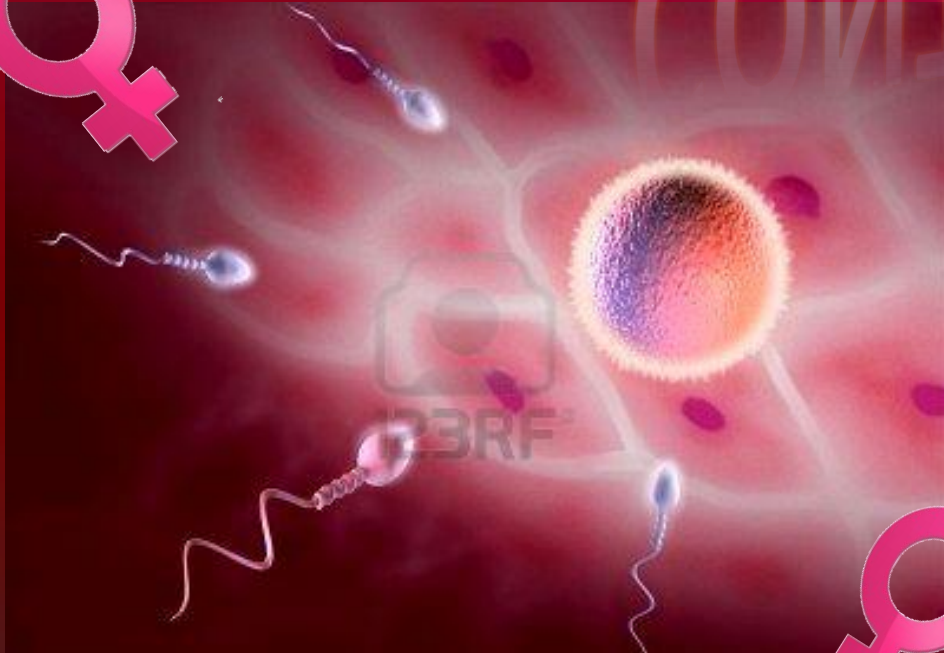


PHARMACOLOGY OF

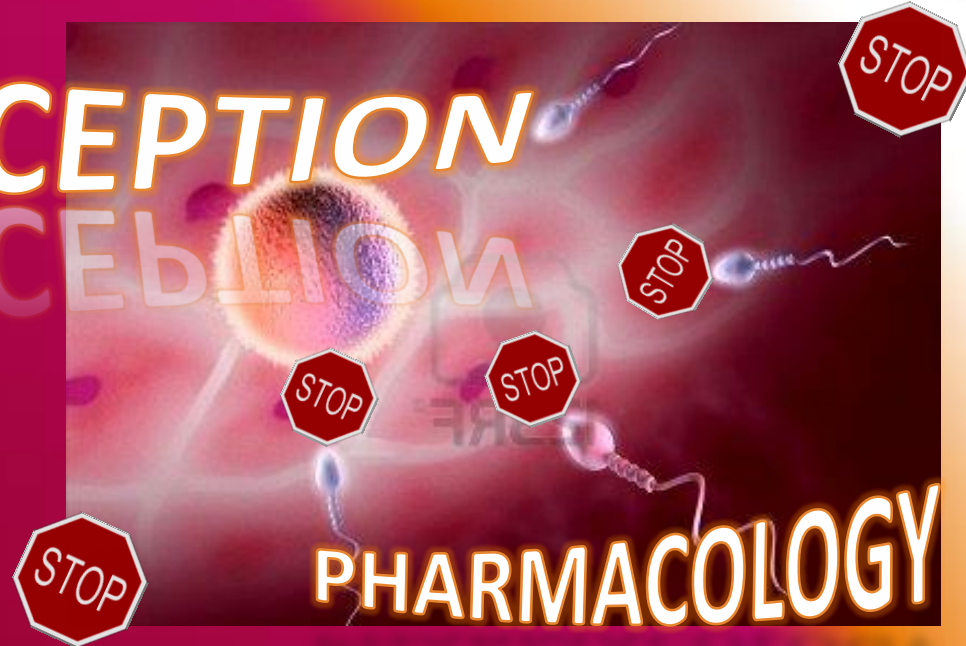
CONTRACEPTION

КОНТРАЦЕПЦИЯ



CONTRACEPTION

CONTRACEPTION

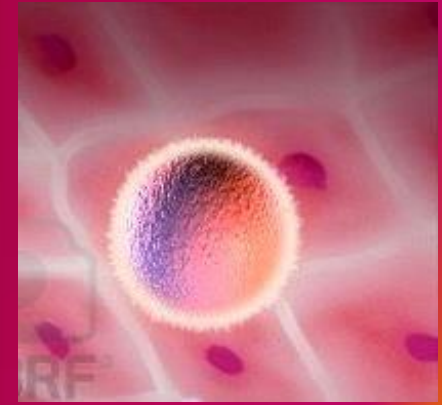
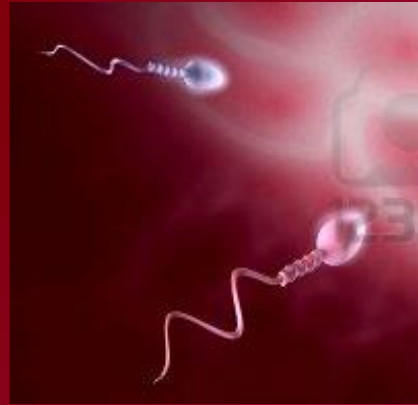


ILOS

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.



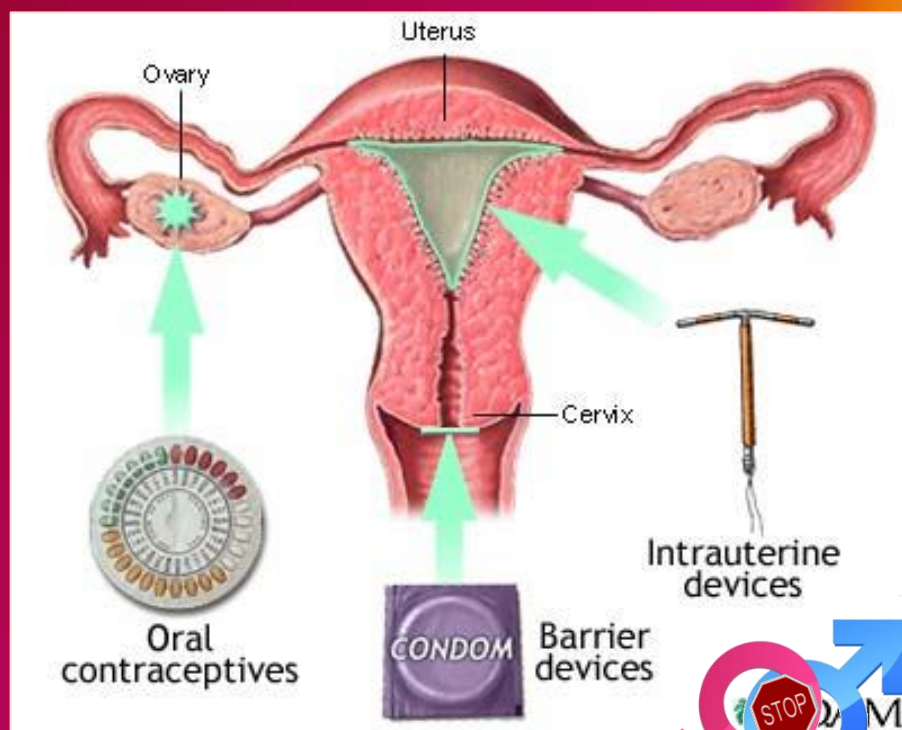
IN CONTRACEPTION → we are preventing this fusion to occur
This achieved by interfering with



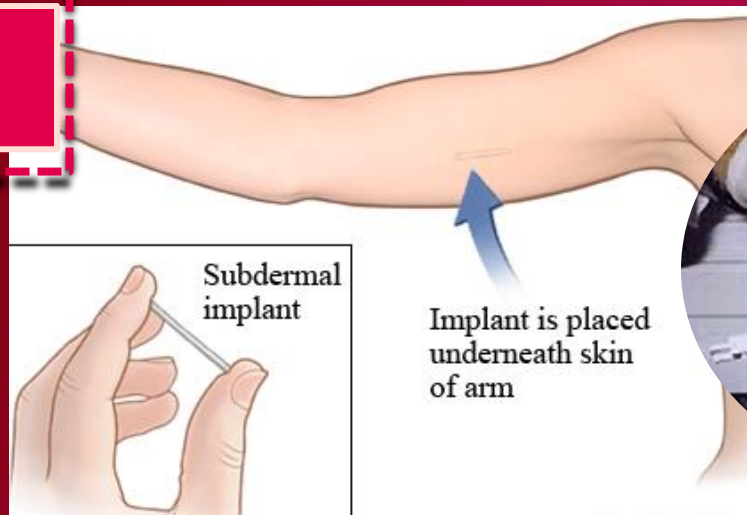
CONTRACEPTIVE UTILITIES AVAILABLE



SITE OF ACTION OF CONTRACEPTIVES



Interruption of normal process of ovulation



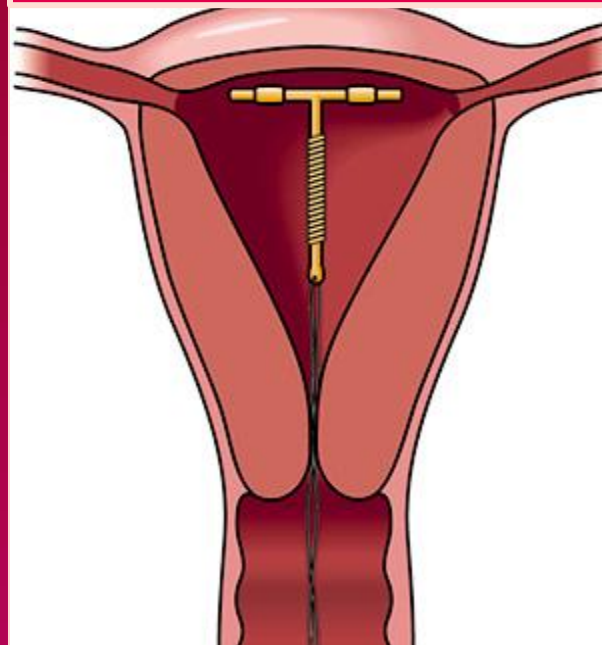
Interruption by a barrier



Barrier method:
The cervical cap fits snugly over the cervix, preventing sperm from entering the uterus



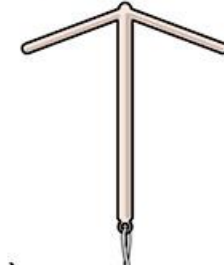
Interruption of Implantation by IUD



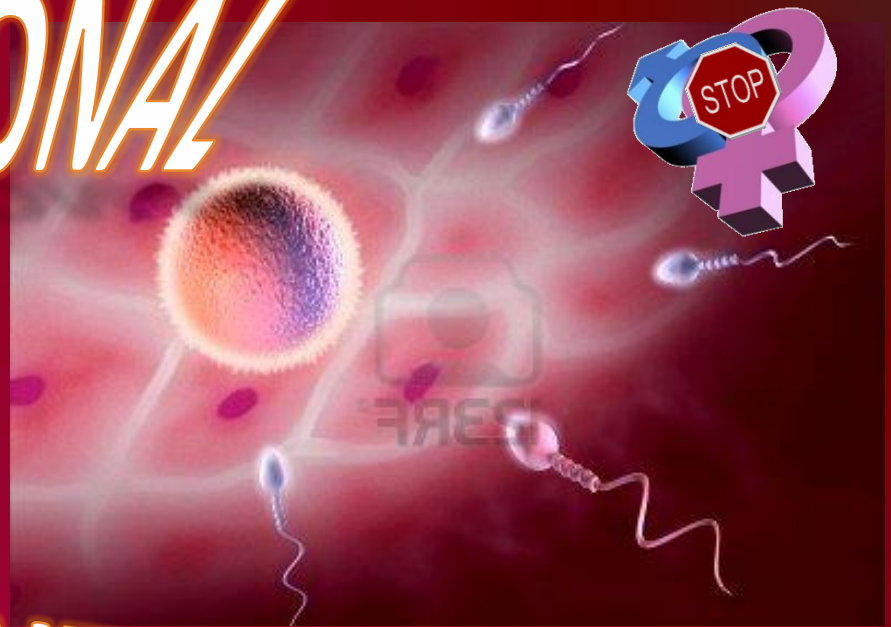
Copper T 380A

IUD

Progestasert

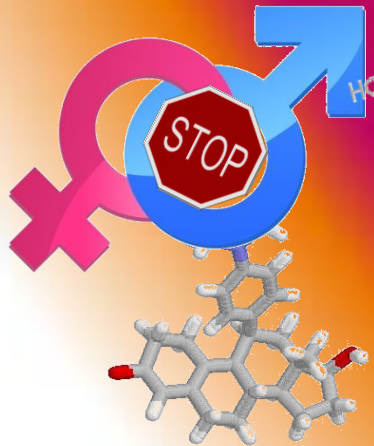
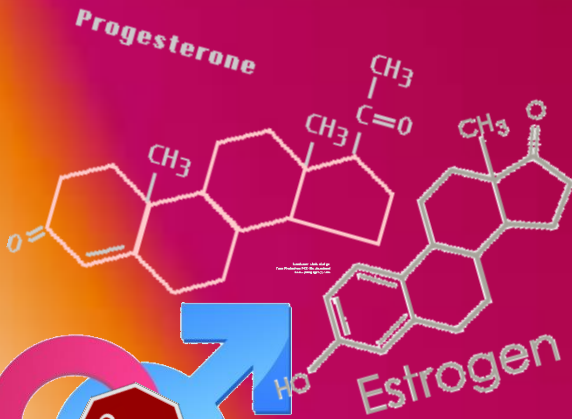


HORMONAL



CONTRACEPTION

CONTRACEPTION



Types

ORAL CONTRACEPTIVE Pills

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

COMBINED Pills(COC)

Contain estrogens & progestin

MINI Pills(POP)

Contain only a progestin

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

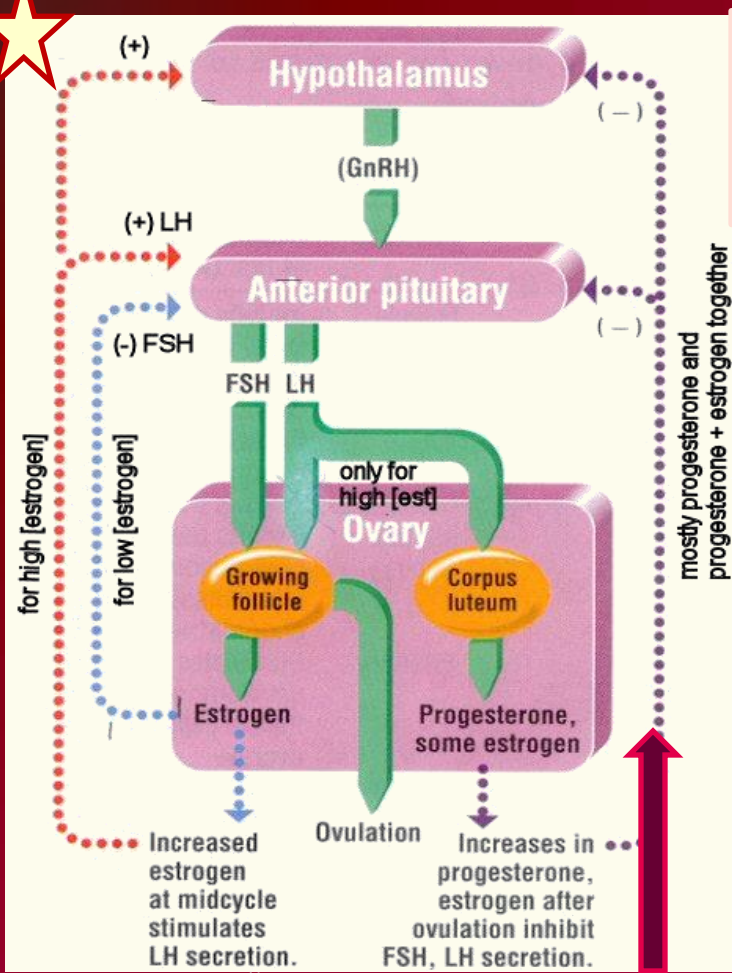
- ☒ Norethindrone
- ☒ Levonorgestrel (*Norgestrel*)
- ☒ Medroxyprogesterone acetate

Show systemic androgenic effects; acne, hirsutism, weight gain, & deleterious effects on lipid & CHO metabolism.

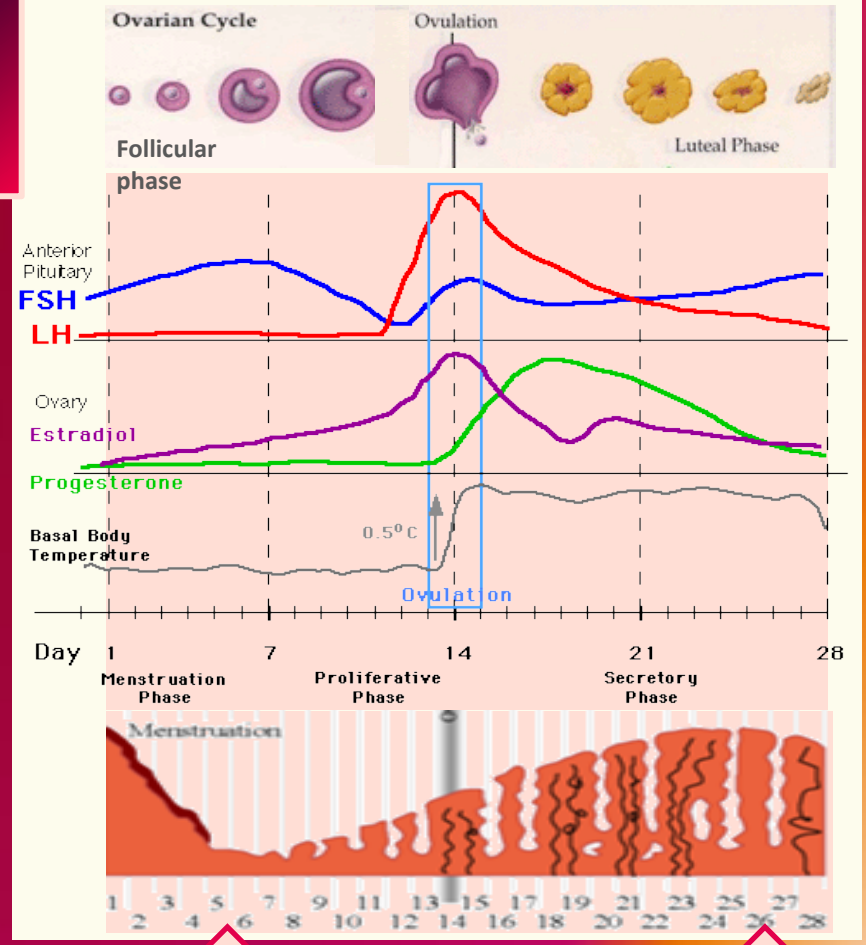
- Currently
- ☒ Norgestimate
 - ☒ Desogestrel
 - ☒ **Drospirenone**

Has no systemic androgenic effects

➔ Has also antimineralocorticoid activity



MECHANISM OF ACTION OF COC



Thus COC act mainly by **Preventing OVULATION** by **SUPPRESSING THE RELEASE OF GONADOTROPHINS** → Yet, by doing so they also →

- 📌 **Inhibit IMPLANTATION** by → ↓ endometrial proliferation → no ovum can be embedded + ↓ secretion & peristalsis in fallopian tubes → hinder transport
- 📌 **Inhibit FERTILIZATION** → ↑ viscosity of cervical secretion → no sperm pass



- They were essentially designed to mimic the menstrual cycle by producing a monthly withdrawal bleeding.
- Currently, their formulation were more improved to also mimic the natural on going changes in hormonal profile → **PHASE FORMULATIONS**
 - 1. Monophasic** → (fixed amount of estrogen & progesterin)
 - 2. Multiphasic** → (fixed amount of estrogen [or variable] + amount of progesterin ↑↑ [in second half or 3 successive phases of cycle)

Methods of administration

- 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**



Seasonal Pills

COMBINED Pills [COC] *Continued*

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 on pill free days.

📊 **Disadvantages;** Higher incidence of breakthrough bleeding & spotting during early use.

Indications of COC

📊 **As a contraceptive;** In women seeking; a reliable, reversible, coitally-independent method of contraception. Efficacy reach up to (99.9%) in preventing pregnancy if a woman is compliant.

📊 **Other indications;**

- As a HRT
- Endometriosis; specially the extended cycle pills.

**ADRs****A. Estrogen Related**

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

B. Progestin Related

1. Nausea, vomiting
2. Headache
3. Fatigue, depression of mood
4. Menstrual irregularities
5. Weight gain
6. Hirsutism , masculinization
7. Ectopic pregnancy.



Contraindications

- 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
- Fibroid tumors – use mini pill
- Dyslipidemia, diabetes, hypertension, migraine.....
- Lactating mothers – use mini pill

N.B. Females that are obese, smokers

Females > 35 years

better given the mini pills



Interactions

Medications that cause contraceptive failure

Medications that ↑ COC toxicity

Medications that is altered in clearance by COC

Impairing absorption
CYT P450 Inducers

CYT P450 Inhibitors

Medications that cause contraceptive failure

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

Medications that ↑ COC toxicity

Microsomal Enzyme Inhibitors; ↓ metabolism of OC → ↑ toxicity
Acetaminophen, Erythromycin, SSRIs

Medications of altered clearance (↓) by COC:

→ ↑ 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....

Mechanisms

- The main mechanism of action ; → increase cervical mucous plug
→ no sperm penetration → inhibit **FERTILIZATION** .



Indications

- ✚ Are alternative when oestrogen is contraindicated (specially in cardiovascular, 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*

Method of administration

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

ADRs & Contraindications

- ✚ That related to progestins only

N.B. There is slightly higher contraception failure rates when used



Types

ORAL CONTRACEPTIVE Pills

COMBINED Pills

MINI Pills

MORNING-AFTER Pills

Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse

Post Coital Contraception

Emergency Hormonal Contraception [EHC]

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	A single dose	Within 120 hrs	85 - 100%



Mechanism

Exact mechanism(s) is questionable depending on the time it is taken in relevance to the menstrual cycle.

N.B. Mifepristone → is a competitive progesterone antagonist → luteolytic → abortifacient → potentiated by addition of **Misoprostol**

Indications

- When desirability for avoiding pregnancy is obvious
- Inevitable ↓ efficacy of other forms of contraception:
 - Unsuccessful withdrawal before ejaculation
 - Torn, leaking condom
 - Missed pills
 - Detached contraceptive patch.....etc
 - Medico-legal insult: Rape

ADRs

Depending on formulations used.

If **Mifepristone**

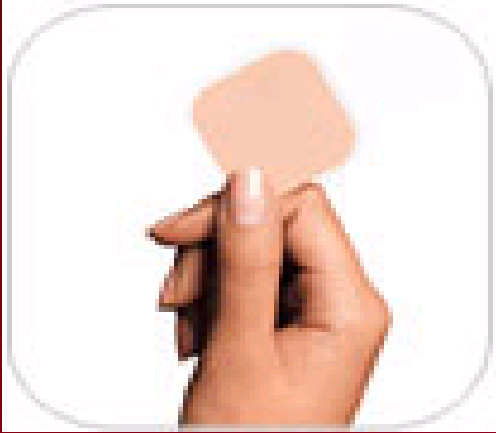
→ uterine bleeding could be problematic
must be under medical supervision



OTHER HORMONAL CONTRACEPTIVE MODALITIES

Other Application MODALITIES	Hormonal Content Within	Dosing Frequency	Reported Efficacy
Patch (<i>Transdermal System</i>)	Like COC, having both hormones	On same day every week for three weeks, 1 week free	99%
Injectable (given IM)	Depot medroxyprogesterone acetate	Every three month	99.7%
Implant (6 rods)	Levonorgestrel	Every three –five years	98-99%
Vaginal Ring	Releases a continuous low dose of hormones	Worn for 3 weeks, one week free to get the cycle	85 - 100%
IUR	Levonorgestrel	Regular contraception Worn for 5 years	97%
	Levonorgestrel	For EHC → Worn for a week / within 5 days	

OTHER HORMONAL CONTRACEPTIVE MODALITIES



CONTRACEPTION

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