ORIFE EMMANUELLA

15/MHS06/052

MLS 514

1a. The anterior pituitary often is referred to as the “master gland” because, together with the hypothalamus, it orchestrates the complex regulatory functions of many other endocrine glands. A major organ of the endocrine system, the anterior pituitary (also called the adenohypophysis or pars anterior) is the glandular, anterior lobe that together with the posterior lobe (posterior pituitary, or the neurohypophysis) makes up the pituitary gland (hypophysis). The anterior pituitary regulates several physiological processes, including stress, growth, reproduction, and lactation. The pituitary gland is a small gland that sits in the sella turcica (‘Turkish saddle’), a bony hollow in the base of the skull, underneath the brain and behind the bridge of the nose. The pituitary gland has two main parts, the anterior pituitary gland and the posterior pituitary gland. The anterior pituitary contains five types of endocrine cell, and they are defined by the hormones they secrete: somatotropes (GH); Lactotropes (PRL); gonadotropes (LH and FSH); corticotropes (ACTH) and thyrotropes (TSH).[6] It also contains non-endocrine folliculostellate cells which are thought to stimulate and support the endocrine cell populations. The anterior pituitary gland produces six major hormones which are;

• Adrenocorticotropic Hormone (ACTH): It is a polypeptide, it acts on the adrenal gland and makes it secretes glucorticoid, mineralocorticoid and androgens as an effect. It triggers the adrenals to release the hormone cortisol, which regulates carbohydrate, fat, and protein metabolism and blood pressure. The adrenal glands sit above the kidneys and are also responsible for the body's fight or flight response.

• Thyroid Stimulating Hormone (TSH): it is a glycoprotein causes the thyroid gland to produce and release thyroid hormones. Thyroid hormone controls the basal metabolic rate and plays an important role in growth and maturation. Thyroid hormones affect almost every organ in the body.

• Growth hormone (GH): It is a polypeptide, made up of cells known as somatotrophs. It is released when anterior pituitary when acted on by the growth hormone releasing hormone. GH is essential in early years to maintaining a healthy body composition and for growth in children. In adults, it aids healthy bone and muscle mass and affects fat distribution.

• Prolactin: It is a polypeptide made up of cells known as lactotrophs. When released by the anterior pituitary. Stimulates the breasts to produce milk. This hormone is secreted in large amounts during pregnancy and breast feeding, but is present at all times in both men and women.

• Leutinizing Hormone (LH): It is a glycoprotein made up of gonadotrophs. It is released by the anterior pituitary when acted on by the gonadotrophin releasing hormone from the hypothalamus. LH acts on the gonads which leads to the production of sex hormones.

• Follicle-stimulating hormone (FSH): It is a glycoprotein made up of gonadotrophs. It is released by the anterior pituitary when acted on by the gonadotrophin releasing hormone from the hypothalamus. Stimulates the growth of follicles in the ovaries and sperm development in the testes. In females, as the follicle grows and matures, the egg is readied for ovulation.

1b. Letrozole: Letrozole is an aromatase inhibitor which prevents the conversion of androgen to estrogen. It also improves endometrial thickness and encourages healthy ovarian follicular development. While not approved by the FDA for this use, it has been shown to induce ovulation in women who do not ovulate. For this reason, some infertility specialists are using the drug in women who cannot tolerate or who do not respond well to Clomid. Letrozole is a drug that is commonly used to treat estrogen-dependent tumors, particularly breast cancer in older, post-menopausal women. Letrozole is used treat early breast cancer in women who have experienced menopause (change of life; end of monthly menstrual periods) and who have had other treatments, such as radiation or surgery to remove the tumor. It is also used to treat early breast cancer in women who have experienced menopause and who have already been treated with a medication called tamoxifen (Nolvadex) for 5 years. Letrozole is also used in women who have experienced menopause as a first treatment of breast cancer that has spread within the breast or to other areas of the body or in women whose breast cancer has worsened while they were taking tamoxifen. Letrozole is in a class of medications called nonsteroidal aromatase inhibitors. It works by decreasing the amount of estrogen produced by the body. This can slow or stop the growth of some types of breast cancer cells that need estrogen to grow. It has the potential to enhance FSH release, not by the inhibiting estradiol-receptor interaction, but rather by inhibition of estradiol synthesis. One such inhibitor, letrozole, was approved for use in 1997 for the treatment of breast cancer. By 2001, it had been used in anovulatory women with great success, and at present the drug is extremely popular among physicians and patients in the treatment of both ovulation dysfunction and for controlled ovarian hyperstimulation: the drug has a half-life of only 45 hours, and side effects, while similar to those of clomiphene, are far milder and less frequent.

Clomiphene: Clomifene, also known as clomiphene, is a medication used to treat infertility in women who do not ovulate. Clomiphene is a long trusted oral medication relied upon for its safety, effectiveness and relatively low cost. Clomiphene is used to treat absent or irregular menstrual cycles (ovulation induction), to address a condition called luteal phase defect by increasing progesterone secretion during the second half of the cycle and to make menstrual cycle lengths more predictable, thus improving the timing of intercourse or artificial insemination. Clomiphene may also be used to enhance ovulation in women who are already ovulating. Clomiphene triggers the brain's pituitary gland to secrete an increased amount of follicle stimulating hormone (FSH) and LH (luteinizing hormone). This action stimulates the growth of the ovarian follicle and thus initiates ovulation. During a normal menstrual cycle only one egg is ovulated. The use of clomiphene often causes the ovaries to produce two or three eggs per cycle. Clomiphene is taken orally for 5 days and is active only during the month it is taken.

Menotrophin: Menotropin (also called human menopausal gonadotropin or hMG) is a hormonally active medication for the treatment of fertility disturbances. Menotropins are a standardized mixture of follicle-stimulating hormones and luteinizing hormones. These chemicals are derived from the urine of postmenopausal women. Clomiphene is a synthetic ovulation stimulant. Urine of postmenopausal women reflects the hypergonadotropic state of menopause -levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH) are high - and contain a mixture of these gonadotropins. It is used when clomiphene is not effective

For induction of ovulation and assisted reproductive technologies (ART): Menotropins prepare the ovarian follicle for ovulation. The combination of FSH and LH stimulates follicular growth and maturation. Chorionic gonadotropin, whose actions are nearly identical to those of LH, is administered following menotropins treatment to mimic the naturally occurring surge of LH that triggers ovulation.

2a. Menstruation, also known as a period or monthly, is the regular discharge of blood and mucosal tissue (known as menses) from the inner lining of the uterus through the vagina.

This condition is called Amenorrhea. Amenorrhea may be defined as the absence of menstruation for 3 or more months in women with past menses (i.e., secondary amenorrhea) or the absence of menarche by the age of 15 years in girls who have never menstruated (i.e., primary amenorrhea). Amenorrhea (absence of menses) can be a transient, intermittent, or permanent condition resulting from dysfunction of the hypothalamus, pituitary, ovaries, uterus, or vagina. In this case the 24years of woman has a condition called the secondary amenorrhea. This is the more common form of amenorrhea. Amenorrhea indicates failure of the hypothalamic-pituitary-gonadal axis to induce cyclic changes in the endometrium that normally result in menses and also may result from the absence of end organs or from obstruction of the outflow tract. Symptoms may include; Milky nipple discharge, hair loss, headache, vision changes, excess facial hair and pelvic pain. Causes of secondary amenorrhea may include; malnutrition, anorexia nervosa, exercising too much, polycystic ovary syndrome (PCOS), ovarian cancer, noncancerous ovarian cysts, uterine scarring from D and C (dilation and curettage), removal of the ovaries or uterus, issues with the thyroid gland, hormonal imbalances etc.

Laboratory findings;

1. Pregnancy test would be negative. This is done to rule out pregnancy especially in cases of secondary amenorrhea.
2. Thyroid stimulating hormone (TSH) and prolactin levels are estimated if the prolactin level is normal and TSH is abnormal this could be as a result of a thyroid disease, if TSH is normal and the prolactin level is ˃ 100ng per mL, a magnetic resonance imaging (MRI) is performed to evaluate for prolactinoma.
3. Elevated follicle-stimulating hormone (FSH) or luteinizing hormone (LH) levels suggest an ovarian abnormality (hypergonadotropic hypogonadism). Normal or low FSH or LH levels suggest a pituitary or hypothalamic abnormality (hypogonadotropic hypogonadism).
4. Basal plasma gonadotropins: Basal plasma gonadotropins in patients of amenorrhea include:
* Reduced luteinizing hormone (LH) and FSH, suggestive of hypothalamic and pituitary diseases or premature ovarian failure.
* Reduced LH, suggestive of complete androgen insensitivity syndrome.
1. Dehydroepiandrosterone sulfate (DHEAS): Some patients with amenorrhea may have elevated concentration of dehydroepiandrosterone sulfate (DHEAS), which is usually suggestive of amenorrhea due to polycystic ovary syndrome (PCOS).
2. Fasting glucose (FBS): Some patients with amenorrhea may have elevated concentration of fasting glucose (FBS), which is usually suggestive of amenorrhea due to polycystic ovary syndrome (PCOS).

2b. This condition is known as menopause. Menopause occurs when a woman has not menstruated in 12 consecutive months and can no longer become pregnant naturally. It usually begins between the ages of 45 and 55, but can develop before or after this age range. Menopause is a natural process that occurs as the ovaries age and produce less reproductive hormones. The body begins to undergo several changes in response to lower levels of estrogen, progesterone, testosterone, follicle-stimulating hormone (FSH), luteinizing hormone (LH). Signs and symptoms may include; Irregular periods, vaginal dryness, hot flashes, chills, night sweats, sleep problems, mood changes etc. Causes of menopause include; Natural decline of reproductive hormones, hysterectomy, chemotherapy and radiation therapy and Primary ovarian insufficiency.

Laboratory findings;

* FSH levels increase and estradiol levels decrease as menopause occurs
* Thyroid-stimulating hormone (TSH), because an underactive thyroid (hypothyroidism) can cause symptoms similar to those of menopause

3a. Infertility is defined as the inability of a couple to conceive after one year of unprotected intercourse. Many factors can affect fertility, including the presence of sperm and egg at the right time in a receptive environment. Tests can evaluate these different aspects of fertility.

**INVESTIGATION OF MALE INFERTILITY**

Diagnosing male infertility problems usually involves:

* **General physical examination:** this includes overall body habitus (e.g obesity, muscular development, and virilisation). Location, size and consistency of the testes and presence and absence of ductal structures.
* **Medical history:** this includes medical illness and medications, surgical interventions in the past, sexual ability/ limitation, lifestyle factors (smoking drinking), supplement usage (vitamins, oral antioxidant) and history of malignancy.
* **Semen analysis:** A sample is studied with a microscope to determine the number of sperm, the appearance of the sperm, and the ability of the sperm to move. A low sperm count decreases fertility.
* **Hormone testing:** Hormones produced by the pituitary gland, hypothalamus and testicles play a key role in sexual development and sperm production. Abnormalities in other hormonal or organ systems also might contribute to infertility. A blood test measures the level of testosterone and other hormones.
* **Post-ejaculation urinalysis:** Sperm in the urine can indicate that the sperm are traveling backward into the bladder instead of out the penis during ejaculation (retrograde ejaculation).
* **Genetic tests:** When sperm concentration is extremely low, there could be a genetic cause. A blood test can reveal whether there are subtle changes in the Y chromosome which are signs of a genetic abnormality. Genetic testing might be ordered to diagnose various congenital or inherited syndromes e.g Klinefelter’s syndrome (47 XXY chromosome makeup instead of 46XY).
* **Testicular biopsy:** This test involves removing samples from the testicle with a needle. If the results of the testicular biopsy show that sperm production is normal, the problem is likely caused by a blockage or another problem with sperm transport
* **Transrectal ultrasound:** A small, lubricated wand is inserted into the rectum. It allows the doctor to check the prostate and look for blockages of the tubes that carry semen (ejaculatory ducts and seminal vesicles).
* **Chlamydia test:** Chlamydia can affect fertility, but antibiotics can treat it.

**INVESTIGATION OF FEMALE INFERTILITY**

* **Medical history:** this includes medical illness and medications, surgical interventions in the past, sexual ability/ limitation, lifestyle factors (smoking drinking), supplement usage (vitamins, oral antioxidant) and history of malignancy.
* **Ovulation testing:** An at-home, over-the-counter ovulation prediction kit detects the surge in luteinizing hormone (LH) that occurs before ovulation. A blood test for progesterone can also show if someone is ovulating. Other hormone levels, such as prolactin, also may be checked.
* **Hysterosalpingography:** Fluid is injected into the woman’s uterus and X-rays are taken to determine whether the fluid travels properly out of the uterus and into the fallopian tubes. If a blockage is present, surgery may be necessary.
* **Thyroid function test:** This may affect the hormonal balance
* **Genetic testing:** Genetic testing helps determine whether there is a genetic defect causing infertility. Some patients carry genetic diseases that can cause infertility, such as Fragile X syndrome. Some women can have rearrangements of their chromosomes such that their eggs and sperm can have abnormal chromosomes and this can lead to repeated miscarriage or infertility. These problems are rare but do exist.
* **Ovarian reserve testing:** This testing helps determine the quality and quantity of eggs available for ovulation.

3b. Surgery, medication, and assisted reproductive technology (ART) can help couples achieve conception. Assisted reproductive technology (ART) refers to any fertility treatment or procedure for assisting reproduction that includes the handling of human eggs, sperms or embryos. ART falls into the category of field endocrinology and cryopreservation, reproductive technology and infertility treatments. ART procedures involve surgically removing eggs from woman ovaries, combining them with sperm in the laboratory and returning them to the woman’s body or donating them to another woman. There are several forms of assisted reproductive technology and they include;

* **In vitro fertilization (IVF):** In vitro fertilization is a technique which involves fertilization outside the body in an artificial environment. Sperm are placed with unfertilized eggs in a petri dish, where fertilization can take place. The embryo is then placed in the uterus to begin a pregnancy. Sometimes the embryo is frozen for future use.
* **Intracytoplasmic sperm injection (ICSI):** Intracytoplasmic sperm injection (ICSI) is the injection of single mature immobilized normal spermatozoa into the cytoplasm of a mature metaphase II oocyte. This procedure is most commonly used to overcome male infertility problems, although it may also be used where eggs cannot easily be penetrated by sperm and occasionally in addition to sperm donation. ICSI is the technique of choice in cases of obstructive azoospermia since it enables the best use of micro surgically retrieved spermatozoa from the epididymis or testis.
* **Intrauterine insemination:** Intrauterine Insemination (IUI) is a fertility treatment that involves placing sperm inside a woman’s uterus to facilitate fertilization. The goal of IUI is to increase the number of sperm that reach the fallopian tubes and subsequently increase the chance of fertilization.
* **Surrogacy:** Surrogacy is an arrangement, often supported by a legal agreement, whereby a woman (the surrogate mother) agrees to bear a child on behalf of another person who is will become the parent of the child. Surrogacy is considered one of many assisted reproductive technologies. Surrogacy may be either traditional or gestational, which are differentiated by the genetic origin of the egg.
* **Sperm or egg donation:** If necessary, sperm or eggs can be received from a donor. Fertility treatment with donor eggs is usually done using IVF.

Other assisted reproductive technology may include;

* Zygote intrafallopian transfer (ZIFT)
* Gamete intrafallopian transfer (GIFT)
* Artificial embryo twinning
* Embryo donation