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**ESTROGEN**

Estrogen, or oestrogen, is the primary female [sex hormone](https://en.wikipedia.org/wiki/Sex_steroid). It is responsible for the development and regulation of the female [reproductive system](https://en.wikipedia.org/wiki/Reproductive_system) and [secondary sex characteristics](https://en.wikipedia.org/wiki/Secondary_sex_characteristic). Estrogen contributes to [cognitive health](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4491541/), bone health, the function of the [cardiovascular system](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3398381/), and other essential bodily processes.

However, most people know it for its role alongside [progesterone](https://www.medicalnewstoday.com/articles/277737.php) in female sexual and reproductive health. The ovaries, adrenal glands, and fat tissues produce estrogen. Both female and male bodies have this hormone, but females create more of it. Like all [steroid hormones](https://en.wikipedia.org/wiki/Steroid_hormone), estrogens readily [diffuse](https://en.wikipedia.org/wiki/Diffusion) across the [cell membrane](https://en.wikipedia.org/wiki/Cell_membrane). Once inside the cell, they bind to and activate [estrogen receptors](https://en.wikipedia.org/wiki/Estrogen_receptor) (ERs) which in turn [modulate](https://en.wikipedia.org/wiki/Regulation_of_gene_expression) the [expression](https://en.wikipedia.org/wiki/Gene_expression) of many [genes](https://en.wikipedia.org/wiki/Gene). Estrogens also have important actions in males, including effects on bone, spermatogenesis, and behavior. Estrogens and progestins are used in menopausal hormone therapy (MHT) and contraception in women. Estrogen- and progesterone-receptor antagonists also are available. Antiestrogens are employed in treating hormone-responsive breast cancer and infertility. The main use of antiprogestins has been for medical abortion. Selective estrogen receptor modulators (SERMs) with tissue-selective agonist or antagonist activities are increasingly available.

Types of Estrogen

There are different types of estrogen:

1. Estrone

This type of estrogen is present in the body [after menopause](https://www.hormone.org/your-health-and-hormones/glands-and-hormones-a-to-z/hormones/estrone). It is a weaker form of estrogen and one that the body can convert to other forms of estrogen, as necessary.

1. Estradiol

Both males and females produce estradiol, and it is the most common type of estrogen in females during their reproductive years.

[Too much](https://www.hormone.org/your-health-and-hormones/glands-and-hormones-a-to-z/hormones/estradiol) estradiol may result in acne, loss of sex drive, osteoporosis, and depression. Very high levels can increase the risk of uterine and breast cancer. However, low levels can result in weight gain and cardiovascular disease.

1. Estriol

Levels of estriol rise [during pregnancy](https://www.hormone.org/your-health-and-hormones/glands-and-hormones-a-to-z/hormones/estriol), as it helps the uterus grow and prepares the body for delivery. Estriol levels peak just before birth.

Physiological and Pharmacological Actions

DEVELOPMENTAL ACTIONS

Estrogens in girl’s cause growth and development of the vagina, uterus, and fallopian tubes, and contribute to breast enlargement, molding the body con- tours, shaping the skeleton, and causing the pubertal growth spurt of the long bones and epiphyseal closure. Growth of axillary and pubic hair, pigmentation of the genital region, and the regional pigmentation of the nipples and areolae that occur after the first trimester of pregnancy are also estrogenic actions.

Estrogens also play developmental roles in males. In boys, estrogen deficiency diminishes the pubertal growth spurt and delays skeletal maturation and epiphyseal closure so that linear growth continues into adulthood. Estrogen deficiency in men leads to elevated gonadotropins, macroorchidism, and increased testosterone levels and also may affect carbohydrate and lipid metabolism and fertility.

NEUROENDOCRINE CONTROL OF THE MENSTURAL CYCLE

A neuroendocrine cascade involving the hypothalamus, pituitary, and ovaries controls the menstrual cycle. A neuronal oscillator or “clock” in the hypothalamus fires at intervals that coincide with bursts of gonadotropin-releasing hormone (GnRH) release into the hypothalamic-pituitary portal vasculature. GnRH interacts with its receptor on pituitary gonadotropes to cause release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). The frequency of the GnRH pulses, which varies in the different phases of the menstrual cycle controls the relative secretion of FSH and LH.

The gonadotropins (LH and FSH) regulate the growth and maturation of follicles in the ovary and ovarian production of estrogen and progesterone, which then exert feedback regulation on the pituitary and hypothalamus. Because GnRH release is intermittent, LH and FSH secretion is pulsatile. The pulse frequency is determined by the hypothalamic GnRH pulse generator, but the amount of gonadotropin released in each pulse (i.e., the pulse amplitude) is largely controlled by the actions of estrogens and progesterone on the pituitary. The intermittent, pulsatile nature of hormone release is essential for the maintenance of normal ovulatory menstrual cycles; constant infusion of GnRH inhibits gonadotropin release and ovarian steroid production. Ovarian steroids, primarily progesterone, regulate the frequency of GnRH release by direct and indirect effects on GnRH neurons.

METABOLIC EFFECTS

Estrogens increase bone mass, largely by decreasing the number and activity of osteoclasts, thereby decreasing bone resorption. Estrogens increase high-density lipoprotein (HDL) levels and decrease the levels of low-density lipoprotein (LDL) and Lp(a). Estrogens also increase biliary cholesterol secretion and decrease bile acid secretion, leading to increased saturation of bile with cholesterol that results in gallstone formation in some women receiving estrogens. The decline in bile acid biosynthesis may contribute to the decreased incidence of colon cancer in women receiving combined estrogen-progestin treatment. Estrogens affect many serum proteins, particularly those involved in hormone binding and clotting cascades. In general, estrogens increase plasma levels of corticosteroid-binding globulin (CBG), thyroxine-binding globulin (TBG), and sex hormone–binding globulin (SHBG), which binds both androgens and estrogens.

Estrogens alter a number of pathways that affect the cardiovascular system. Systemic effects include changes in lipoprotein metabolism and in hepatic production of plasma proteins. Estrogens slightly increase coagulation factors II, VII, IX, X, and XII, and decrease the anticoagulation factors protein C, protein S, and antithrombin III. Fibrinolytic pathways also are affected; several studies of women treated with estrogen or estrogen with a progestin demonstrate decreased levels of plasminogen-activator inhibitor protein-1 (PAI-1) with a concomitant increase in fibrinolysis. Thus, estrogens increase both coagulation and fibrinolytic pathways. Estrogen actions on the vascular wall include induction of inducible NO synthase and increased production of NO and prostacyclin, all of which promote vasodilation.

Biosynthesis of Estrogen

Estrogens, in females, are produced primarily by the [ovaries](https://en.wikipedia.org/wiki/Ovary), and during pregnancy, the [placenta](https://en.wikipedia.org/wiki/Placenta). [Follicle-stimulating hormone](https://en.wikipedia.org/wiki/Follicle-stimulating_hormone) (FSH) stimulates the ovarian production of estrogens by the [granulosa cells](https://en.wikipedia.org/wiki/Granulosa_cell) of the [ovarian follicles](https://en.wikipedia.org/wiki/Ovarian_follicle) and [corpora lutea](https://en.wikipedia.org/wiki/Corpus_luteum). Some estrogens are also produced in smaller amounts by other tissues such as the [liver](https://en.wikipedia.org/wiki/Liver), [pancreas](https://en.wikipedia.org/wiki/Pancreas), [bone](https://en.wikipedia.org/wiki/Bone), [adrenal glands](https://en.wikipedia.org/wiki/Adrenal_gland), [skin](https://en.wikipedia.org/wiki/Skin), [brain](https://en.wikipedia.org/wiki/Brain), [adipose tissue](https://en.wikipedia.org/wiki/Adipose_tissue),and the [breasts](https://en.wikipedia.org/wiki/Breast). These secondary sources of estrogens are especially important in postmenopausal women. The pathway of estrogen biosynthesis in extragonadal tissues is different. These tissues are not able to synthesize C19 steroids, and therefore depend on C19 supplies from other tissues and the level of aromatase.

In females, synthesis of estrogens starts in [theca interna](https://en.wikipedia.org/wiki/Theca_interna) cells in the ovary, by the synthesis of [androstenedione](https://en.wikipedia.org/wiki/Androstenedione) from [cholesterol](https://en.wikipedia.org/wiki/Cholesterol). Androstenedione is a substance of weak androgenic activity which serves predominantly as a [precursor](https://en.wikipedia.org/wiki/Precursor_(biochemistry)) for more potent androgens such as testosterone as well as estrogen. This compound crosses the [basal membrane](https://en.wikipedia.org/wiki/Basal_membrane) into the surrounding granulosa cells, where it is converted either immediately into estrone, or into testosterone and then estradiol in an additional step. The conversion of androstenedione to testosterone is catalyzed by [17β-hydroxysteroid dehydrogenase](https://en.wikipedia.org/wiki/17%CE%B2-hydroxysteroid_dehydrogenase) (17β-HSD), whereas the conversion of androstenedione and testosterone into estrone and estradiol, respectively is catalyzed by aromatase, enzymes which are both expressed in granulosa cells. In contrast, granulosa cells lack [17α-hydroxylase](https://en.wikipedia.org/wiki/17%CE%B1-hydroxylase) and [17,20-lyase](https://en.wikipedia.org/wiki/17,20-lyase), whereas theca cells express these enzymes and 17β-HSD but lack aromatase. Hence, both granulosa and theca cells are essential for the production of estrogen in the ovaries. Estrogen levels vary through the [menstrual cycle](https://en.wikipedia.org/wiki/Menstrual_cycle), with levels highest near the end of the [follicular phase](https://en.wikipedia.org/wiki/Follicular_phase) just before [ovulation](https://en.wikipedia.org/wiki/Ovulation).

Note that in males, estrogen is also produced by the [Sertoli cells](https://en.wikipedia.org/wiki/Sertoli_cell) when FSH binds to their FSH receptors.

Pharmacokinetics of Estrogen

ABSORPTION, FATE, AND ELIMINATION

Various estrogens are available for oral, parenteral, transdermal, or topical administration. For many uses, preparations are available as an estrogen alone or in combination with a progestin. Oral administration may utilize estradiol, conjugated estrogens, esters of estrone and other estrogens, and ethinyl estradiol. A micronized preparation of estradiol (ESTRACE, others) can be given orally, but high doses must be used due to first-pass metabolism. Ethinyl estradiol is used orally, as the ethinyl substitution at C17 inhibits first-pass hepatic metabolism. Other common oral preparations contain conjugated equine estrogens (PREMARIN); esterified esters; or mixtures of conjugated estrogens prepared from plant-derived sources (CENESTIN).

Transdermal administration of estradiol (ESTRADERM, VIVELLE, ALORA, CLIMARA, others) provides slow, sustained release of the hormone, systemic distribution, and more constant blood levels than oral dosing. Estradiol is also available as a topical cream (ESTRASORB) or as a gel (ESTROGEL). The transdermal route does not lead to the high level of the drug that enters the liver via the portal circulation after oral administration and is thus may decrease estrogen effects on hepatic protein synthesis, lipoprotein profiles, and triglyceride levels. Estradiol and conjugated estrogen creams also are available for topical administration to the vagina. These are effective locally, but systemic effects also are possible due to significant absorption. A 3-month vaginal ring (ESTRING, FEMRING) may be used for slow release of estradiol, and tablets are also available for vaginal use (VAGIFEM). Other preparations are available for intramuscular injection. The esters of estradiol become less polar as the size of the substituents increases; thus, the rate of absorption of oily preparations is progressively slowed, and the duration of action can be prolonged. A single intra- muscular injection of compounds such as estradiol valerate (DELESTROGEN) or estradiol cypionate (DEPO-ESTRADIOL) in oil may be absorbed over several weeks.

Estrogens are extensively bound to plasma proteins. Estradiol and other naturally occurring estrogens are bound mainly to SHBG; ethinyl estradiol is bound extensively to serum albumin but not SHBG. Due to their size and lipophilic nature, unbound estrogens distribute rapidly and extensively.

Estrogens undergo rapid hepatic biotransformation, with a plasma t1/2 measured in minutes. Estradiol is converted primarily by 17β-hydroxysteroid dehydrogenase to estrone, which under- goes conversion by 16α-hydroxylation and 17-keto reduction to estriol, the major urinary metabo- lite. A variety of sulfate and glucuronide conjugates also are excreted in the urine. Estrogen conjugates also undergo enterohepatic recirculation.

Ethinyl estradiol is cleared more slowly than is estradiol due to decreased hepatic metabolism, with an elimination t1/2 of 13–27 hours. Its primary route of biotransformation is via 2-hydroxylation and subsequent formation of the corresponding 2- and 3-methyl ethers.

Adverse Effects of Estrogen

The amount of estrogens (and progestins) in oral contraceptives has been markedly decreased, significantly diminishing the risks associated with their use.

CONCERN ABOUT CARCINOGENIC ACTIONS

Early studies established that estrogens can induce tumors of the breast, uterus, testis, bone, kidney, and other tissues in various animal species. Thereafter, an increased incidence of vaginal and cervical adenocarcinoma was noted in female offspring of mothers who had taken diethyl- stilbestrol during the first trimester of pregnancy. Estrogen use during pregnancy also can increase the incidence of nonmalignant genital abnormalities in both male and female offspring; pregnant women should not be given estrogens.

The use of unopposed estrogen in postmenopausal women increases the risk of endometrial carcinoma by 5–15-fold, an increase that can be prevented if a progestin is coadministered with the estrogen. Randomized, clinical trials of estrogen-progestin and estrogen-only use in post- menopausal women have established a small but significant increase in the risk of breast cancer, apparently due to the medroxyprogesterone. In women without a uterus who received estrogen alone, the relative risk of breast cancer was insignificantly decreased. Thus, the data suggest that the progestin component in hormone-replacement therapy plays a major role in this increased risk of breast cancer. Importantly, the excess risk of breast cancer associated with menopausal hor- mone use apparently abates within 5 years after discontinuing therapy.

METABOLIC AND CARDIOVASCULAR EFFECTS

Although they may slightly elevate plasma triglycerides, estrogens generally have favorable over- all effects on plasma lipoprotein profiles. However, concurrent administration of progestins may reduce these favorable actions. Currently prescribed doses of estrogens do not increase the risk of hypertension.

Observational studies, clinical trials using surrogate markers of cardiovascular disease, and animal studies suggested that estrogen therapy in postmenopausal women would reduce the risk of cardiovascular disease. In randomized clinical trials, however, conjugated equine estrogens alone or in combination with medroxyprogesterone acetate (MPA) did not protect against coronary heart disease (CHD). It is unclear whether these results (single dose; relatively older population) apply to other preparations, doses, and patient populations (e.g., women closer to age 50 who typically initiate hormone therapy for relief of vasomotor symptoms). Clearly, oral estrogens significantly increase the risk of thromboembolic disease in healthy women and in women with preexisting cardiovascular disease.

EFFECTS ON COGNITION

Retrospective studies suggested that estrogens had beneficial effects on cognition and delayed the onset of Alzheimer’s disease. However, in randomized trials, no protective effect was observed, and the incidence of dementia in the treated group was actually increased.

OTHER POTENTIAL ADVERSE EFFECTS

Nausea and vomiting occur in some women but often disappear with time and may be minimized by taking estrogens with food or just prior to sleeping. Breast fullness and tenderness and edema may occur, which may be diminished by lowering the dose. A more serious concern is that estro- gens may cause severe migraine in some women. Estrogens also may reactivate or exacerbate endometriosis.

Therapeutic Uses of Estrogen

The two major uses of estrogens are as components of combination oral contraceptives (*see* below) and for MHT. Historically, conjugated estrogens have been the most common agents for post- menopausal use (typically 0.625 mg/day). In contrast, most combination oral contraceptives in cur- rent use employ 20–35 *μ*g/day of ethinyl estradiol*.* The “effective” dose of estrogen used for MHT is less than that in oral contraceptives when one considers potency. The doses of estrogens employed in both settings have decreased substantially in recent years and untoward effects have a lower incidence and severity than those reported in older studies.

MENOPAUSAL HORMONE THERAPY

Established benefits of estrogen therapy in post- menopausal women include amelioration of vasomotor symptoms and the prevention of bone fractures and urogenital atrophy.

Vasomotor Symptoms:

The decline in ovarian function at menopause is associated with vasomotor symptoms, typically hot flashes. Treatment of vasomotor symptoms with estrogen is specific and is the most efficacious pharmacotherapy.

Osteoporosis:

Osteoporosis is associated with the loss of bone mass and an increased incidence of fractures. Estrogen therapy clearly is efficacious in decreasing the incidence of fractures, although bone loss resumes when treatment is discontinued. However, because of potential risks associated with estrogen use, first-line use of other drugs should be carefully considered. Estrogens are more effective at preventing than restoring bone loss and are most effective if initiated before significant bone loss occurs.

Vaginal Dryness and Urogenital Atrophy:

Loss of tissue lining the vagina or bladder in postmenopausal women leads to a variety of symptoms, including dryness and itching of the vagina, dyspareunia, swelling of tissues in the genital region, pain during urination, a need to urinate urgently or often, and sudden or unexpected urinary incontinence. When estrogens are being used solely for relief of vulvar and vaginal atrophy, local administration as a vaginal cream, ring device, or tablets may be considered.

Cardiovascular Disease:

Prospective studies unexpectedly indicated that the incidence of heart disease and stroke in older postmenopausal women treated with conjugated estrogens and a progestin was initially increased, although the trend reversed with time. While it is not clear if similar results would occur with different drugs/doses or in different patient populations, estrogens (alone or in combination with a progestin) should not be used for the treatment or prevention of cardiovascular disease.

MENOPAUSAL HORMONE REGIMENS

Estrogen-replacement therapy, or ERT (i.e., estrogens alone), in postmenopausal women was associated with an increased incidence of endometrial carcinoma; this led to the use of hormone-replacement therapy, or HRT, which includes a progestin to limit estrogen-related endometrial hyperplasia. “Hormone-replacement” therapy (now generally referred to as “menopausal hormone” therapy) with both an estrogen and progestin now is recommended for postmenopausal women with a uterus. For women who have undergone a hysterectomy, estrogen alone avoids the possible deleterious effects of progestins. Regardless of the specific agent or regimen, MHT with estrogens should use the lowest dose and shortest duration necessary to achieve an appropriate therapeutic goal.

Conjugated estrogens and MPA have been used most commonly in menopausal hormone regi- mens, although estradiol, estrone, and estriol have been used as estrogens, and norethindrone, norgestimate, levonorgestrel, norethisterone, and progesterone also have been widely used (espe- cially in Europe). Various “continuous” or “cyclic” regimens that include drug-free days have been used. An example of a cyclic regimen is: (1) administration of an estrogen for 25 days, (2) the addition of MPA for the last 12–14 days of estrogen treatment, and (3) 5–6 days with no hor- mone treatment, during which withdrawal bleeding normally occurs due to breakdown and shed- ding of the endometrium. Continuous administration of combined estrogen plus progestin does not lead to regular, recurrent endometrial shedding, but may cause intermittent spotting or bleeding. Other regimens include a progestin intermittently (e.g., every third month), but the long-term endometrial safety of these regimens remains to be firmly established. PREMPRO (conjugated estrogens plus MPA given as a fixed dose daily) and PREMPHASE (conjugated estrogens given for 28 days plus MPA given for 14 out of 28 days) are widely used combinations. Other combina- tion products available in the U.S. are FEMHRT (ethinyl estradiol plus norethindrone acetate), ACTIVELLA (estradiol plus norethindrone), and PREFEST (estradiol and norgestimate).

Another pharmacological consideration is the route of administration. Oral administration exposes the liver to higher concentrations of estrogens than transdermal administration and may increase SHBG, other binding globulins, angiotensinogen; and the cholesterol content of bile. Transdermal estrogen appears to cause smaller beneficial changes in LDL and HDL profiles but may be preferred in women with hypertriglyceridemia.

Tibolone (LIVIAL) is widely used in Europe for treatment of vasomotor symptoms and pre- vention of osteoporosis but is not approved in the U.S. The parent compound is metabolized in a tissue-selective manner to metabolites that have predominantly estrogenic, progestogenic, and androgenic activities. The drug increases bone mineral density and decreases vasomotor symp- toms without stimulating the endometrium, but its effects on fractures, breast cancer, and long- term outcomes remain to be established.

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](https://www.medicalnewstoday.com/articles/192590.php)
* mood changes
* sleep disorders
* anxiety
* 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
* vaginal bleeding
* fluid retention, leading to swelling

Some types of hormone therapy can also [increase the risk](https://www.menopause.org/for-women/menopauseflashes/menopause-symptoms-and-treatments/news-you-can-use-about-hormone-therapy) of a stroke, blood clots, and uterine and breast cancer. A doctor can advise a person on whether estrogen therapy is suitable for them.

In addition to menopause, estrogen therapy can also [help resolve](https://www.ncbi.nlm.nih.gov/books/NBK538260/):

* primary ovarian insufficiency
* other ovarian issues
* some types of acne
* some cases of prostate cancer
* [delayed puberty](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5810248/), for example, in Turner’s syndrome

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 include:

* 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
* the use of certain medications, including steroids, ampicillin, estrogen-containing drugs, phenothiazines, and tetracyclines
* some congenital conditions, such as Turner’s syndrome
* [high blood pressure](https://www.medicalnewstoday.com/articles/159283.php)
* [diabetes](https://www.medicalnewstoday.com/info/diabetes/)
* primary ovarian insufficiency
* an underactive pituitary gland
* 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
* more severe premenstrual or menopausal symptoms
* hot flashes, night sweats, or both
* noncancerous lumps in the breast and uterus
* mood changes and sleeping problems
* weight gain, mainly in the hips, thighs, and waist
* 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.

**ANTIFERTILITY DRUGS**

Antifertility drugs refer to hormonal contraceptives (oral contraceptives). Oral contraceptives are widely used worldwide and have had a revolutionary impact by providing a convenient, affordable, and reliable means of contraception. Myriad agents with substantially different components, doses, and side effects provide real therapeutic options. In addition to contraceptive actions, these agents have substantial health benefits.

Types of Hormonal Contraceptives

A. COMBINATION ORAL CONTRACEPTIVES;

They are combination oral contraceptives containing both an estrogen and a progestin. Their theo- retical efficacy is considered to be 99.9%. Ethinyl estradiol and mestranol are the two estrogens used (with ethinyl estradiol being much more frequently used). The progestins are 19-nor com- pounds in the estrane or gonane series that have varying degrees of androgenic, estrogenic, and antiestrogenic activities that may be responsible for some side effects.

Mechanism of Action

Combination oral contraceptives act by preventing ovulation. Plasma LH (Luteinizing Hormone) and FSH (Follicle Stimulating Hormone) levels are suppressed, the midcycle surge of LH is absent, endogenous steroid levels are diminished, and ovulation does not occur. While either component alone can exert these effects, the combination synergistically decreases plasma gonadotropin levels and suppresses ovulation more consistently than either alone.

Side Effects

1. Nausea

2. Vomiting

3. Edema

4. Migraine headache in few individuals

B. PROGESTIN-ONLY CONTRACEPTIVES

Progestin-only contraceptives are only slightly less efficacious than combination oral contraceptives, with theoretical efficacy of 99%. Specific preparations include the “minipill”; low doses of progestins or 75 *μ*g of norgestrel taken daily without interruption; subdermal implants of 216 mg of norgestrel for slow release and resultant long-term contraceptive action and crystalline suspensions of MPA (Medroxyprogesteron acetate) for intramuscular injection of 150 mg of drug, which provides effective contraception for 3 months.

Mechanism of Action

Progestin-only pills and levonorgestrel implants are highly efficacious for contraception. The pills block ovulation in only 60–80% of cycles; effectiveness is thought to be due largely to local effects in the cervix and uterus; such effects also account for the efficacy of intrauterine devices that release progestins. Depot injections of MPA yield plasma levels of drug high enough to prevent ovulation in virtually all patients, pre- sumably by decreasing the frequency of GnRH (Gonadotropin Releasing Hormone) pulses.

Side Effects

1. Episodes of irregular, unpredictable spotting and breakthrough bleeding.

2. Amenorrhea becomes common after a year or more of use.

C. POSTCOITAL OR EMERGENCY CONTRACEPTIVES

The FDA has approved two preparations for postcoital contraception. PLAN-B is two doses of the “minipill” (0.75 mg lev- onorgestrel per pill) separated by 12 hours. It is contraindicated in cases of confirmed pregnancy.

Side Effects

1. Nausea

2. Vomiting

**REFRENCES;** [www.medicalnewstoday.com](http://www.medicalnewstoday.com)

en.wikipedia.org

Goodman & Gilman textbook