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The pituitary gland is located in the bony cavity known as sella turcica, which is found at the base of the brain. The pituitary has three lobes: anterior pituitary lobes also known as adenohypophysis, posterior pituitary lobe also known as neurohypophysis and the pass intermedia.

The anterior pituitary gland secrete hormones which are regulated by the hypothalamic releasing or inhibitory hormones. The hypothalamus triggers the anterior pituitary gland through the action of the appropriate releasing hormones. There are six anterior pituitary hormones and they are:

i. Growth hormone (GH, somatotrophin): it is a large 191 amino acid polypeptide which release inhibitory hormone known as somatostatin. It may control its own secretion through short-loop negative feedback on hypothalamic somatostatin. Dopamine enhance growth hormone secretion in a healthy individual. Growth hormone affects:

- Carbohydrate metabolism as it upset insulin effect on glucose uptake by cells, thus excess growth hormone production leads to glucose intolerance
- Fat metabolism is also affected by growth hormone through lipolysis stimulation leading to high concentration of plasma free fatty acids which then antagonizes insulin action and secretion.
- Protein metabolism via Somatomedic C or IGF-I (insulin like growth factor-1), it increases protein production in concurrence with insulin by stimulating cell uptake of amino acids.
- Growth hormone promotes bone growth in both thickness and length by stimulating osteoblast activity and epiphyseal cartilage proliferation.

ii. Thyroid stimulating hormone (TSH or thyrotrophin): this is a glycoprotein with molecular weight of 28,300 daltons. It is a dimer and has two different subunit, an alpha subunit and beta subunit which is specific to TSH. TSH simulates adenylate cyclase in thyroid cells and increases iodine uptake and production of thyroid hormone (T3 &T4). It also controls thyroid hormone secretion, it maintain the size of the thyroid gland and the rate of its blood flow.

iii. Follicle stimulating hormone: this is a glycoprotein like TSH with basic structure similar to luteinizing hormone. Its secretion is regulated by factors similar to LH. In addition to this factor, it is controlled by inhibin, which is a protein hormone. Inhibin is mainly produced in the sertoli cells and a liitle amount by the leydig cells of the testes in male and in the female by the granulosa cells of the ovary. FSH stimulates gametogenesis and follicle development along with locally produced estrogen and androgens in females and spermatogenesis in males acting along with LH-testosterone.

iv. Luteinizing hormone (LH): is a glycoprotein and can also be referred to as interstitial cell stimulating hormone. It is a dimer composed of an alpha subunit and a hormone specific beta subunit. Like FSH, it also function differently in both sexes. This hormone and FSH induce growth of the gonad and they are the major stimulant of gonadal steroid production. LH in the presence of FSH stimulates leydig cells of the testis to produce and secrete testosterone and small amount of 5α-dihydrotestosterone. In females, the target organs are the ovaries, the mid cycle surge of LH is responsible for the rupture of ovarian follicle and helps in the formation of corpus luteum from the ruptured follicle and may require the concomitant presence of FSH. It controls the ovarian secretion of estrogen and progesterone.

v. Adrenocorticotrophic hormone (ACTH): this is a single polypeptide chain of 39 amino acids. ACTH has dual regulatory stimulation. The major pathways is the corticotrophin or ACTH- releasing hormone and the minor stimulating factor is the vasopressin. The molecular weight of ACTH is about 4500 Daltons. The amino terminal 24 amino acids (24 N-terminal peptide) are essential for its biological action i.e. the regulation of production and secretion of glucocorticoid including adrenal cortex sex hormone maintenance of the size and blood flow of the adrenal cortex. The blood or plasma of ACTH is highest between 6am -8am and very low in the evening, at about 11pm.

vi. Prolactin is a single chain glycoprotein. It contains about 198 amino acids and has a molecular weight of about 22,500 Daltons. Prolactin is similar in structure to growth hormone. Its secretion is pulsatile and increased secretion occurs in the afternoon than in the morning, while the peak level are at night. Its inhibitory factor is known to be dopamine (prolactin inhibiting factor), which is secreted in the hypothalamus. The secretion of prolactin is increased in pregnancy and reaches the peak during delivery. Suckling of breast by the baby may initiate the release of prolactin. Prolactin has the following action:

- It is essential with estrogen and adrenal steroid for normal enlargement of breast
- In pregnancy, prolactin along placental lactogen, estrogen and free progesterone, is responsible for breast enlargement and milk secretion.
- Production of breast tissue and sensation of menstruation.
- Increased concentration of prolactin in the bloodstream interfere with the gondal function

1b.i. Letrozole is an orally active, nonsteroidal and an aromatase inhibitor whose primary action is suppression of the estrogen production, thereby decreasing the negative feedback of estrogens in the hypothalamus leading to increased GnRH production and FSH secretion and subsequent ovarian follicular development. It is used for ovulation induction, treating certain types of breast cancer such as hormone-receptor positive breast cancer in women after menopause. Some breast cancers are made to grow faster by a natural hormone called estrogen. Letrozole decrease the concentration of estrogen in the body and reverse/ slow the growth of these breast cancer

ii. Clomiphene is a non-steroidal compound which blocks hypothalamic steroid receptor, thereby preventing a negative feedback to the hypothalamus. This result in the release of gondotrophin releasing hormone (luteinizing hormone and follicle stimulating hormone releasing hormone)

which causes increased secretion of luteinizing hormone and follicle stimulating hormone from anterior pituitary gland to stimulate ovulation. It is the first choice of drug in ovulation induction in women with certain medical conditions such as polycystic ovary syndrome that prevent naturally occurring ovulation.

iii. Gonadotropins are fertility drugs that contain follicle stimulating hormone, luteinizing hormone or combination of the two. These drugs are used to stimulate ovulation. Early in the menstrual cycle, a woman with low hormone level who is not ovulating have daily human menopausal gonadotropin or recombinant human FSH injections for the average of 12 days. This helps in the development of mature follicle making the ovary ready to ovulate. One dose of human chorionic gonadotropin is then used to stimulate ovulation.

2. The cessation and lack of menstruation for at least 3month is a condition known as amenorrhea. Amenorrhea is a normal feature in pre-puberty, pregnant and postmenopausal females. In a woman of about 24years, diagnosing amenorrhea is a matter of first determining whether pregnancy is the etiology. In the absence of pregnancy, the challenge is to determine the exact cause of lack of menses. Amenorrhea is classified into primary and secondary amenorrhea

Primary amenorrhea is the failure of menses to occur by age 16years, in the presence of normal growth and secondary sexual characteristics

Secondary amenorrhea is defined as absence of periodic menstruation for at least 6 months in women who have previously experienced menses. The 24 years woman may be suffering from secondary amenorrhea.

Causes of secondary amenorrhea

- Weight loss/anorexia
- Non-specific hypothalamic
- Chronic anovulation including PCOS
- Hypothyroidism
- Cushing syndrome
- Pituitary tumor
- Polycystic ovarian syndrome
- Ovarian tumor

Evaluation of secondary amenorrhea

i. History: includes a complete description of menstrual patterns, medications prescribed, nutritional history, patterns of exercise, previous contraceptive use, weight changes, stress and chronic disease.
ii. Microscopic, culture and sensitive.

Pregnancy is the most common cause of secondary amenorrhea. A pregnancy test (measurement of serum or urinary human chorionic gonadotropin) is recommended as a first step in evaluation of a secondary amenorrhea.

After pregnancy testing, all women who present with 3 months of secondary amenorrhea should have a diagnostic evaluation initiated at that visit. A complete blood cell count, urinalysis, and serum chemistries should be evaluated to help rule out systemic disease. Serum prolactin, FSH, estradiol, and thyrotropin levels should also be measured routinely in the initial evaluation of amenorrhea once pregnancy has been excluded. In the future, determination of anti-müllerian hormone levels may become the preferred initial test for diagnosing PCOS.

iii. Pelvic ultrasonography may identify congenital abnormalities of the uterus, cervix, and vagina, or absence of these organs. Magnetic resonance imaging can detect hypothalamic/pituitary lesions. Hysterosalpingography and hysteroscopy are indicated in cases of possible Asherman syndrome.

iv. Hormonal studies may include assays of prolactin, FSH, LH, estradiol, thyroid hormones, or androgens.

- Prolactin levels in excess of 200 ng/mL are not observed except in the case of prolactin-secreting pituitary adenoma (prolactinoma) or anti-depressants such as Risperidone. Psychotropic drugs, hypothyroidism, stress, and meals can also raise prolactin levels. FSH, LH, and estradiol
- An FSH level of approximately 40 mIU/mL is indicative of ovarian insufficiency. If a repeat value in 1 month confirms this finding and amenorrhea still persists, then the diagnosis of premature ovarian failure/primary ovarian insufficiency is confirmed.
- LH levels are elevated in cases of 17, 20 lyase deficiency, 17-hydroxylase deficiency, and premature ovarian failure.
- Serum estradiol levels undergo wide fluctuations during the normal menstrual cycle. During the early follicular phase of the menstrual cycle, levels may be lower than 50 pg/mL. During the preovulatory estradiol surge, levels in the range of 400 pg/mL are not uncommon. In healthy menopausal women, estradiol levels are routinely lower than 20 pg/mL.
- Thyroid hormones: Disorders of the thyroid gland may result in menstrual irregularities, measure thyrotropin and free thyroxine (T4) if symptoms of hypothyroidism or hyperthyroidism are present.
- Androgens: Checking levels of testosterone and dehydroepiandrosterone sulfate helps identify hyperandrogenic conditions resulting in amenorrhea.

2b. If the woman is 60years, she could have attained the menopausal stage. Menopause is defined as the permanent cessation of menstruation resulting from loss of ovarian follicular activity. It begins with the ovaries failing to produce adequate amounts of estrogen and inhibin as a result, gonadotropin production is increased in a continued attempt to stimulate the ovary. Hormonal changes begin about 5 years before the actual menopause, as the response of the ovary to gonadotropins begins to decrease and menstrual cycles become increasingly irregular. The term perimenopausal refers to the time interval from onset of these menstrual irregularities to menopause itself. This transition phase will last from 2 to 8 years. At this time, FSH concentrations increase and E2 concentrations decrease, whereas LH and progesterone

concentrations remain unchanged, indicating that menstrual cycles remain ovulatory. As estrogen continues to decline, an associated decrease in prolactin concentrations is noted. The decrease in estrogen concentrations gives rise to vasomotor instability and so-called “hot flashes.” After menopause, the ovary continues to produce androgens, particularly testosterone and androstenedione, as a result of increased LH concentrations. In addition, the adrenal gland continues to secrete androgens. The resulting decrease in the estrogen/androgen ratio is the cause of the hirsutism seen in some postmenopausal women.

3a. 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 refers to couples or patients who have had no previous successful pregnancies. Secondary infertility encompasses patients who have previously conceived but are currently unable to conceive.

Cause of infertility

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
	Postsurgical

Investigation of infertility

- History

Male

A history of drug or alcohol abuse, frequent hot-tub baths, excess stress, occupation, fatigue, medical conditions, excessive or infrequent coitus should be elicited.

Female

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

- Laboratory tests

Specific male fertility tests may include:

Semen analysis: Semen is generally obtained by masturbating or by interrupting intercourse and ejaculating your semen into a clean container. Semen analysis measures ejaculate volume, pH, sperm count, motility, forward progression, and morphology. Semen
should be analyzed within 1 hour after collection.

Hormone testing: level of testosterone and other male hormones.

Genetic testing. Genetic testing may be done to determine whether there's a genetic defect causing infertility.

Testicular biopsy. In select cases, a testicular biopsy may be performed to identify abnormalities contributing to infertility or to retrieve sperm for assisted reproductive techniques, such as IVF.

Imaging. In certain situations, imaging studies such as a brain MRI, transrectal or scrotal ultrasound, or a test of the vas deferens (vasography) may be performed.

Other specialty testing. In rare cases, other tests to evaluate the quality of the sperm may be performed, such as evaluating a semen specimen for DNA abnormalities.

Specific female fertility tests may include:

Ovulation testing: measurement of hormone levels to determine whether ovulation occurs or not.

Hysterosalpingography: Hysterosalpingography evaluates the condition of the uterus and fallopian tubes and looks for blockages or other problems. X-ray contrast is injected into your uterus, and an X-ray is taken to determine if the cavity is normal and to see if the fluid spills out of your fallopian tubes.

Ovarian reserve testing. This testing helps determine the quantity of the eggs available for ovulation. This approach often begins with hormone testing early in the menstrual cycle.

Other hormone testing. Other hormone tests check levels of ovulatory hormones, as well as pituitary hormones that control reproductive processes.

Imaging tests. Pelvic ultrasound looks for uterine or ovarian disease. Sometimes a sonohysterogram, also called a saline infusion sonogram, is used to see details inside the uterus that are not seen on a regular ultrasound.

Hysteroscopy: this involve the insertion of a thin, lighted device through the cervix into the uterus to view any potential abnormalities.

Laparoscopy. This minimally invasive surgery involves making a small incision beneath the navel and inserting a thin viewing device to examine the fallopian tubes, ovaries and uterus. A laparoscopy may identify endometriosis, scarring, blockages or irregularities of the fallopian tubes, and problems with the ovaries and uterus.

3b. To achieve conception in expectant couple, the couple will be encouraged to attend a counselling section where necessary treatment would be taken, such as:

- 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, break from work 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.