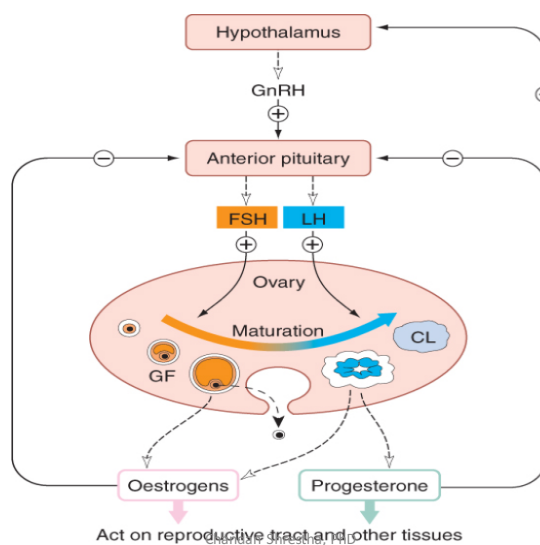


# Estrogen

- Estrogen is produced by the ovaries and in smaller amounts by the adrenal cortex, testes (testicles) and fetoplacental unit (the fetus and the placenta).
- May be
  1. Natural: Estradiol
  2. Synthetic
    - a) *Steroidal*: Ethinyl estradiol, Mestranol, Tibolone.
    - b) *Non steroidal*: Diethylstilbestrol (stilbestrol), Hexestrol, Dienestrol

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# Regulation of secretion



## Estrogen Receptor

- Two ERs designated ER $\alpha$  and ER $\beta$  have been identified.
- ER $\alpha$  predominates in uterus, vagina, breast, hypothalamus and blood vessels.
- ER $\beta$  predominates in prostate gland of males and ovaries in females.

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## Estrogen

### Uses

- [Birth control](#) (Oral Contraceptive Pills)
- [Hormone replacement therapy](#)
- Advanced prostate or postmenopausal breast carcinoma treatment.
- [Osteoporosis](#) prophylaxis.

### Adverse Effect

- Nausea and breast tenderness (common)
- Postmenopausal uterine bleeding can occur.
- Increased risk of thromboembolic events, myocardial infarction, and breast and endometrial cancer.

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## Estrogen

### Contraindication

- Known or suspected pregnancy
- lactation
- Undiagnosed [abnormal genital](#) bleeding.
- Breast cancer
- History of thromboembolic disease (e.g., [stroke](#), MI).
- [Liver dysfunction](#) or disease.

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## Anti Estrogen

### Clomiphene citrate

#### MOA

- It binds to both ER $\alpha$  and ER $\beta$  and acts as a pure estrogen antagonist.

**Uses:** **Infertility** due to failure of ovulation: 50 mg once daily for 5 days starting from 5th day of cycle. Treatment is given monthly.

If 1-2 months treatment does not result in conception-the daily dose may be doubled for 2-3 cycles (max 200 mg/ day).

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**Other uses:** *Oligozoospermia* (low sperm count): In men also clomiphene increases Gn secretion → promotes spermatogenesis and testosterone secretion. For male infertility- 25 mg daily given for 24 days in a month with 6 days rest for upto 6 months has been recommended. However, success rates are low.

#### **Adverse effects**

Polycystic ovaries, multiple pregnancy, hot flushes, gastric upset, vertigo, allergic dermatitis. Risk of ovarian tumour may be increased.

#### **Precaution and Contraindication**

Patient with enlarged ovaries

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## Anti Estrogen

### **Selective estrogen receptor modulators (SERMs)**

- are synthetic molecules that bind to estrogen receptors but act either as agonists or antagonists in different tissues.
- Drugs that acts like estrogen in some tissues but like an anti-estrogen in others are called a *selective estrogen receptor modulator* or SERM.
- **Tamoxifen**
- **Raloxifene**

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## Tamoxifen

- tamoxifen acts like an anti-estrogen in breast cells, it acts like an estrogen in other tissues, like the uterus and the bones.
- **Used** in breast cancer, infertility, gynecomastia

**Adverse effect:** hot flashes and nausea (Common).  
Menstrual irregularities, vaginal bleeding and increased risk of venous thromboembolism can also occur

**Dose:** 10-20 mg BD.

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## Raloxifine

- has estrogenic actions on bone and anti-estrogenic actions on the uterus and breast.
- **Uses:** prevention and treatment of osteoporosis (decrease bone resorption and overall bone turnover)
- **Adverse Effect:** Hot flushes, leg cramps are generally mild; vaginal bleeding is occasional.

The only serious concern is 3-fold **increase in risk of deep vein thrombosis and pulmonary embolism.**

- **Dose:** 60mg/day

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## Progestin

- These are substances which convert the estrogen primed endometrium to secretory and maintain pregnancy after conception (**Progestin**=favouring pregnancy).

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## Progestin

### 1. Natural: Progesterone

### 2. Synthetic

a. Progesterone derivative: Medroxyprogesterone acetate, Megestrol acetate, Hydroxyprogesterone caproate

*Newer compound*: Nomegestrol acetate

### b. 19-Nortestosterone derivatives

*Older compounds*

Norethindrone (Norethisterone)

Lynestrenol (Ethinylestrenol)

Allylestrenol

Levonorgestrel (**Gonane**)

*Newer compounds*

**(Gonanes)**

Desogestrel

Norgestimate

Gestodene

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## Progestin

### Uses

- As contraceptive
- Hormonal replacement therapy (HRT)
- Dysfunctional uterine bleeding
- Endometriosis
- Premenstrual syndrome/tension
- Endometrial carcinoma

### Adverse Effect

- Breast engorgement, headache, rise in body temperature, edema, esophageal reflux, acne and mood swings may occur with higher doses.
- Irregular bleeding or amenorrhoea can occur if a progestin is given continuously.

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## Anti-Progestin

### Mifepristone

- potent competitive antiprogestational and significant antiglucocorticoid as well as antiandrogenic activity.

### Uses

- Termination of pregnancy of up to 7 weeks  
(Mifepristone 600mg + misoprostol 400mg)
- Postcoital contraceptive (Mifepristone 600mg within 72 hr)
- Induction of labour
- Once a month contraceptive (mifepristone: 200mg; 2 days after mid cycle)
- Cushing's syndrome

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# Oral Contraceptive Pills

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## Oral Contraceptive pill (OCP)

- Birth control Pill
- Taken orally

### **Types of OCP**

1. Combined pill
2. Minipill
3. Postcoital (emergency) contraceptive pills

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## Combined pill

- the most popular and most efficacious method.
- contain both estrogen and progesterone.
- One tablet is taken daily for 21 days, starting on the 5th day of menstruation.
- Calendar packs of pills are available.



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## Combined pill

### MOA

- prevent ovulation by suppressing the release of gonadotropins.
- Inhibits follicular development and prevent ovulation
- All progestogen-containing contraceptives is inhibition of sperm penetration through the cervix into upper genital tract by decreasing the water content and increasing the viscosity of the cervical mucus.

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## Combined pill

### Adverse Effect

- Nausea, vomiting, headache, bloating, breast tenderness, swelling of the ankles/feet (fluid retention), or weight change may occur.
- Vaginal bleeding or missed/irregular periods may occur, especially during the first few months of use.

### Contraindication

1. cardiovascular disease
2. Moderate-to-severe hypertension; hyperlipidaemia.
3. Active liver disease, hepatoma or h/ o jaundice during past pregnancy.

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## Mini Pill (Progestin only pill)

- Do not contain estrogen
- A low-dose progestin only
- pill is taken daily continuously without any gap.
- The menstrual cycle tends to become irregular and ovulation occurs in 20-30% women.

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## Postcoital (Emergency) contraceptive Pills

- Morning after pill
- used after sexual intercourse to prevent pregnancy.
- are drugs intended to disrupt or delay ovulation or fertilization.

### Types

1. Combined estrogen and progestin pills
2. Progestin (levonorgestrel) only pills
3. Antiprogestin pills (Mifepristone 600 mg single dose taken within 72 hours of intercourse)

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## Progestin only pill

- contain 1.5 mg of levonorgestrel, either as a single 1.5 mg tablet (**E72**) or as a split dose of two 0.75 mg tablets (**eCON**) taken 12 hours apart, effective up to 72 hours after intercourse.
- Adverse Effect: nausea, vomiting, abdominal pain, fatigue, headache, dizziness and breast tenderness.

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