**NAME: MICHEAL CHISOM IMMACULATE**

**DEPARTMENT: PHARMACOLOGY**

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**COURSE: PHA 306 ENDOCRINE AND REPRODUCTIVE SYSTEM PHARMACOLOGY**

**ASSIGNMENT: 1. WRITE ON ESTROGEN AND PROGESTIN**

 **2. ANTIFERTILITY DRUGS**

 **ESTROGEN**

**Estrogen**, any of a group of [hormones](https://www.britannica.com/science/hormone) that primarily influence the female reproductive tract in its development, maturation, and function. There are three major hormones—estradiol, estrone, and estriol—among the estrogens, and estradiol is the predominant one.

Estrogen is a hormone that plays various roles in the body. In females, it helps develop and maintain both the reproductive system and female characteristics, such as breasts and pubic hair.

The major sources of estrogens are the [ovaries](https://www.britannica.com/science/ovary-animal-and-human) and the [placenta](https://www.britannica.com/science/placenta-human-and-animal) (the temporary [organ](https://www.britannica.com/science/organ-biology) that serves to nourish the [fetus](https://www.britannica.com/science/fetus) and remove its wastes); additional small amounts are secreted by the [adrenal glands](https://www.britannica.com/science/adrenal-gland) and by the male [testes](https://www.britannica.com/science/testis). It is believed that the [egg](https://www.britannica.com/science/egg-biology) follicle (the saclike structure that holds the immature egg) and interstitial cells (certain cells in the framework of [connective tissue](https://www.britannica.com/science/connective-tissue)) in the [ovaries](https://www.britannica.com/science/ovary-animal-and-human) are the actual production sites of estrogens in the female. Estrogen levels in the bloodstream seem to be highest during the egg-releasing period ([ovulation](https://www.britannica.com/science/ovulation)) and after [menstruation](https://www.britannica.com/science/menstruation), when tissue called the [corpus luteum](https://www.britannica.com/science/corpus-luteum) replaces the empty egg follicle.

**Types of estrogen**

There are different types of estrogen:

* Estradiol is produced in women of childbearing age, mostly by the ovaries.
* Estriol is the main estrogen produced during pregnancy, mostly in the placenta.
* Estrone, produced by the adrenal glands and fatty tissue, is the only type of estrogen produced after menopause.

**Fuction of estrogen**

Estrogen enables the following organs to function:

**Ovaries:** Estrogen [helps stimulate](https://www.britannica.com/science/estrogen) the growth of the egg follicle.

**Vagina:** In the vagina, estrogen [maintains the thickness](https://www.ncbi.nlm.nih.gov/books/NBK538260/) of the vaginal wall and promotes lubrication.

**Uterus:** Estrogen enhances and maintains the mucous membrane that lines the uterus. It also regulates the flow and thickness of uterine mucus secretions.

**Breasts:** The body uses estrogen in the formation of breast tissue. This hormone also helps stop the flow of milk after weaning.

## Synthesis and secretion of estrogen

[Cholesterol](https://www.britannica.com/science/cholesterol) is the parent [molecule](https://www.britannica.com/science/molecule) from which all ovarian [steroid](https://www.britannica.com/science/steroid) hormones are formed. Cholesterol is converted to pregnenolone, and pregnenolone is converted to [progesterone](https://www.britannica.com/science/progesterone). The steps in the conversion of progesterone to the main estrogens—estradiol and estrone—include the intermediate formation of several [androgens](https://www.britannica.com/science/androgen) (male [sex](https://www.britannica.com/science/sex) hormones): dehydroepiandrosterone, androstenedione, and [testosterone](https://www.britannica.com/science/testosterone). In short, androgens are [precursors](https://www.merriam-webster.com/dictionary/precursors) of estrogens; they are converted to estrogens through the action of an [enzyme](https://www.britannica.com/science/enzyme) known as [aromatase](https://www.britannica.com/science/aromatase). The ovaries are the richest source of aromatase, although some aromatase is present in [adipose tissue](https://www.britannica.com/science/adipose-tissue), which is also an important source of estrogen in postmenopausal women. [Estradiol](https://www.britannica.com/science/estradiol), the most potent estrogen, is synthesized from testosterone. [Estrone](https://www.britannica.com/science/estrone) can be formed from estradiol, but its major [precursor](https://www.merriam-webster.com/dictionary/precursor) is androstenedione. [Estriol](https://www.britannica.com/science/estriol), the weakest of the estrogens, is formed from both estrone and estradiol.

Once secreted into the [blood](https://www.britannica.com/science/blood-biochemistry), estrogens bind reversibly to a [protein](https://www.britannica.com/science/protein) known as sex hormone-binding [globulin](https://www.britannica.com/science/globulin). Thus, some of the [hormone](https://www.britannica.com/science/hormone) in [serum](https://www.britannica.com/science/serum) is bound and some is free, or unbound. At its target tissues, the free hormone penetrates the [cell](https://www.britannica.com/science/cell-biology) surface and then binds to a protein known as an estrogen [receptor](https://www.britannica.com/science/receptor-nerve-ending) in the [cytoplasm](https://www.britannica.com/science/cytoplasm) of the cells. The estrogen-receptor complexes enter the cell [nucleus](https://www.britannica.com/science/nucleus-biology), where they modulate [protein synthesis](https://www.britannica.com/science/translation-genetics) by influencing the rate at which particular [genes](https://www.britannica.com/science/gene) are transcribed. Gene transcription is the process by which [DNA](https://www.britannica.com/science/DNA) (deoxyribonucleic acid) codes for certain proteins by producing specific molecules of [messenger RNA](https://www.britannica.com/science/messenger-RNA) (ribonucleic acid) that direct the synthesis of those [proteins](https://www.britannica.com/science/protein). In the case of estrogens, there are two types of cytoplasmic receptors—estrogen receptor-alpha and estrogen receptor-beta—that have a different tissue distribution but similar capacities to activate DNA synthesis.

**Levels of estrogen**

Estrogen levels vary among individuals. They also fluctuate during the menstrual cycle and over a female’s lifetime. This fluctuation can sometimes produce effects such as mood changes before menstruation or hot flashes in menopause.

Factors that can affect estrogen levels includes:

* pregnancy, the end of pregnancy, and breastfeeding
* puberty
* menopause
* older age
* overweight and [obesity](https://www.medicalnewstoday.com/info/obesity/how-much-should-i-weigh.php)
* extreme dieting or [anorexia nervosa](https://www.medicalnewstoday.com/articles/267432.php)
* strenuous exercise or training
* [high blood pressure](https://www.medicalnewstoday.com/articles/159283.php)
* [diabetes](https://www.medicalnewstoday.com/info/diabetes/)
* polycystic ovary syndrome (PCOS)
* tumors of the ovaries or adrenal glands

**Estrogen imbalance**

An imbalance of estrogen [leads to](https://www.hormone.org/hormones-and-health/hormones/estrogen):

* irregular or no menstruation
* light or heavy bleeding during menstruation
* low sexual desire
* vaginal dryness and vaginal atrophy
* [fatigue](https://www.medicalnewstoday.com/articles/248002.php)
* mood swings
* feelings of [depression](https://www.medicalnewstoday.com/articles/8933.php) and [anxiety](https://www.medicalnewstoday.com/articles/323454)
* dry skin

Some of these effects are common during menopause. Some hereditary and other conditions can lead to high levels of estrogen in males, which can result in:

* [infertility](https://www.medicalnewstoday.com/articles/165748.php)
* [erectile dysfunction](https://www.medicalnewstoday.com/articles/5702.php)
* larger breasts, known as gynecomastia

Males with low estrogen levels may have excess belly fat and low libido.

**Estrogen therapy**

Estrogen therapy can help manage menopause symptoms as part of hormone therapy, which people usually refer to as [hormone replacement therapy](https://www.medicalnewstoday.com/articles/181726).

The treatment may consist solely of estrogen (estrogen replacement therapy, or ERT), or it may involve a combination of estrogen and progestin, a synthetic form of progesterone.

Hormone treatment is available as a pill, nasal spray, patch, skin gel, injection, vaginal cream, or ring.

It can help manage: hot flashes, vaginal dryness, painful intercourse, mood changes, sleep disorders, anxiety and decreased sexual desire.

It may also help reduce the risk of osteoporosis, which increases when people enter [menopause](https://www.medicalnewstoday.com/articles/155651).

**Side effects** [**include**](https://www.nhs.uk/conditions/hormone-replacement-therapy-hrt/side-effects/)**:**

* bloating
* breast soreness
* headaches
* leg cramps
* indigestion
* nausea
* fluid retention, leading to swelling

 **PROGESTIN**

Progestins are synthetic steroid hormones that activate the progesterone receptor in a similar way to progesterone but each individual progestin has its own distinctive effect.

Progestin are used to treat amenorrhea, premenstrual tension and abnormal uterine bleeding. As they prevent ovulation, progestins are a major constituent of oral contraceptives and other forms of contraception. Progestins can also act to decrease levels of some hormones so can be used to treat hormonally sensitive cancers, for transgender hormone suppression and for precocious puberty.

**Uses of progestin**

Uses for progestin include treatment for:

**•** Birth control

• Hormone replacement therapy

• Menstrual disorders

• Abnormal uterine bleeding

• Amenorrhea, or absence of menstruation

• Endometriosis

• Endometrial hyperplasia, an abnormal thickening of the uterus wall

• Breast, kidney, or uterine cancer

• Changes in hair growth

• Changes in sexual desire

• Anticancer hormonal therapy

• Breast pain

• Preventing premature birth

• Acne

• Infertility treatment, when used as a cream

• Breastmilk production

**Mechanism of action**

Similar to estrogens, but binds to different receptors in the cytoplasm or nucleus which then interact with progesterone-response elements to activate gene transcription.

progestins work as contraceptives via negative feedback on GnRH release.

**Physiological effects of progestin**

• Promote secretory activity of endometrium “primed” by estrogen

• Negative feedback on anterior pituitary release of FSH and LH, this prevents follicular maturation & ovulation

• Important (along with estrogen) in breast development & lactation

• The cause of mid-cycle increase in body temperature at ovulation

**Indications for progestins (synthetic):**

• Contraception - most commonly used in combination with estrogens

• Progestin only “mini pills” are not as effective as combination pills

• Control of functional uterine bleeding

• Management of endometriosis (ectopic endometrial tissue)

• Management of dysmenorrhea (painful menstruation)

**Pharmacokinetics**:

progesterone itself is rapidly metabolized, which limits its use as a therapeutic agent.

synthetic progestins are not rapidly inactivated by first pass metabolism, and can be administered orally.

**Side Effects**:

• weight gain

• Edema

• Depression

• Pulmonary embolism

• The more potent progestins, if used for a long period of time, will decrease HDL levels and lead to atherosclerosis.

 **ANTIFERTILITY DRUGS**

These are the chemical substances used to control the pregnancy. These are also called oral contraceptives. The basic aim of antifertility drugs is to prevent conception or fertilization.

Oral contraceptives belong to the class of natural products known as steroids.These control the female menstrual cycle and ovulation. The birth control pills are essentially a mixture of esterogen and progesterone derivatives which are more potent than the natural hormones.These common pills are used for a combination of progesterone, norethindrone and estrogen ethynylestradiol.

#### Benefits of antifertility drugs

Antifertility drugs generally do not have many side effects, weight gain is the only issue known to be reported. These drugs are very useful if taken in proper dose, following are its significant benefits:

1. They cause no interference in sexual activities and risk of pregnancy is reduced.

2. They might cause reduction in menstrual bleeding.

3. They can be taken immediately after childbirth.

**Classification of antifertiity drugs**

**GnRH antagonist**: Either Gonadotropin releasing hormone or any Gonadotropin releasing hormone agonist may be used. GnRH stimulates the release of gonadotropins from the pituitary in the body.

**Estrogen antagonist**: fertility medication inhibiting in the effects of estrogen includes clomiphene and aromatase inhibitors.

**Clomiphene:** It is a selective estrogen receptor modulation. It is the most widely used fertility drug.

**Aromatises inhibitors**: Although primarily a breast cancer treatment, aromatase inhibitors can also work as fertility medication, probably through a mechanism similar to clomiphene.

**Gonadotropins:** Gonadotropins are the hormones in the body that normally stimulate the gonad. For medication, they can be extracted from urine or by genetic modification. For example, the so called menotropins consist of LH and FSH extracted from human from menopausal woman.

**Human chorionic gonadotropin (Hcg):** hcG is normally produced during pregnancy. However it can also replace LH as an ovulation inducer.

**Other:** Hmg is a medication containing a follicle stimulating hormone and lutenizing.

**Methods for female**

Female antifertility agents might be acting through following mechanism:

* inhibition of ovulation
* prevention of fertilization
* interference with transport of ova from oviduct to endometrium of the uterus
* interference with the implication of fertilizes ovum
* distraction of early implanted embryo.