of their infertility and this information should be carefully reviewed. Couples may not understand the complexity of a thorough infertility evaluation.

1. **Physical Examination**

**Female**

A thorough general physical examination is necessary to help define factors that may lead to infertility. Special attention to signs of endocrine disturbance such as abnormal size or consistency of the thyroid gland, skin pigmentation, or the presence of abdominal stria should be documented. The presence of acne, oily skin, and hirsutism indicates androgen excess. Acanthosis nigricans, the presence of galactorrhea, surgical scars, or significant variation from normal body weight or percent body fat should be noted. The degree of estrogenization of the vagina and the quality and quantity of cervical mucus should be observed in the context of the current phase of the menstrual cycle. The presence of vaginal or cervical infection should be evaluated by microscopic examination of a wet preparation of a vaginal smear. The cervix is also carefully examined for anatomic abnormalities resulting from intrauterine exposure to diethylstilbestrol or prior cervical surgery, including cryotherapy, cautery, or laser. Cervical cultures for gonococcus, chlamydia, and Pap smears should be obtained. A thorough pelvic examination should detect the presence of cervical, uterine, adnexal tenderness, and pelvic masses. The size and contour of the uterus and adnexa should also be described. A careful rectovaginal examination may be performed to palpate uterosacral nodularity found in endometriosis. The length and direction of uterine cavity should be gently measured with a sterile plastic catheter to check for cervical stenosis as well as depth and direction of the uterine cavity. This information may aid in future intrauterine inseminations or embryo transfers.

**Male**

Physical examination of the male can be performed by the gynecologist, urologist, or family physician. The examination should focus on the degree of secondary sexual development, general body habitus, height, arm span, and presence of gynecomastia. A general physical examination is performed and should include evaluation of perineal sensation and rectal sphincter tone. Examination of the male genitals begins with careful inspection of the penis. Size and location of the urethral meatus as well as any discharge or evidence of stricture is evaluated. The testes are individually palpated and the relative weights, sizes, and consistency should be evaluated. The average volume for an adult testis is 25 mL or approximately 5 × 3 cm. Very small or soft testes are usually associated with a decrease in germinal tissue mass due to either testicular failure or some abnormality in the hypothalamic-pituitary axis leading to hypogonadotropic hypogonadism. The epididymis is palpated along its course to evaluate for swelling or tenderness consistent with epididymitis. The vas deferens should be evaluated by palpation. The presence of a varicocele should be looked for following valsalva. The prostate should be evaluated for size and evidence of prostatitis.

After the history and physical examination of both partners has been completed, an initial diagnosis should be made. The history and physical examination may clearly point to one or more etiologies. During the first evaluation initial laboratory and diagnostic tests should be ordered.

**INITIAL LABORATORY AND DIAGNOSTIC TESTS**

**Basic Laboratory Testing female**

While routine preobstetrical screening of infertile women is not mandatory, it is extremely helpful to screen for patients for anemia and blood type, including Rh or antibody status. Women may need Rhogam after early spontaneous abortions or ectopic pregnancies. Women with a negative titer for rubella will require immunization prior to therapy for infertility. Human immunodeficiency virus (HIV) testing is essential in high-risk populations, those undergoing ART, or those receiving cryopreserved gametes.

**Ovulation Documentation**

Ovulatory factors account for up to 25% of infertility and may be caused by a multitude of factors that may be elicited in the initial history. This includes a history compatible with polycystic ovarian disease, oligomenorrhea, or amenorrhea associated with weight loss or excessive obesity, exercise, eating disorders, and galactorrhea.

**Basal body temperature chart.**

The basal body temperature chart, although much maligned, is still a useful and cost-effective index of evaluating ovulation.

**Serum progesterone.**

The use of serum progesterone levels obtained at midluteal phase evaluates the occurrence and adequacy of ovulation and corpus luteum function. Most clinicians agree that a level of 10 ng/mL or greater is indicative of adequate ovulation (luteinization). Other investigators have suggested that three samples obtained in the luteal phase totaling 15 ng/mL constitutes normal ovulation.

**Endometrial biopsy.**

The endometrial biopsy may also be used to confirm ovulation and diagnose a luteal phase defect. It is usually performed late in the cycle, 1 to 2 days before expecting menstruation. The couple should refrain from intercourse or use barrier contraception during the cycle in which the endometrial biopsy is obtained.

**Preovulatory sonography.**

Preovulatory transvaginal sector sonography is a highly useful tool for evaluating adequate follicle development, endometrial assessment and oocyte release. A triple-line endometrial pattern seen on sonography before ovulation is predictive of subsequent pregnancy.

**Clomiphene challenge test to assess ovarian reserve.**

It has long been documented that the development of diminished ovarian reserve reflects the process of follicular depletion and a decline in oocyte quality. This is a natural physiologic occurrence for women in their mid- to late 30s, even when they have ovulatory cycles. This process is associated with a rise in a woman’s FSH levels, especially in the follicular phase. Currently basal FSH is the best marker to assess ovarian reserve and predict response to supra-ovulation. The clomiphene challenge tests the ovarian reserve in women 35 years and older by measuring FSH levels on cycle day number 3 and then on day 10 after the administration of 100 mg of clomiphene citrate on cycle day 5 to 9. An abnormal test is when the day 10 sample is elevated. The mechanism is unknown, but is based on the fact that women with normal ovarian function and reserve should be able to overcome the impact of clomiphene by day 10. Adding clomiphene allows one to unmask patients who may not be detectable by basal FSH screening alone.

**Other laboratory tests.**

Serum TSH and prolactin levels are obtained in most women with infertility, and in all women with amenorrhea and or galactorrhea, Serum androgens are only obtained in hirsute women and gonadotropins are obtained in women over age 35 and in women with amenorrhea.

Hysterosalpingogram

Laparoscopy/Hysteroscopy

**BASIC LABORATORY TESTING MALES**

**Semen Analysis**

A semen specimen should be examined in all couples presenting with infertility. The specimen is obtained by masturbation into a sterile collection cup. Forty-eight to 72 hours of abstinence is recommended prior to analysis. The sample should be delivered to the laboratory within 1 hour of collection. The semen analysis should have a volume of 2 to 5 mL, 20 to 200 million sperm per milliliter with 50% directional motility, 0% to 40% abnormal forms, liquefaction at room temperature in 1 to 20 minutes, and a pH of 7.0 with a range of 7.5 to 8.0. There is great variation from sample to sample in terms of volume, number, and motility. In addition, there may be seasonal variation in these values. Therefore, it is recommended that if an abnormality is found, a repeat analysis should be carried out 2 to 3 months later to determine the presence of a male factor. It is inappropriate to designate a male as infertile based on a single semen analysis.

**ADDITIONAL OPTIONAL TESTS**

1. **Postcoital Testing**

A postcoital test has been advocated to evaluate the presence of cervical factors

1. **Male Immunologic Causes of Infertility**

The testis is an immunologically protected site because of the blood-testis barrier. Although there are other causes of male immune infertility such as autoimmune orchitis, the most common cause of male immunologic infertility is anti-sperm antibodies (ASA).

1. **Female Immunologic Causes of Infertilty**

Immune assault on the components of the ovary can lead to diminished ovarian function and even premature ovarian failure. Autoimmunity has been shown to cause up to 20% of premature ovarian failures. Addison’s disease is the most common cause of autoimmune infertility. Further evaluation of the female immune factor is difficult secondary to a lack of standardized ovarian antibody assays

**PSYCHOLOGICAL EVALUATION**

Every aspect of the infertility evaluation evokes some emotional and psychological stress for the couples involved. Many times in a large, busy medical practice, it may be difficult for physicians to spend the time necessary to allow frustrated couples to verbalize their feelings and give feedback on management and outcomes. Investigators have found a higher incidence of emotional disturbance in infertile women than among matched controls. Infertile couples have described themselves as being “damaged,” “defective,” “hollow,” and “empty.”[23](https://www.glowm.com/section_view/heading/Evaluation%20and%20Management%20of%20the%20Infertile%20Couple/item/320#r23)

The physical and mental consequences of the infertility workup, subsequent treatment, and lack of success may either cause or greatly exacerbate a psychological problem.

 **QUESTION 3B.**

In order to enable the couple achieve conception, a treatment plan can be developed

Some causes of infertility can't be corrected. In cases where spontaneous pregnancy doesn't happen, couples can often still achieve a pregnancy through use of assisted reproductive technology. Infertility treatment may involve significant financial, physical, psychological and time commitments.

**Treatment for men**

Men's treatment for general sexual problems or lack of healthy sperm may include:

* **Changing lifestyle factors.** Improving lifestyle and certain behaviors can improve chances for pregnancy, including discontinuing select medications, reducing or eliminating harmful substances, improving frequency and timing of intercourse, exercising regularly, and optimizing other factors that may otherwise impair fertility.
* **Medications.** Certain medications may improve sperm count and likelihood for achieving a successful pregnancy. These medicines may increase testicular function, including sperm production and quality.
* **Surgery.** For some conditions, surgery may be able to reverse a sperm blockage and restore fertility. In other cases, surgically repairing a varicocele may improve overall chances for pregnancy.
* **Sperm retrieval.** These techniques obtain sperm when ejaculation is a problem or when no sperm are present in the ejaculated fluid. They may also be used in cases in which assisted reproductive techniques are planned and sperm counts are low or otherwise abnormal.

**Treatment for women**

Some women need only one or two therapies to improve fertility. Other women may need several different types of treatment to achieve pregnancy.

* **Stimulating ovulation with fertility drugs.** Fertility drugs are the main treatment for women who are infertile due to ovulation disorders. These medications regulate or induce ovulation. Talk with your doctor about fertility drug options — including the benefits and risks of each type.
* **Intrauterine insemination (IUI).** During IUI, healthy sperm are placed directly in the uterus around the time the ovary releases one or more eggs to be fertilized. Depending on the reasons for infertility, the timing of IUI can be coordinated with your normal cycle or with fertility medications.
* **Surgery to restore fertility.** Uterine problems such as endometrial polyps, a uterine septum, intrauterine scar tissue and some fibroids can be treated with hysteroscopic surgery. Endometriosis, pelvic adhesions, and larger fibroids may require laparoscopic surgery or surgery with a larger incision of the abdomen.

**Assisted reproductive technology**

Assisted reproductive technology (ART) is any fertility treatment in which the egg and sperm are handled. There are several types of ART.

In vitro fertilization (IVF) is the most common ART technique. IVF involves stimulating and retrieving multiple mature eggs, fertilizing them with sperm in a dish in a lab, and implanting the embryos in the uterus several days after fertilization.

Other techniques are sometimes used in an IVF cycle, such as:

* **Intracytoplasmic sperm injection (ICSI).** A single healthy sperm is injected directly into a mature egg. ICSI is often used when there is poor semen quality or quantity, or if fertilization attempts during prior IVF cycles failed.
* **Assisted hatching.** This technique assists the implantation of the embryo into the lining of the uterus by opening the outer covering of the embryo (hatching).
* **Donor eggs or sperm.** Most ART is done using a couple's own eggs and sperm. However, if there are severe problems with either the eggs or the sperm, you may choose to use eggs, sperm or embryos from a known or anonymous donor.
* **Gestational carrier.** Women who don't have a functional uterus or for whom pregnancy poses a serious health risk might choose IVF using a gestational carrier. In this case, the couple's embryo is placed in the uterus of the carrier for pregnancy.

**Complications of treatment**

Complications of infertility treatment may include:

* **Multiple pregnancy.** The most common complication of infertility treatment is a multiple pregnancy — twins, triplets or more. Generally, the greater the number of fetuses, the higher the risk of premature labor and delivery, as well as problems during pregnancy such as gestational diabetes. Babies born prematurely are at increased risk of health and developmental problems. Talk to your doctor about any concerns you have about a multiple pregnancy before starting treatment.
* **Ovarian hyperstimulation syndrome (OHSS).** Fertility medications to induce ovulation can cause OHSS, particularly with ART, in which the ovaries become swollen and painful. Symptoms may include mild abdominal pain, bloating, and nausea that lasts about a week, or longer if you become pregnant. Rarely, a more severe form causes rapid weight gain and shortness of breath requiring emergency treatment.
* **Bleeding or infection.** As with any invasive procedure, there is a rare risk of bleeding or infection with assisted reproductive technology or reproductive surgery.