

Oral contraceptives

1-COMBINED Oral contraceptives (COC) most common (100% effective)

Drug	Formulation	Administration	MOA	ADRs	Contraindication
A-Estrogens ✓ Ethinyl estradiol ✓ mestranol [a "prodrug" converted to ethinyl estradiol]	✓ Currently, their formulation is improved to mimic the natural ongoing changes in hormonal profile . Accordingly we have now the phase formulations: 1. Monophasic → (a fixed amount of estrogen & progestin) 2. Biphasic (2 doses) → (a fixed amount of estrogen , while amount of progestin increases stepwise in the second half of the cycle) 3. Triphasic (3 doses) → (amount of estrogen ; fixed or variable & amount of progestin increases stepwise in 3 phases).	<ul style="list-style-type: none"> • Pills are taken for 21 days, starting on 5th day of the cycle & ending at day 26. This is followed by a 7 day pill free period • TO IMPROVE COMPLIANCE a formulation of 28 pills available, but the last 7 pills of the 28 pills are actually placebo (non hormonal). • Pills are better taken at same time of day 	The main action is: It inhibits ovulation by suppressing the release of Gonadotrophs (FSH & LH) → no action on the ovary → ovulation is prevented . Other actions: ✓ Inhibit implantation of the fertilized zygote by causing abnormal contraction of the fallopian tubes & uterine musculature → ovum will be expelled rather than implanted. ✓ <i>Increase viscosity of the cervical mucus making it so viscous (A progesterone effect)</i> → no sperm pass ✓ Abnormal transport time of sperm through the fallopian tubes.	<ol style="list-style-type: none"> 1. Nausea and breast tenderness 2. Headache 3. Increase Skin Pigmentation 4. Impair glucose tolerance (hyperglycemia) 5. Increase incidence of breast, vaginal & cervical cancer. 6. Cardiovascular - major concern <ol style="list-style-type: none"> a. Thromboembolism b. Hypertension 7. Increase frequency of gall bladder disease (because it's steroid _cholesterol _if it's accumulated it's cause stones) 	<ul style="list-style-type: none"> ✓ Thrombophlebitis / thromboembolic disorders (metabolic syndrome manifestations) ✓ Congestive heart failure or other causes of edema ✓ Vaginal bleeding of undiagnosed etiology ✓ Known or suspected pregnancy ✓ Known or suspected breast cancer, or estrogen-dependent neoplasms ✓ Impaired hepatic functions ✓ Dyslipidemia, diabetes, hypertension, migraine ✓ Lactating mothers - <u>use mini pill</u> (Estrogen down regulates prolactin receptors) <p>N.B. Females that are obese, smokers (It cause interaction with the liver enzymes), Females > 35 years (because she more prone to cancer) are better given the mini pills</p>
B-Progestins <ul style="list-style-type: none"> • Norethindrone • Levonorgestrel (<i>Norgestrel</i>) • Medroxyprogesterone acetate ✓ Norgestimate ✓ Desogestrel ✓ Drospirenone				<ol style="list-style-type: none"> 1. Nausea, vomiting ,headache 2. Slightly higher failure rate of contraception. 3. Fatigue, depression of mood 4. Menstrual irregularities 5. Weight gain (It stimulates lipoprotein lipase activity and seems to favor fat deposition.) 6. Hirsutism 7. Masculinization (Norethindrone) 8. Ectopic pregnancy. 	

Interaction: →

A) Medications that cause contraceptive failure

- ✓ Antibiotics that interfere with normal GI flora → ↓ absorption
→ ↓ its bioavailability
- ✓ Microsomal **Enzyme Inducers** → ↑ catabolism of OC
e.g.: **Phenytoin , Phenobarbitone, Rifampin**

B) Medications that ↑ COC toxicity

Microsomal **Enzyme Inhibitors**; ↓ metabolism of OC → ↑ toxicity e.g.: **Acetaminophen, Erythromycin , SSRI (antidepressant)**

C) Medications that alter the clearance of COC → ↑ toxicity

e.g.: **Cyclosporine ,Warfarin, Theophylline**

Drug	Indication	Administration	MOA	ADRs & Contraindications
2-MINI Pills Progestin-Only Pills (POP) Contains only a progestin (97% effective) → as norethindrone or desogestrel and are used when estrogen containing pills are contraindicated	<ul style="list-style-type: none"> Are alternative when estrogen is contraindicated (e.g.: during breast feeding, hypertension, cancer, smokers over the age of 35). 	<ol style="list-style-type: none"> Oral tablets should be taken every day, all year round I.M injection e.g. medroxy-progesterone acetate 150 mg every 3 months.. 	<p>➤ <i>The main effect is that it increases cervical mucus, so no sperm penetration & therefore, no fertilization. (the efficacy is lower than COC drugs)</i></p>	<p>✓ That are related to progestins only</p> <p>N.B. There is slightly higher contraception failure rates when mini pills are used</p>

3- MORNING-AFTER Pills

Also known as:

- Post Coital Contraception
- Emergency Hormonal Contraception (EHC)

This is a form Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse

Contain both **hormones** or **each one alone (high dose)** or **Mifepristone + Misoprostol**

Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse

Indication: When desirability for avoiding pregnancy is obvious for emergency_after sexual intercourse

Summary

- ✓ Rising levels of **Estrogens (β-ESTRADIOL)** AND **Progesterone** inhibit the secretion of **GnRH** in hypothalamus & the secretion of the **Gonadotrophs** from the A. pituitary
- ✓ In contraception the goal is to prevent the sperm from fertilizing the ovum. This done by many different method e.g. (**Hormonal therapy** like Oral Contraceptives, **Intrauterine devices** that interferes with implantation, or **preventing sperm from fertilizing the ovum** through Condoms and spermaticidals)
- ✓ The most controlled and effective way of contraception is **using oral contraceptives**.
- ✓ They are divided according to composition & intent of use into three types
- ✓ **1-COMBINED Oral contraceptives (COC)** that Contain estrogen & progestin(100% effective)
- ✓ **A-Estrogens** like **Ethinyl estradiol or mestranol** [a “prodrug” converted to ethinyl estradiol]
- ✓ **B-Progestins are divided into 2 subgroups:**
- ✓ **1) Preparations that have systemic androgenic effect;** acne, hirsutism, weight gain. E.g(**Norethindrone ,Levonorgestrel (Norgestrel) ,and Medroxyprogesterone acetate**
- ✓ **2)Preparations that do not have, and are the ones currently used** e.g (**Norgestimate,Desogestrel,Drospirenone**)
- ✓ **COC’s main action is:** that It **inhibits ovulation** by **suppressing the release of Gonadotrophs (FSH & LH)** → **no action on the ovary** → **ovulation is prevented.**
- ✓ Currently, their formulation is improved to mimic the natural ongoing changes in hormonal profile.

- ✓ **Monophasic** → (a fixed amount of **estrogen** & **progestin**)
- ✓ **Biphasic (2 doses)** → (a fixed amount of **estrogen**, while amount of **progestin** increases stepwise in the second half of the cycle)
- ✓ **Triphasic (3 doses)** → (amount of **estrogen**; fixed or variable & amount of **progestin** increases stepwise in 3 phases).
- ✓ **Pills are taken for 21 days, starting on 5th day of the cycle & ending at day 26. This is followed by a 7 day pill free period**
- ✓ **TO IMPROVE COMPLIANCE**; a formulation of **28 pills available**, but the **last 7 pills** of the 28 pills are **actually placebo**.
- ✓ **Estrogen ADRs**: Impaired glucose tolerance (hyperglycemia), Increased incidence of breast, vaginal & cervical cancer, Thromboembolism, Hypertension.

Progestin ADRs: Menstrual irregularities, Weight gain, **Hirsutism**, **Masculinization** (The latter two are seen **Norethindrone derivatives**)

- ✓ **Females that are obese, smokers, Females > 35 years are better given the mini pills**

✓ **Interactions:**

- 1) **Antibiotics** that interfere with normal GI flora → ↓ in its absorption
- 2) **Microsomal Enzyme Inducers** → e.g.: **Phenytoin, Phenobarbitone, Rifampin**
- 3) **Microsomal Enzyme Inhibitors** e.g.: **Acetaminophen, Erythromycin**
- 4) **Medications that alter the clearance of COC** → ↑ toxicity e.g.: **Cyclosporine, Warfarin, Theophylline**

- ✓ **2-MINI Pills Progestin-Only Pills (POP)** e.g. (**norethindrone, desogestrel**) Contains only a progestin (97% effective). They are used as an alternative when **estrogens are contraindicated** (e.g.: during breast feeding, hypertension, cancer, smokers over the age of 35).
- ✓ *The main effect is that they increase cervical mucus, so no sperm penetration & therefore, no fertilization.*
- ✓ **There is slightly higher contraception failure rates when mini pills are used**
- ✓ **3- MORNING-AFTER Pills** **or** Post Coital Contraception (Emergency Hormonal Contraception [EHC])
- ✓ **It either contains both synthetic hormones (Ethinyl estradiol and Levonorgestrel) or each one alone (in high doses) or Mifepristone with or without Misoprostol**
- ✓ They are used when **When desirability for avoiding pregnancy is obvious**: Torn, leaking condom, Missed pills, Exposure to teratogen e.g. Live vaccine, or Rape