

# Pharmacology of Contraception



Ismail Raslan

Eman Alrashidi , Nouf Alzendi

**Plz Focus on mechanism & indication**

# Pharmacology of contraception

This page imp.  
For  
understanding  
only

- **What is contraception?**

- Prevention of pregnancy

- **How do we achieve contraception pharmacologically?**

- Three types :

1. Interfering with normal ovulation:

❖ This type is called hormonal therapy (most important) Can be in the form of:

- Oral Contraceptives
- Contraceptive Patches
- Injectable
- Implants
- Vaginal rings
- IUD (with hormone)

See the last page

2. Interfering with implantation:

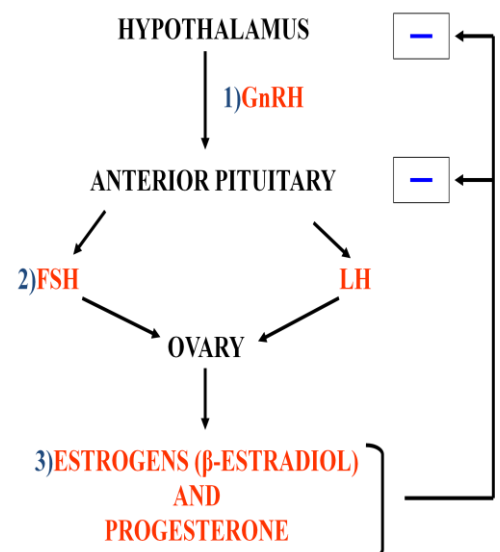
❖ Intra uterine device ( IUD) that contains copper (copper is toxic to sperm , spermicidal)

3. Interfering with the sperm from getting to the ovum:

- ❖ Kill the sperm ( gel, foam, ovules)
- ❖ Interrupt by a barrier (condoms , cervical caps)

- **What is hormonal therapy? And how does it work?**

- Hormonal therapy is when we give the patient amounts of estrogens or progesterone or both to make her body think that she is pregnant and that will lead to preventing ovulation
- So GnRH causes the anterior pituitary to release LH and FSH
- LH and FSH act on the ovaries and cause ovulation
- LH and FSH are stopped from releasing by a negative feedback mechanism through estrogens and progesterone
- So we give the patient estrogens and progesterone to inhibit the GnRH release which inhibit LH and FSH so there will be no ovulation



# Oral Contraceptives (OC)

We have three main types of oral contraceptive pills:

- 1- Combined oral contraceptives (COC)
- 2- MINI pills – progesterone only pills (POP)
- 3- Morning after pills

## 1. Combined oral contraceptives (COC):

- a. Contain both estrogens and progesterone
- b. Nowadays the dose of estrogens in COC is being decreased (new generation of COC has low estrogens .. ) Why?  
To get rid of harmful side effects of estrogens (as we will see later in ADRs)
- c. Two types of estrogens are used :
  - ✓ Ethinyle estradiol
  - ✓ Mestranol ( converted into Ethinyle estradiol in the body )
- d. Progesterone are androgen precursors
  - ✓ so the **less the selectivity for the receptors** the more it might **cause androgen effect in female** like : acne, hirsutism, weight gain, and deleterious effects on lipid & carbohydrate metabolism; drugs that have low selectivity :
    1. Norethindrone
    2. Norethindrone acetate
    3. Levonorgestrel (*Norgestrel*)
    4. Medroxyprogesterone acetate
  - ✓ nowadays we give more specific receptor drugs to reduce progesterone side effects; preparations that are more specific :
    1. Norgestimate
    2. Desogestrel
    3. Drospirenone
- e. Mechanism of action of COC (4 mechanisms) (suppress ovulation)
  1. Like discussed before : inhibits release of LH FSH >> no ovulation (most imp.)
  2. Causes abnormal contraction of fallopian tubes and uterus > no implantation
  3. Increasing viscosity of cervical mucus > sperms can't pass
  4. Abnormal transport time through fallopian tubes

Old drugs >> less receptor-selective >> androgen effect

New drugs >> more receptor-selective >> less androgen effect

5. the ratio of progesterone and estrogens are being developed to mimic the natural hormonal changes in the body SO They are essentially designed to mimic the menstrual cycle by producing a monthly withdrawal bleeding (**menstruation**) (**use of them doesn't prevent menstruation** ).

**f. We have three types of preparation:**

- Monophasic: levels of estrogens and progesterone are the same throughout the 21 pills
- Biphasic : level of estrogens is fixed; however levels of progesterone increase gradually at the second half of the cycle
- Triphasic : level of estrogens is fixed; levels of progesterone is variable and increases 3 times throughout the monthly dosage

**g. Indications :** As a contraceptive for any woman looking for: a reliable, reversible, coitally-independent (**not affect sexual intercourse** ) method of contraception.

**h. Methods of administration :**

- Pills are taken for 21 days, starting on day 5 & ending at day 26. This is followed by a 7 day pill free period "**remember: day 1 is the 1<sup>st</sup> day of bleeding** " (**يعني تأخذها لمدة ٢١ يوم تبدأ فيها في اليوم الخامس من الدورة وتوقفها بعد ٢١ يوم يعني قبل الدورة الثانية بثلاث أيام تقريبا وترجع تأخذهم مره ثانية في اليوم الخامس من الدورة وهكذا** )
- Pills are better taken at same time of day
- If females are compliant (**well use**) the efficacy of COC can reach as high as (99.9%) in preventing pregnancy (**if a dose is missed , ovulation might occur**)
- TO IMPROVE COMPLIANCE (**improve use in case of forgetfulness** ); there exist a formulation of 28 pills that resemble the biphasic or triphasic formulation, but the last 7 pills to be taken of the 28 pills are actually placebo .

(يعني في حالات الحريم المسطولات D : على قولت الدكتور (اللي ممكن تنسى وتستمر تأخذ الحبوب في الأيام المفروض توقف فيها على أساس إنها تعودت) سوا نوعية من الحبوب تؤخذ وما توقفها لكن السبع حبات الأخيرة ما تحتوي على هرمونات ولا حاجة عبارة عن دواء وهمي (ما يضر طبعا ) )



**i. Adverse effects of COC and contraindications :**

It can be estrogens related and can be progesterone related

( Keep in mind that estrogens related side effect is less now due to the decrease in dosage)

- **Estrogens related adverse effects:**

- Nausea and breast tenderness
- Headache
- ↑Skin Pigmentation; due to vitamin B6 deficiency
- Impair glucose tolerance (hyperglycemias) ( can be very serious)
- Incidence of breast, vaginal & cervical cancer??
  - Nowadays it is not a problem because the levels of estrogen are low in COC
  - However it is contraindicated to give COC to patients with history of cervical or vaginal or breast cancer
- Cardiovascular — major concern
  - a. Thromboembolism
  - b. Hypertension : due to water/sodium retention and it is reversible
- ↑ frequency of gall bladder disease

- **Progesterone related adverse effects:**

- Nausea, vomiting&headache
- Slightly higher failure rate
- Fatigue, depression of mood
- Menstrual irregularities
- Weight gain
- Hirsutism
- Masculinization (Norethindrone)
- Ectopic pregnancy.

Due to androgenic properties of progesterone

- **Contraindication : it's very simple if you understand the side effects**

- CVS disorders
  - Thrombophlebitis /Thromboembolic disorders
  - Congestive heart failure or edema
- Vaginal bleeding of unknown etiology. **Why?** could be due to cancer
- Pregnancy / or suspected pregnancy
- Known or suspected neoplasms of the breast or estrogen dependant neoplasms

- Impaired hepatic functions
- Fibroid tumors –use mini pill
- Dyslipidemia, diabetes, hypertension, migraine.....
- Lactating mothers **Why? because estrogens suppress prolactin which leads to stopping milk production SO better give them mini pills**
- NB. If a mother is a smoker, obese and over 35 we give her Mini pills( **which are progesterone only** )

**imp!! Lactating mothers+ fibroid tumor+ obese+ smoker+ above 35 >>> use mini pills , COC contraindicated**

#### **j. Drug interaction:**

There are three types of interactions with COC

##### **1. Medication that cause the contraceptives to fail**

- Impaired absorption : like taking antibiotics that kill GI flora > this will lead to ↓absorption> ↓ its bioavailability > failure of the drug
- Drug inducers(CYT P450 inducers) : ↑ catabolism of OC; like:
  - i. Phenytoin
  - ii. Phenobarbitone
  - iii. Rifampin

##### **2. Medications that increase COC toxicity (CYT P450 inhibitors ):**

- ↓ metabolism of OC ➔ ↑ toxicity e.g.:
  - i. Acetaminophen
  - ii. Erythromycin.

##### **3. Medications of altered clearance (↓) by COC;**

- ↑ toxicity e.g.:
  - i. Cyclosporine
  - ii. WARFARIN
  - iii. Theophylline

## 2. MINI pills – progesterone only pills ( POP)

### a. Contains only progesterone

- ✓ norethindrone
- ✓ desogestrel

### b. Mechanism of action

#### 1. Very low dose (*most regularly used*):

→ no sperm penetration (cuz of increased the viscosity & thickness of secretion of the cervix ) → inhibits fertilization (not ovulation).

#### 2. Intermediate dose(*recent preparations*):

→ Inhibit fertilization and ovulation

### c. Indications :

- ✓ Are alternative when oestrogen is contraindicated (specially in cardio-vascular, hepatobiliary, cancer and some metabolic disorders)
- ✓ Are used with no age limits, in smokers & during lactation.
- ✓ **N.B.** They became popular because no worry of estrogenic side effects & are better tolerated

### d. Route of admission : Should be taken every day, all the year round

### e. ADRs : Slightly higher failure rates

### 3. Morning after pills

a. also called EHC ( emergency hormonal contraception) OR Post Coital Contraception

(Contraception on instantaneous (immediate) demand, 2ndry to unprotected sexual intercourse)

(this type of OC are used after sexual intercourse occurs when the fertilization is not wanted)

b. Used for :






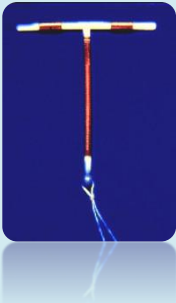
1. Medico-legal (emergencies ) insult: Rape (حالات الاغتصاب)
2. Inevitable (expected) ↓ efficacy of other forms of contraception!
  - Unsuccessful withdrawal before ejaculation
  - Torn, leaking condom
  - Missed pills
  - Detached contraceptive patch.....etc

c. Adverse effects depends on the formulation, if mifepristone is used it can cause uterine bleeding so must be done under medical supervision

Composition	Method of Administration	Timing of 1st dose After Intercourse	Reported Efficacy
Ethinyl estadiol + Levonorgestrel	2 tablets twice with 12 hrs in between	Better within 12 hrs only up to 72hrs	75%
High-dose only Ethinyl estadiol	Twice daily for 5 days	Better within 12 hrs only up to 72hrs	75 - 85%
High dose only levonorgestrel	Twice daily for 5 days	Better within 12 hrs only up to 72hrs	70 – 75%
Mifepristone ± Misoprostol (lyses the corpus leuteum > > endometrial shedding)	A single dose	Within 120 hrs	85 - 100%



## OTHER HORMONAL CONTRACEPTIVE MODALITIES

Other Application MODALITIES	Hormonal Content Within	Dosing Frequency	Reported Efficacy
<b>Patch (Transdermal System)</b> 	Like COC, having both hormones	On same day every week for three weeks, 1 week free	99%
<b>Injectable (given IM)</b> 	Depot medroxyprogesterone acetate	<b>Every three month</b> ■ Rarely used because patient might get pregnant first 1 or 2 cycles & We do not know about long term safety	99.7%
<b>Implant ( 6 rods)</b>  	Levonorgestrel	Every three –five years	98-99%
<b>Vaginal Ring</b> 	Releases a continuous low dose of hormones	Worn for 3 weeks, one week free to get the cycle	85 - 100%
<b>IUR</b> 	Levonorgestrel	Regular contraception Worn for 5 years	97%
	Levonorgestrel	For EC→ Worn for a week / within 5 days	