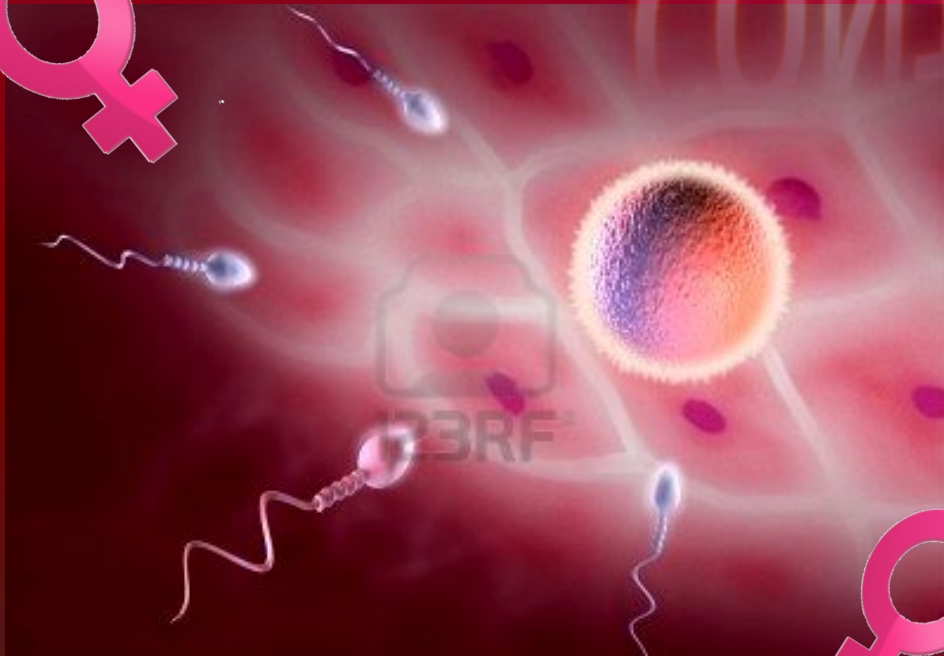


PHARMACOLOGY OF

CONTRACEPTION

CONTRACEPTION



CONTRACEPTION

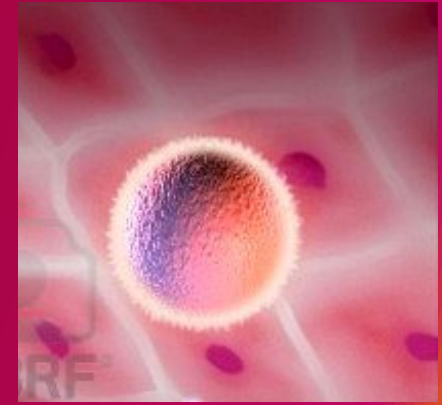


ILOS

By the end of this lecture you will be able to:

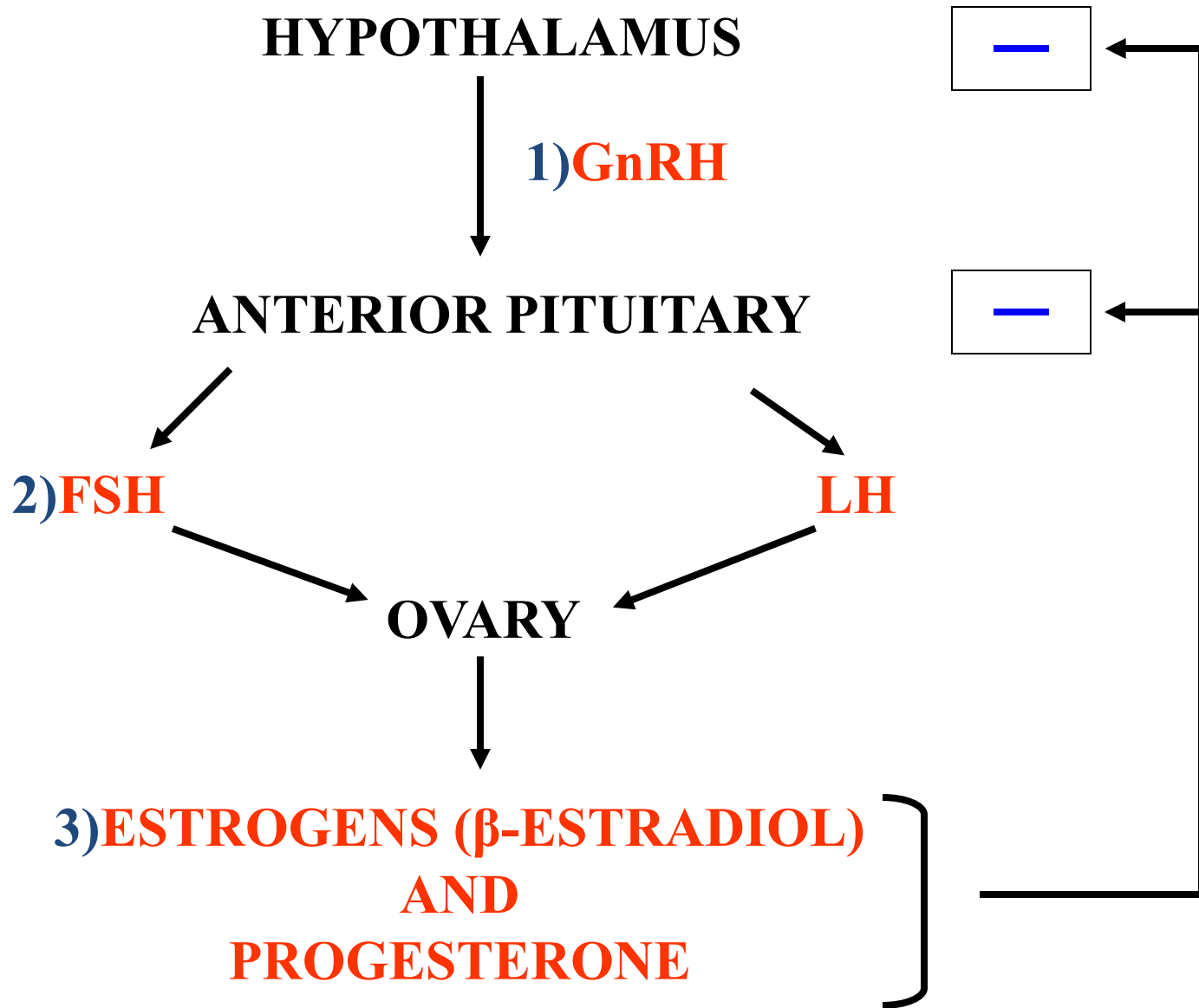
- ⊗ Perceive the different contraceptive utilities available
- ⊗ Classify them according to their site and mechanism of action
- ⊗ Justify the existing hormonal contraceptives present
- ⊗ Compare between the types of oral contraceptives pills with respect to mechanism of action, formulations, indications,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

IN CONCEPTION → there is fusion of the sperm & ovum to produce a new organism.

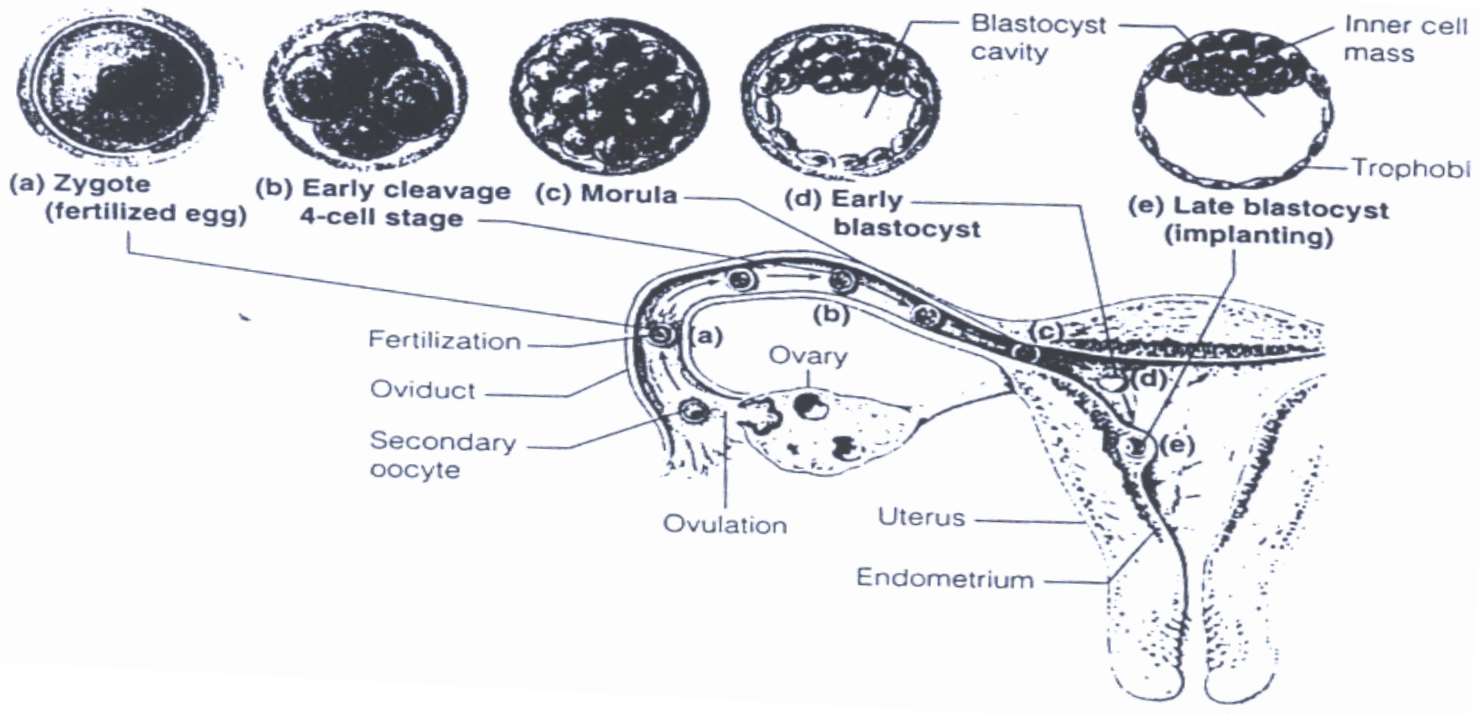
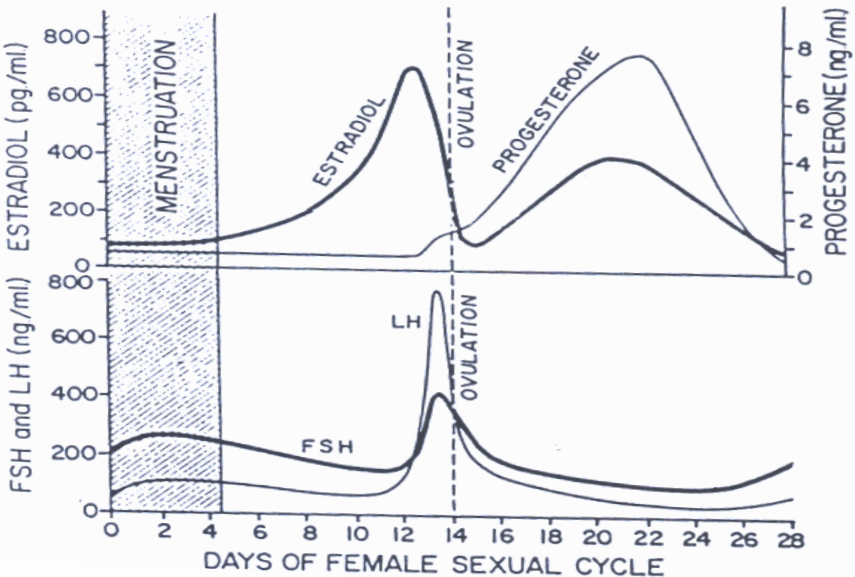


IN CONTRACEPTION → we are preventing this fusion to occur
This achieved by interfering with





Plasma concentrations of the gonadotropins & ovarian hormones during the normal female sexual cycle



Types

ORAL CONTRACEPTIVE Pills

According to composition & intent of use; OC are divided into three types

COMBINED Pills(COC)

Contain estrogen & progestin(100% effective)

MINI Pills(POP)

Contain only a 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

Has systemic androgenic effect; acne, hirsutism, weight gain.

- Currently
- 📊 Norgestimate
 - 📊 Desogestrel
 - 📊 Drospirenone

Has no systemic androgenic effect

MECHANISM OF ACTION OF COC

INHIBIT OVULATION by **SUPPRESSING THE RELEASE OF GONADOTROPHINS (FSH & LH)** → no action on the ovary → ovulation is prevented.

🚧 **Inhibit IMPLANTATION** by causing abnormal contraction of the fallopian tubes & uterine musculature → ovum will be expelled rather than implanted.

🚧 **Increase viscosity of the cervical mucus** making it so viscous → no sperm pass

🚧 **Abnormal transport time through the fallopian tubes .**

COMBINED Pills [COC] *Continued*

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**





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

✚ **Benefit;** 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.

COMBINED Pills [COC] *Continued*

Monthly Pills

🏠 Currently, their formulation is improved to mimic the natural on going 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).

COMBINED Pills [COC]

	Estrogen (mg)		Progestin (mg)	
Monophasic combination tablets				
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	<small>D,L</small> -Norgestrel	0.5
Norinyl 1/50, Ortho-Novum 1/50	Mestranol	0.05	Norethindrone	1.0
Biphasic combination tablets				
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

COMBINED Pills [COC] *Continued*

	Estrogen (mg)		Progestin (mg)	
Triphasic combination tablets				
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

ADRs**A. Estrogen Related**

1. Nausea and breast tenderness
2. Headache
3. ↑ Skin Pigmentation
4. Impair glucose tolerance (hyperglycemia)
5. ↑ incidence of breast, vaginal & cervical cancer
6. Cardiovascular - major concern
 - a. Thromboembolism
 - b. Hypertension
7. ↑ frequency of gall bladder disease

B. Progestin Related

1. Nausea, vomiting & headache
2. Slightly higher failure rate
3. Fatigue, depression of mood
4. Menstrual irregularities
5. Weight gain
6. Hirsutism
7. Masculinization (Norethindrone)
8. Ectopic pregnancy

Contraindications of estrogen containing pills

- Thrombophlebitis / thromboembolic disorders
- CHF 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 – use progestin - only pills(mini pills)

**N.B. Obese Females, smokers,
Females > 35 years**

better given progestin only pills

COMBINED Pills [COC]

Continued

Interactions

Medications that cause contraceptive failure

Impairing absorption

CYT P450 Inducers

Medications that ↑ COC toxicity

CYT P450 Inhibitors

Medications that is altered in clearance by COC

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

Medications that ↑ COC toxicity

Microsomal Enzyme Inhibitors; ↓ metabolism of OC → ↑ toxicity e.g.:
Acetaminophen, Erythromycin

Medications altered in clearance (↓) by COC: → ↑ in their toxicity

WARFARIN, Cyclosporine, Theophylline

Types

ORAL CONTRACEPTIVE Pills

COMBINED Pills

MINI Pills

MORNING-AFTER Pills

Progestin-Only Pills (POP)

Contains only a progestin → as norethindrone or desogestrel....

Mechanism of action

➤ *The main effect is*

→ increase cervical mucus, so no sperm penetration & therefore, no fertilization.

Indications

🚩 Are alternative when oestrogen is contraindicated (e.g.: during breast feeding, hypertension, cancer, smokers over the age of 35).

Contraceptives containing only a progestin

Should be taken **every day**, the **same time**, **all year** round

I.M injection e.g. medroxy progesterone acetate 150 mg every 3 months..

Types

ORAL CONTRACEPTIVE Pills

COMBINED Pills

MINI Pills

MORNING-AFTER Pills

Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse

Post Coital Contraception

Emergency Contraception

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- 120 hrs	85 - 100%

MORNING-AFTER Pills

Continued

Indications

When desirability for avoiding pregnancy is obvious :

- Unsuccessful withdrawal before ejaculation
- Torn, leaking condom
- Missed pills
- Exposure to teratogen e.g. Live vaccine
- Rape



Patch



Cervical Cap



Injectable



Vaginal Ring



Pills



Male Condom



Diaphragm



Female Condom



Spermicides



IUD



IUD