Oral and Other Contraceptives

Lecture

By

Mohammed M. Alanazi, B.Pharm, Ph.D

Assistant Professor

Department of Pharmacology and Toxicology

College of Pharmacy, KSU

Slides adopted from Dr. Sary Alsanea

College of Dentistry, 1st floor \ office 1A 29, momalanazi@ksu.edu.sa

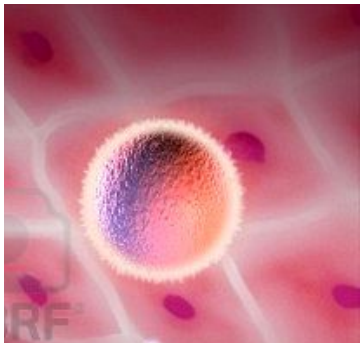
Objectives

- 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

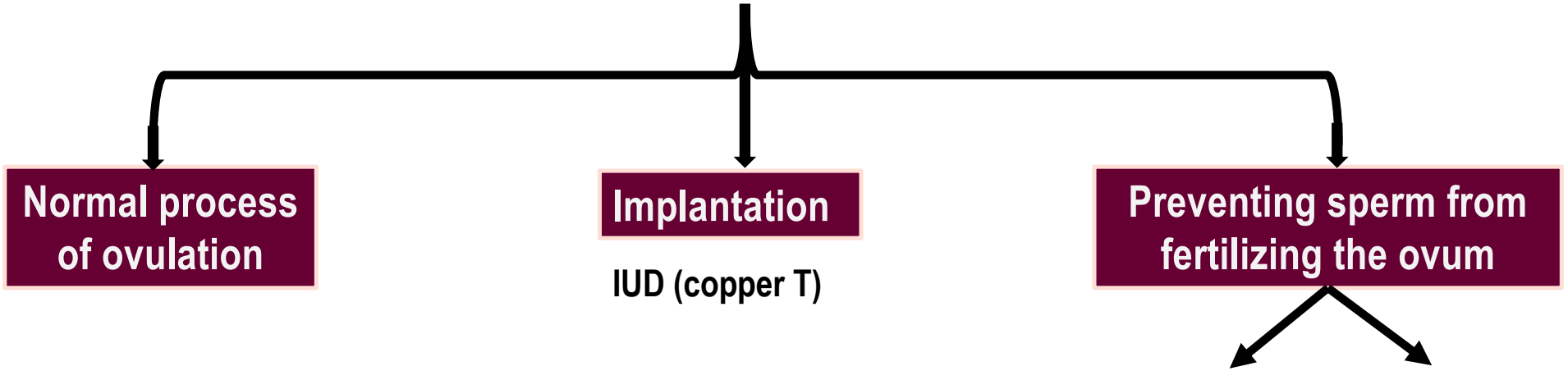
Introduction

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

- **IN CONTRACEPTION ➔ we are preventing this fusion to occur**



Contraception achieved by interfering with:



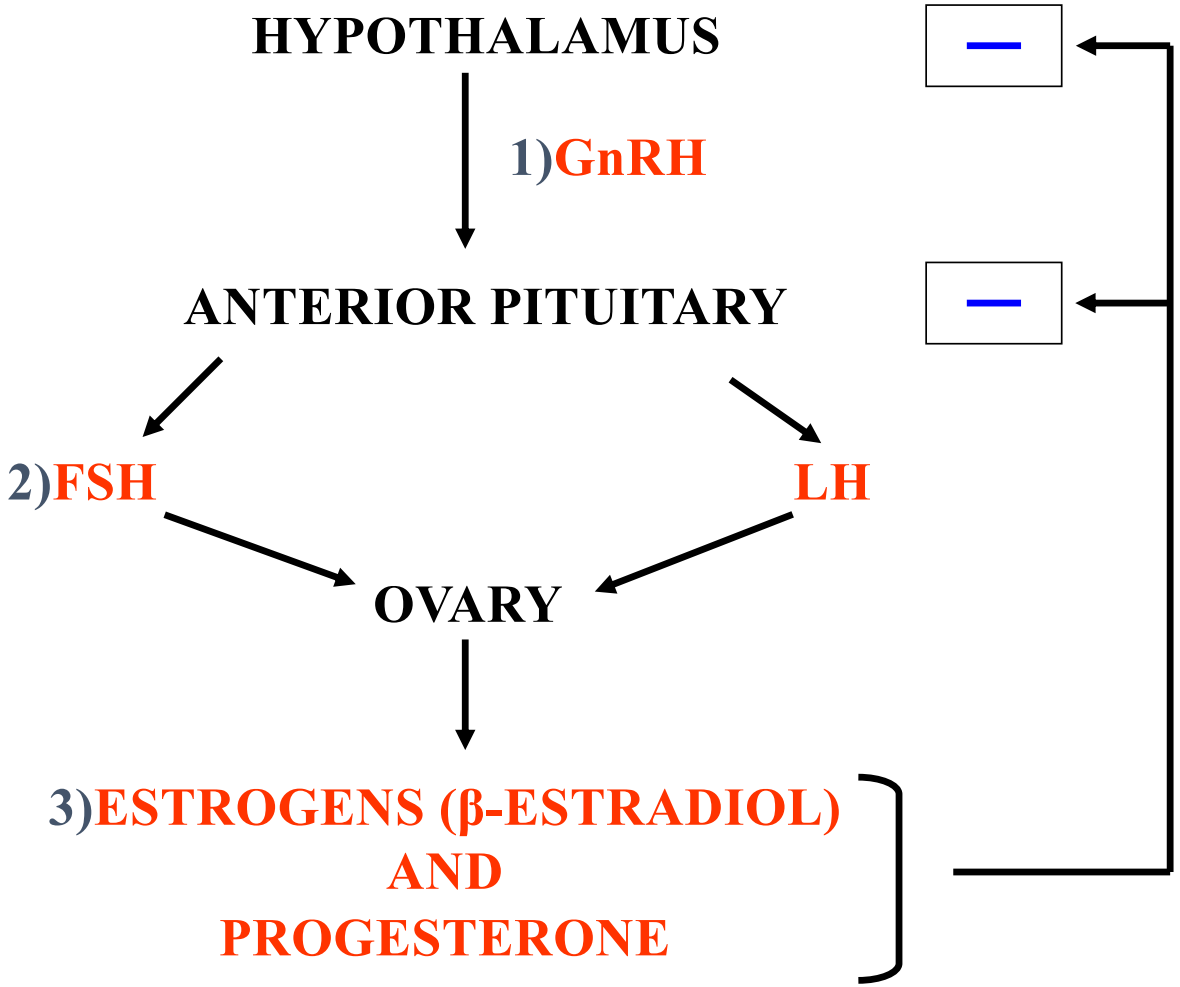
hormonal therapy

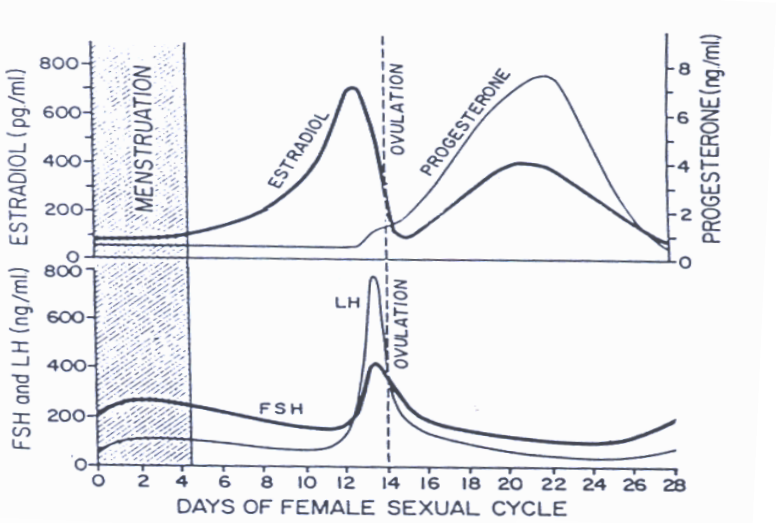
Oral Contraceptive (OC) pills
Contraceptive Patches
Vaginal rings
Injectable
IUD (with hormone)

Spermicidals

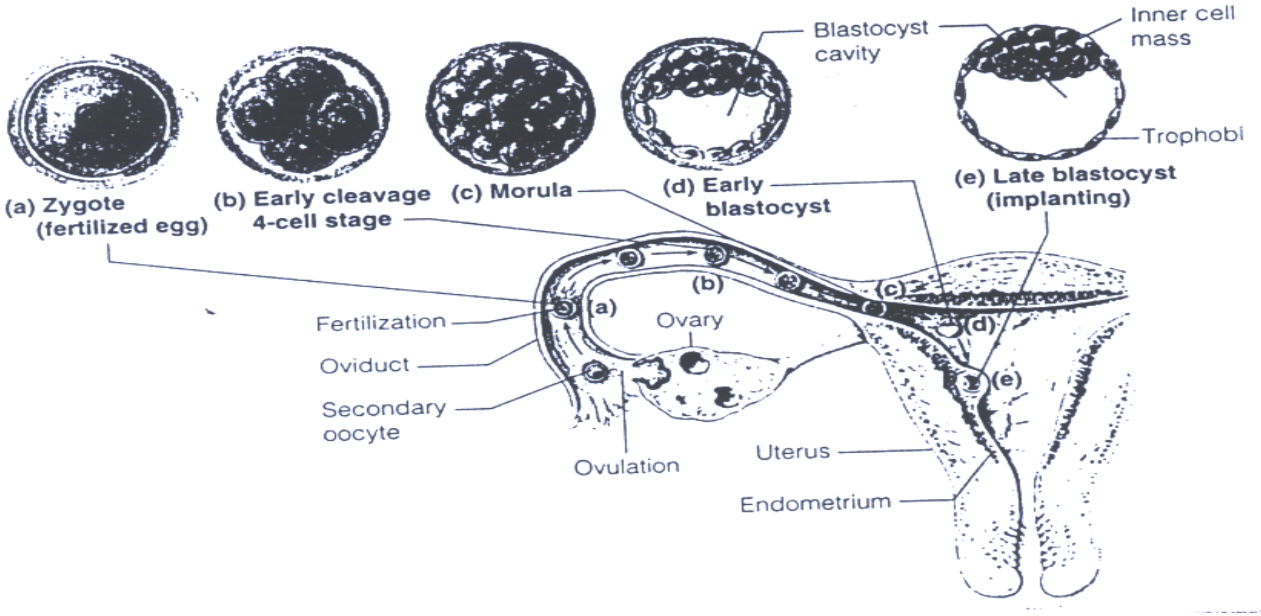
Jells
Foams

Condoms
Cervical caps
Diaphragms
Thin films


HYPOTHALAMUS
1)GnRH
ANTERIOR PITUITARY
2)FSH
LH
OVARY
3)ESTROGENS (β-ESTRADIOL)
AND
PROGESTERONE
–
–



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



Types ORAL CONTRACEPTIVE (OC) Pills According to composition & intent of use

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 (Antiprogestin) + Misoprostol (Pg)

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), and* Medroxyprogesterone acetate • Has systemic androgenic effect; acne, hirsutism, weight gain.
Currently	• Norgestimate, Desogestrel, and Drospirenone • Has no systemic androgenic effect

Combined Oral Contraceptives (COC):

- **Mechanism of Action:**

- **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 Oral Contraceptives (COC):

- **Method 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 medicated**
  - **Followed by the last 7 pills (dummy pills).**

Combined Oral Contraceptives (COC):

- **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**

- ***Benefit:*** **It lessens menstrual periods to 4 times a year (1 period every 3 months) ➔ useful in those who have pain from endometriosis and can prevent migraines during period.**

- ***Disadvantages:*** **Higher incidence of breakthrough bleeding during early use.**

Combined Oral Contraceptives (COC):

- **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).**

	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	Ethynodiol 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 estradlol	0.05	Ethynodiol dlacetate	1.0
Ovcon 50	Ethinyl estradlol	0.05	Norethindrone	1.0
Ovral-28	Ethinyl estradiol	0.05	$_{D,L}$-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 estradlol	0.035	Norethlndrone	1.0

	Estrogen (mg)		Progestin	(mg)
Triphasic combination tablets				
Triphasil, Tri-Levlen, Trivora				
Days 1—6	Ethinyl estradlol	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	Ethiriyl 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	Norgestlmate	0.215
Days 15—21	Ethinyl estradiol	0.035	Norgestimate	0.25

Combined Oral Contraceptives (COC): (Adverse Drug Reactions)

A. Estrogen Related	B. Progestin Related
• Nausea and breast tenderness • Headache • ↑Skin Pigmentation • Impair glucose tolerance (hyperglycemia) • ↑ incidence of breast, vaginal & cervical cancer?? • Cardiovascular - major concern a. Thromboembolism b. Hypertension • ↑ frequency of gall bladder disease	• Nausea, vomiting & headache • Slightly higher failure rate • Fatigue • Depression of mood • Menstrual irregularities • Weight gain • Hirsutism • Masculinization (Norethindrone) • Ectopic pregnancy.

Combined Oral Contraceptives (COC):
(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 Oral Contraceptives (COC): (Interactions)

A. Medications that cause contraceptive failure: (i.e. impairing absorption & CYT P450 Inducers)

- Antibiotics that interfere with normal GI flora → ↓absorption and ↓ enterohepatic recycling → ↓ its bioavailability.
- Microsomal Enzyme Inducers → ↑ catabolism of OC. (Phenytoin , Phenobarbitone, Rifampin)

B. Medications that ↑ COC toxicity: (i.e. CYT P450 inhibitors)

- Microsomal Enzyme Inhibitors; ↓ metabolism of OC → ↑ toxicity. (Acetaminophen, Erythromycin, SSRIs.)

C. Medications of altered clearance (↓) by COC: ↑ toxicity

- WARFARIN, Cyclosporine, Theophylline.

Types ORAL CONTRACEPTIVE (OC) Pills According to composition & intent of use

COMBINED Pills (COC)

MINI Pills (POP)

MORNING-AFTER Pills

Contain only a progestin
(97%effective)

- **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.**

Mini Pills

- **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..

Morning-after pills

- **Indications:**

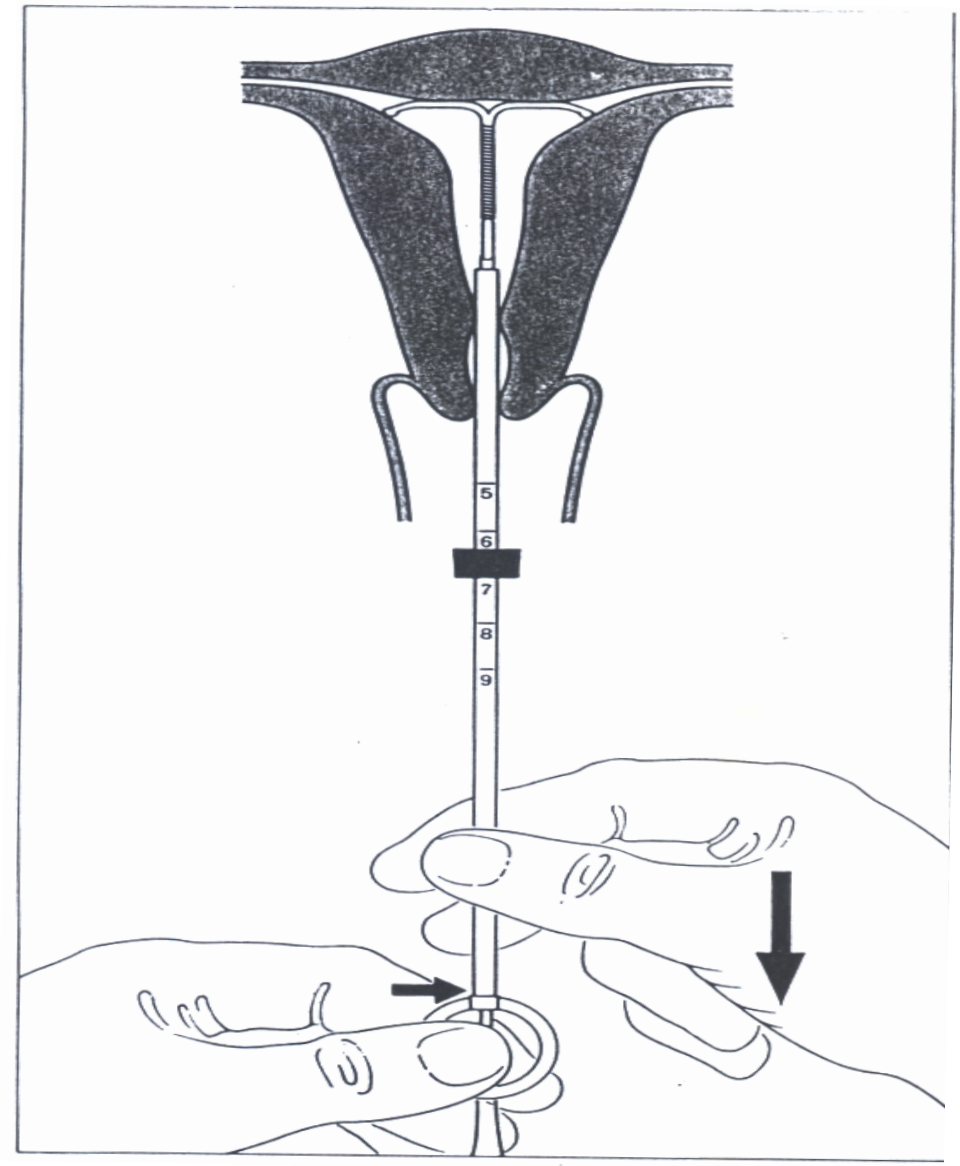
- **When desirability for avoiding pregnancy is obvious:**
- Unsuccessful withdrawal before ejaculation
- Torn, leaking condom
- Missed pills
- Exposure to teratogen e.g. Live vaccine
- Rape

Morning-after pills

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 (Antiprogestin) ± Misoprostol (Pg)	A single dose	0- 120 hrs	85 - 100%

Intrauterine Device (IUD)



Contraceptive Diaphragm

Vaginal ring

Questions ???