



# Lecture 2



## Oral and Other forms of contraception

### Objectives:

- ★ Perceive the different contraceptive utilities available
  - ★ Classify them according to their site and mechanism of action
  - ★ Justify the existing hormonal contraceptives present
  - ★ Compare between the types of oral contraceptives pills with respect to mechanism of action, formulations, indications, adverse effects, contraindications and possible interactions
  - ★ Hint on characteristics & efficacies of other hormonal modalities
- Additional Notes
  - Important
  - Explanation –Extra-

- ❖ In **CONCEPTION**: there is fusion of the sperm & ovum to produce a new organism.
- ❖ IN **CONTRACEPTION**: we are preventing this fusion to occur

If you wanna get “the butter” of this lecture click on the butter icon..  
**HIGHLY RECOMMENDED VIDEO!!**



Contraception is achieved by interfering with:

**Normal process of ovulation**

Hormonal therapy



Oral Contraceptive pills  
Contraceptive Patches  
Vaginal rings  
Injectable  
IUD (with hormone)

**Implantation**

IUD\* (copper T)

\*IUD = Intrauterine device  
(click [HERE](#) for IUD video (at 2:24 mins))

**Preventing sperm from fertilizing the ovum**

**Killing the sperm**



Spermicidals  
**Jells**  
**Foams**

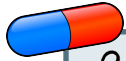
**Interruption by a barrier**



Condoms  
Cervical caps  
Diaphragms  
Thin films

# Types of Oral Contraceptive Pills

According to composition & intent of use



## COMBINED PILLS (COC)

Contain estrogen & progestin  
(100% effective)



## MINI PILLS (POP)

Contain only progestin  
(97% effective)



## MORNING-AFTER PILLS

Contain both hormones or  
Each one alone (high dose)  
or  
Mifepristone ± Misoprostol

## Estrogens

- Ethinyl estradiol or mestranol [a “prodrug” converted to ethinyl estradiol]
- Currently concentration used now is very low to minimize estrogen hazards

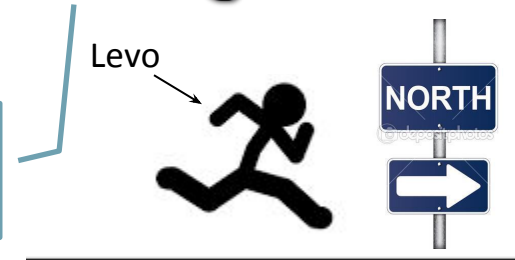
## Progestins

- Norethindrone, Levonorgestrel (Norgestrel), Medroxyprogesterone acetate → Have **systemic androgenic effect**; acne, hirsutism, weight gain.
- Currently: Norgestimate, Desogestrel, Drospirenone → Have **no** systemic androgenic effect

Levo was on a north end run (**noreth-ind-rone**). When he reached the hotel reception, they said: “Levo no register (**levonorgestrel**), you may take the metro (**medroxyprogesterone acetate**). Levo told his friend “We have no register mate (**Norgestimate**)”

Couldn't add desogestrel & drospirenone to Levo's story though.. :/

## Story of Levo



# Combined Pills (COC)

## Estrogens + Norgestimate, Desogestrel and Drospirenone

### MOA

1. Inhibit ovulation by suppressing the release of gonadotrophins (FSH & LH) → no action on the ovary → *ovulation is prevented*. When they do so there will be:
2. Inhibit *implantation* by causing abnormal contraction of the fallopian tubes & uterine musculature → *Ovum will be expelled rather than implanted*.
3. Increase viscosity of the cervical mucus making it so viscous → *No sperm pass*
4. Abnormal *transport* time through the fallopian tubes .

### Seasonal Pills

Are known as Continuous / Extended cycle → Cover 91 days schedule  
 Taken continuously for 84 days, break for 7 days  
 Has very low doses of both estrogens and progestins

#### Advantages

It lessens menstrual periods to 4 times a year → useful in those who have pre-menstrual or menstrual disorders, and in perimenopausal women with vasomotor symptoms.

#### Disadvantages

Higher incidence of breakthrough bleeding & spotting during early use.

### Monthly Pills

Currently, their formulation is improved to mimic the natural on going changes in hormonal profile.

#### Methods of Administration of Monthly Pills:

- ✓ Pills are better taken same time of day
- ✓ For 21 days; starting on day 5 / ending at day 26.
- ✓ This is followed by a 7 day pill free period
- ✓ *To improve compliance*; a formulation of 28 pills
- ✓ The first 21 pills are of multiphasic formulation
- ✓ Followed by the last 7 pills are actually placebo (dummy pills)

# Combined Pills (COC) cont.

## Estrogens + Norgestimate, Desogestrel and Drospirenone

T  
Y  
P  
E  
S

Monthly  
Pills  
cont.

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).

2 and 3 mimics the real cycle

	Estrogen (mg)		Progestin (mg)	
<b>Monophasic combination tablets</b> 1				
Loestrin 21 1/20	Ethinyl estradiol	0.02	Norethindrone acetate	1.0
Desogen, Apri, Ortho-Cept	Ethinyl estradiol	0.03	Desogestrel	0.15
Brevicon, Modicon, Necon 0.5/35	Ethinyl estradiol	0.035	Norethindrone	0.5
Demulen 1/35	Ethinyl estradiol	0.035	Ethinodiol diacetate	1.0
Nelova 1/35 E, Ortho-Novum 1/35	Ethinyl estradiol	0.035	Norethindrone	1.0
Ovcon 35	Ethinyl estradiol	0.035	Norethindrone	0.4
Demulen 1/50	Ethinyl estradiol	0.05	Ethinodiol diacetate	1.0
Ovcon 50	Ethinyl estradiol	0.05	Norethindrone	1.0
Ovral-28	Ethinyl estradiol	0.05	nL-Norgestrel	0.5
Norinyl 1/50, Ortho-Novum 1/50	Mestranol	0.05	Norethindrone	1.0
<b>Biphasic combination tablets</b> 2				
Jenest-28, Ortho-Novum 10/11, Necon 10/11, Nelova 10/11				
Days 1—10	Ethinyl estradiol	0.035	Norethindrone	0.5
Days 11—21	Ethinyl estradiol	0.035	Norethindrone	1.0

2	Estrogen (mg)		Progestin (mg)	
<b>Triphasic combination tablets</b>				
Triphasil, Tri-Levlen, Trivora				
Days 1—6	Ethinyl estradiol	0.03	L-Norgestrel	0.05
Days 7—11	Ethinyl estradiol	0.04	L-Norgestrel	0.075
Days 12—21	Ethinyl estradiol	0.03	L-Norgestrel	0.125
Ortho-Novum 7/7/7, Necon 7/7/7				
Days 1—7	Ethinyl estradiol	0.035	Norethindrone	0.5
Days 8—14	Ethinyl estradiol	0.035	Norethindrone	0.75
Days 15—21	Ethinyl estradiol	0.035	Norethindrone	1.0
Ortho-Tri-Cyclen				
Days 1—7	Ethinyl estradiol	0.035	Norgestimate	0.18
Days 8—14	Ethinyl estradiol	0.035	Norgestimate	0.215
Days 15—21	Ethinyl estradiol	0.035	Norgestimate	0.25

You don't need to memorize drugs, names and doses just be aware of concentrations of each!!

1: Conc. of progestin and estrogen is constant.

2: First 10 days both conc. are constant then the 10-21 days progestin will increase..

# Combined Pills (COC) cont.

## Estrogens + Norgestimate, Desogestrel and Drospirenone

### ADRs

#### Estrogen Related

- ✧ Nausea and breast tenderness.
- ✧ Headache.
- ✧ ↑Skin Pigmentation.
- ✧ impair glucose tolerance (hyperglycemia).
- ✧ ↑Incidence of breast, vaginal & cervical cancer.
- ✧ Cardiovascular - major concern.
- ✧ Thromboembolism.
- ✧ Hypertension.
- ✧ ↑ frequency of gallbladder disease.

#### Progestin Related

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

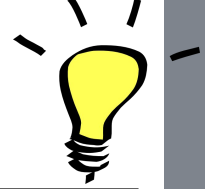
### Contraindications

- ✧ Thrombophlebitis / thromboembolic disorders
- ✧ CHF or other causes of edema
- ✧ Vaginal bleeding of undiagnosed etiology
- ✧ Known or suspected pregnancy cause it may cause miscarriage.
- ✧ Known or suspected breast cancer, or estrogen-dependent neoplasms
- ✧ Impaired hepatic functions
- ✧ **Dyslipidemia, diabetes, hypertension, migraine.....**

Estrogens is contraindicated in : We use **Only the mini pills (Progestin only)**

- ✧ **Lactating mothers.**
- ✧ **Obese**
- ✧ **Smokers,**
- ✧ **Females > 35 years**

# Combined Pills (COC) cont.



## Estrogens + Norgestimate, Desogestrel and Drospirenone

Interactions	Medications that cause contraceptive <b>Failure</b>	Medications that ↑ <b>COC toxicity</b> e.g.: Acetaminophen, Erythromycin.	Medications that is altered in <b>Clearance</b> by COC Warfarin, Cyclosporine, Theophylline
	Impairing absorption	Microsomal Enzyme Inhibitors; ↓ metabolism of OC ↑ toxicity	↑ in their toxicity
	Antibiotics that interfere with normal GI flora = ↓ absorption = ↓ its bioavailability		
	CYT P450 Inducers e.g.: Phenytoin , Phenobarbitone, Rifampin		
	Microsomal Enzyme Inducers □ ↑ catabolism of OC		

# Mini Pills

## Progestin-Only Pills (POP)

<b>Composition</b>	Contains only a progestin → as norethindrone or desogestrel....
<b>Mechanism of Action</b>	The main effect is → increase cervical mucus, so no sperm penetration & therefore, no fertilization.
<b>Indications</b>	Are alternative when oestrogen is contraindicated (e.g.: during breast feeding, hypertension, cancer, smokers over the age of 35).
<b>Instructions for contraceptives containing progestin only</b>	<ul style="list-style-type: none"><li>• Should be taken <b>every day</b>, the <b>same time</b>, <b>all year</b> round</li><li>• I.M injection e.g. medroxy progesterone acetate 150 mg every 3 months..</li></ul>



# Morning-After Pills

## Post Coital & Emergency contraception!

**Indications:** when desirability for avoiding pregnancy is obvious:

1. Unsuccessful withdrawal before ejaculation
2. Torn, leaking condom
3. Missed pills
4. Exposure to teratogen e.g. Live vaccine
5. Rape

Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse

Composition	Method of Administration	Timing of 1st dose after Intercourse	Reported Efficacy
Ethinyl estadiol + Levonorgestrel	2 tablets twice with 12 hrs in between	0- 72hrs	75%
High-dose only Ethinyl estadiol	Twice daily for 5 days	0- 72hrs	75 - 85%
High dose only levonorgestrel	Twice daily for 5 days	0- 72hrs	70 – 75%
Mifepristone ± Misoprostol	A single dose	0-120hrs	85-100%

# MCQs

**Q1: Seasonal combined oral contraceptives are taken:**

- A. 21 days followed by dummy pills for 7 days
- B. Continuously for 84 days with a break for 7 days
- C. 21 days starting at 5<sup>th</sup> / ending at 26<sup>th</sup>
- D. 34 days starting at 5<sup>th</sup> / ending at 39<sup>th</sup>

**Q2: Which one of the following has no systemic androgenic effect?**

- A. Norethindrone
- B. Levonorgestrel
- C. Norgestimate
- D. Medroxyprogesterone acetate

**Q3: A female patient was taking an oral contraceptive drug came to the clinic complaining of weight gain, hirsutism, and masculinization effects. Which of the following OCs is she probably using?**

- A. Mestranol
- B. Desogestrel
- C. Norgestimate
- D. Norethindrone

**Q4: A lady was taking oral contraceptives. One month later she discovered that she got pregnant. Which of the following drugs was she taking with the OCs?**

- A. Acetaminophen
- B. Erythromycin
- C. Ampicillin
- D. Cimetidine

**Q5: A 40-year-old woman who smokes and has hypertension is planning to get oral contraceptive drugs. Which drug is recommended in this case?**

- A. Mifepristone
- B. Ethinyl estradiol
- C. Desogestrel
- D. Mestranol

**Answer key:**

1:B 2:C 3:D 4:C 5:C

1: (becuz we asked about the seasonal not monthly)

# Good luck!

## Pharmacology team 434

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