



Oral and other forms of contraception

Objectives:

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



Color index:
Important Note Extra

Introduction

Definitions

Conception: there is fusion of the sperm & ovum to produce a new organism.

Contraception: we are preventing this fusion to occur

Contraception

Inhibit the normal process of ovulation

Hormone therapy:

- **Oral contraceptive pill** (birth controlling pills)
- Contraceptive Patches (causing slow hormone release 'use for long time')
- Vaginal rings
- Injectable
- IntraUterine Device 'IUD' (with hormone) a device inserted in uterus and secrete hormones which make the uterus contracted 'no good environment for implantation'

Implantation

Intrauterine device 'IUD' (copper T)

the uterus see this loop as foreign body, so it will contract which expel the fertilized ovum (spermicidal)

Preventing sperm from fertilizing the ovum

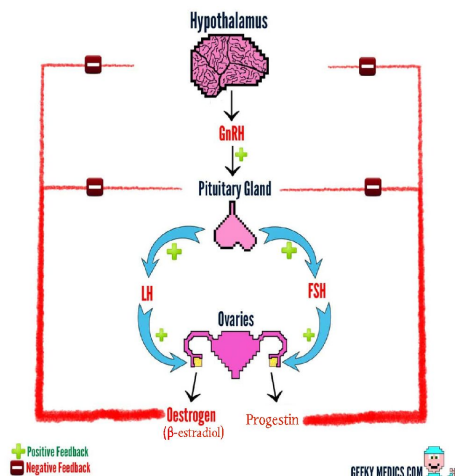
Killing sperms (spermicidal):

- ✓ Jells
- ✓ Foams

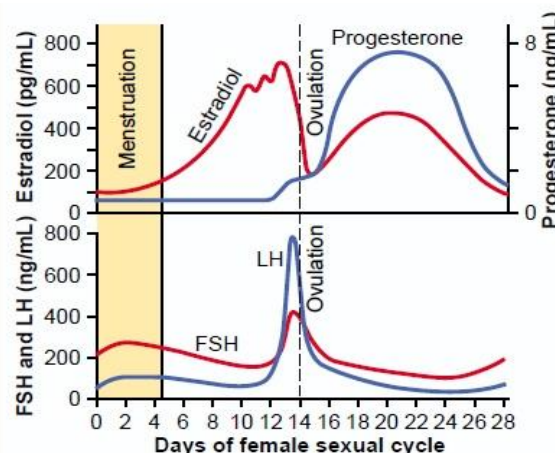
Interruption by a barrier:

- ✓ Condoms
- ✓ Cervical caps
- ✓ Diaphragm
- ✓ Thin films

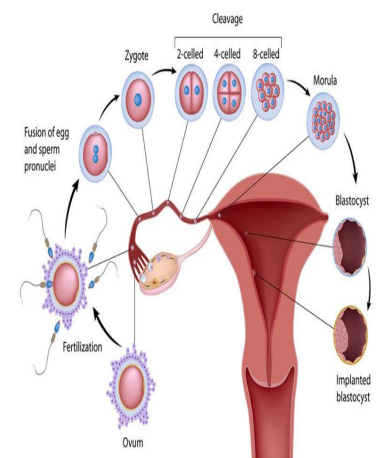
Physiology review



Hypothalamic pituitary gonadal axis

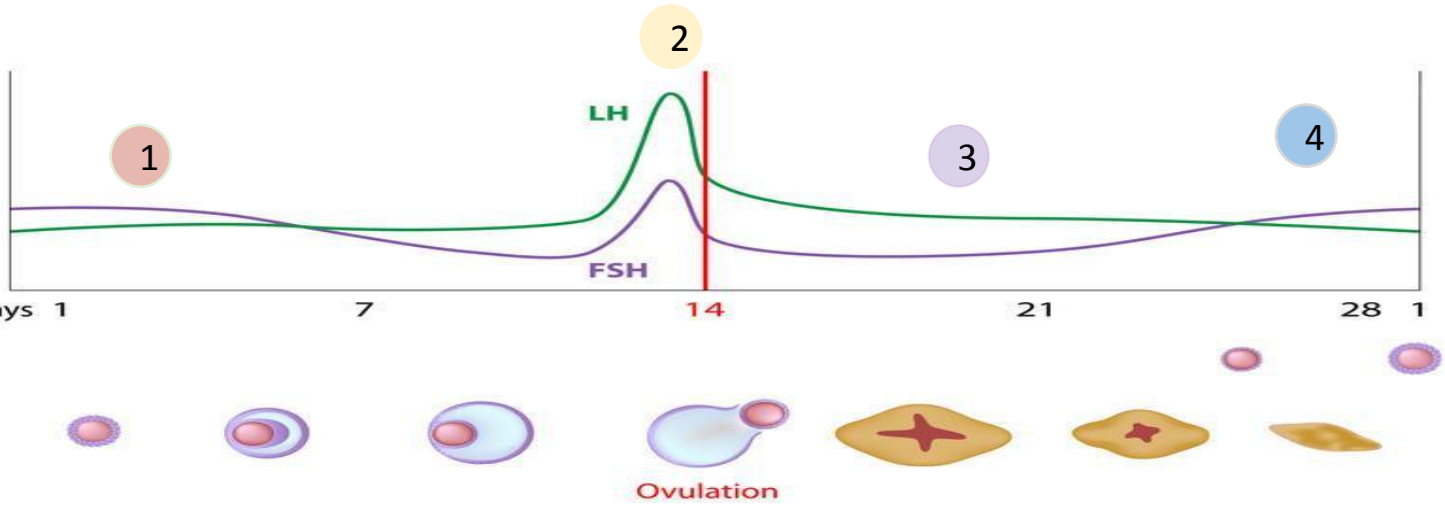


Plasma concentrations of the gonadotropins & ovarian hormones during the normal female sexual cycle



Early development of the fetus

Physiology Review



1

At the beginning of the cycle the FSH increase, with a modest increase in LH ;and that is to prepare the follicle that will contain the oocyte ,at the same time we see an increase in estrogen that helps in producing the perfect environment for the embryo in the uterus by increasing the vascularity and thickness of the endometrium

2

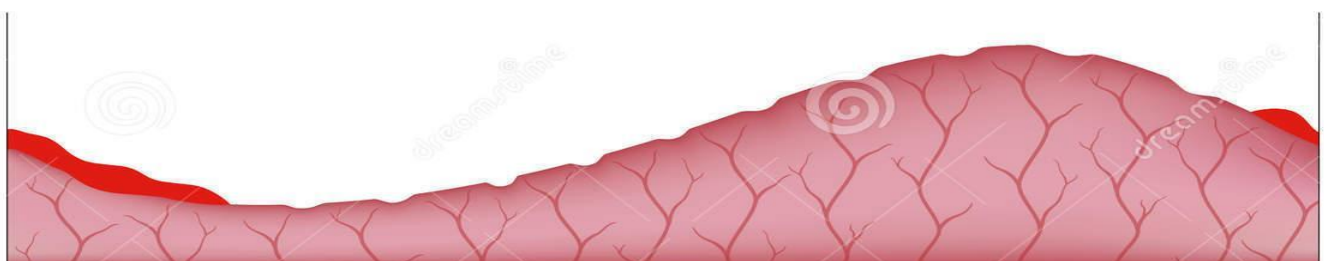
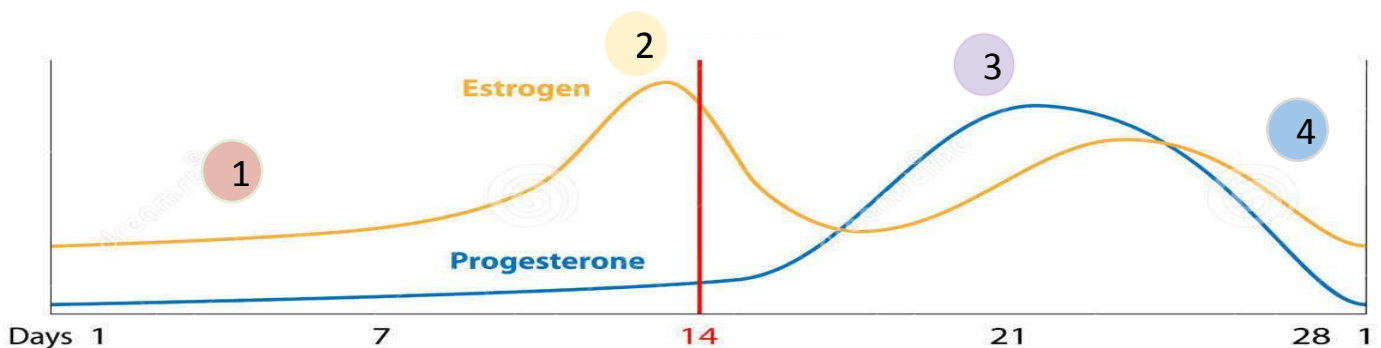
2 days before the ovulation at 12th day : the LH surge then LH will drop ,as well as the **Estrogen** ,and this will lead to ovulation

3

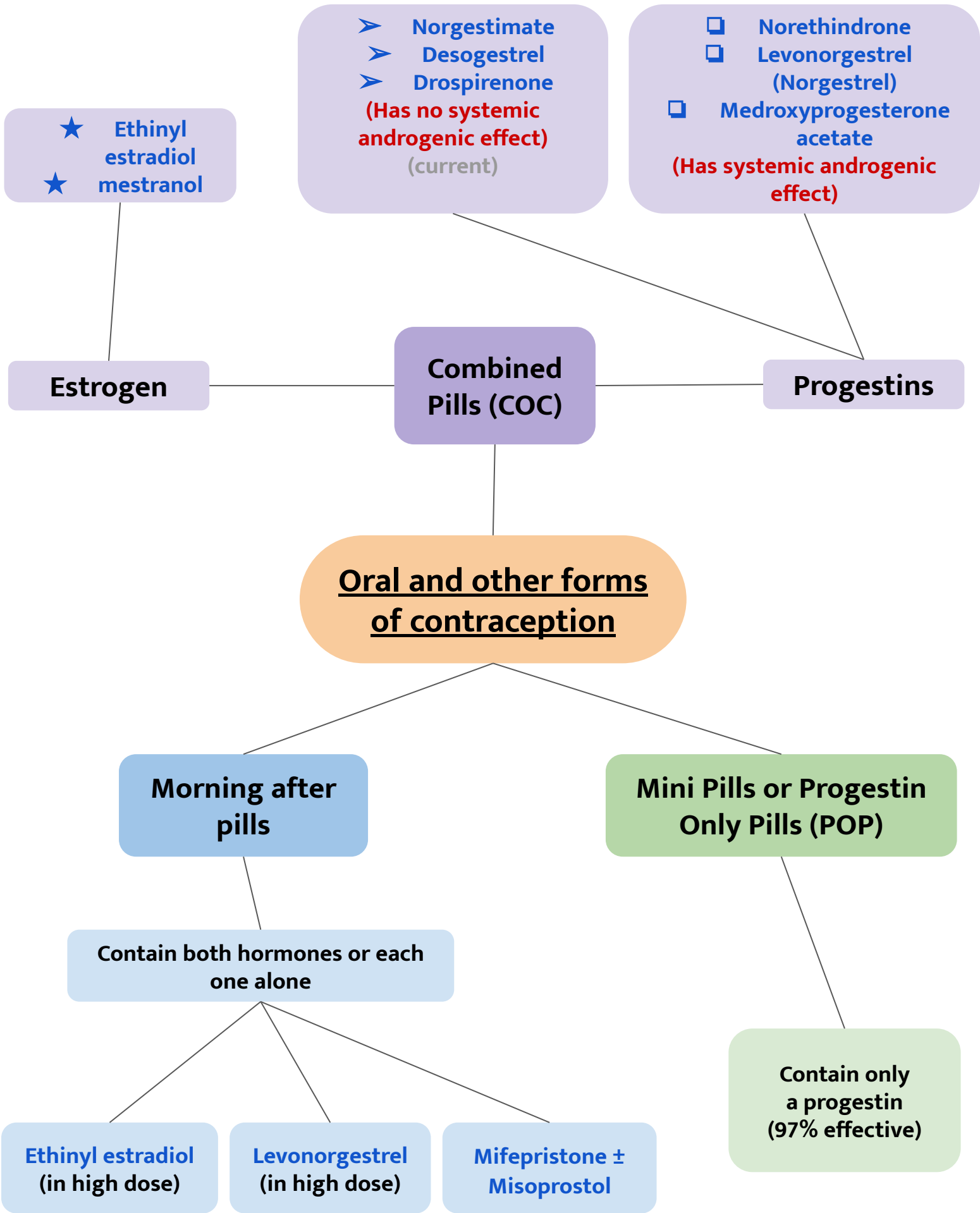
After the ovulation the corpus luteum will secrete **progesterone** and high amount of **estrogen** to prevent the formation of a new ovum by causing a negative feedback to GnRH thus preventing the secretion of **FSH** and **LH**

4

If the ovum is fertilized in the fallopian tube it will implant in endometrium but if not at the 26th day the corpus luteum will lose its secretion (no estrogen and progesterone) and become corpus albican. This will cause the shedding of the endometrium +the cessation of the -ve feedback → repeated cycle



Mindmap



Combined pills (Combined Oral contraceptives)

<p>M.O.A</p>	<ul style="list-style-type: none"> ● Inhibit Ovulation by Suppressing The Release Of Gonadotropins (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 . 	
<p>Methods of administration</p>	<p style="text-align: center;">Monthly Pills</p> <ul style="list-style-type: none"> ● Pills are better taken at the 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 <p><u>To improve compliance: we use a formulation of 28 pills:</u></p> <ul style="list-style-type: none"> ❖ The first 21 pills are of multiphasic formulation (medicated). ❖ Followed by the last 7 placebo pills (dummy pills) 	<p style="text-align: center;">Seasonal Pills</p> <ul style="list-style-type: none"> ● Are known as Continuous / Extended cycle Cover 91 days ● Taken continuously for 84 days, and then a 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 premenstrual or menstrual disorders, and in perimenopausal women with vasomotor symptoms on pill free days Useful in those who have pain from endometriosis and can prevent migraines during period. ● Disadvantages: Higher incidence of breakthrough bleeding & spotting during early use.
<p><u>Monthly Pills</u> Phase Formulations</p>	<ul style="list-style-type: none"> ◆ Currently, the formulation of monthly pills are improved to mimic the natural ongoing changes in hormonal profile. ◆ Accordingly we have now the phase formulations: <ol style="list-style-type: none"> 1. <u>Monophasic</u> (a fixed amount of estrogen & progestin) 2. <u>Biphasic</u> (2 doses) (a fixed amount of estrogen, while the amount of progestin increases stepwise in the second half of the cycle) 3. <u>Triphasic</u> (3 doses) (amount of estrogen; fixed or variable & amount of progestin increases stepwise in 3 phases). 	

Combined Pills (cont.)

- ❖ All you have to know from the tables: Team 435:
 ✓ the Biphasic and Triphasic tablets have a **stepwise increase in the concentration of Progestin** (twice in Biphasic , and 3 times in Triphasic)

الجدول بس لتوضيح المفهوم حق المونو والباي والترافيزك،
 لا تضيعون وقتكم عليه
 + نلاحظ إن الأستروجين غالبًا قليل عشان نقلل أعراضه
 الجانبية

1		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 estradiol	0.05	Ethynodiol diacetate	1.0	
Ovcon 50	Ethinyl estradiol	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 estradiol	0.035	Norethindrone	1.0	
2		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	

دكتور الأولاد ما تكلم عنها لكن بروف يلدز قالت بس اعرفوا نفس ما كتبنا إن في mono الإستروجين والبروجيستيرون ثابتين أما في bi يكون الإستروجين فقط الثابت والبروجيستيرون يتغير على فترتين ، أما tri كلهم يتغيرون الإستروجين و خاصة البروجيستيرون يكون على ثلاث فترات (إذا تلخبطتوا اسحبوا عليه عادي الدكتوراة قالت ما راح نسألكم عنها)

	Estrogen Related	Progestin Related
Adverse Effects	<ol style="list-style-type: none"> 1. Nausea and breast tenderness. 2. Headache. 3. Skin Pigmentation . 4. Impaired glucose tolerance (hyperglycemia) 5. Increase incidence of breast, vaginal & cervical cancer. 6. Cardiovascular: (major concern) A-Thromboembolism B-Hypertension 7. Increased frequency of gallbladder disease. 	<ol style="list-style-type: none"> 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)

C.I	<ul style="list-style-type: none"> ● Thrombophlebitis / thromboembolic disorders ● Chronic heart failure 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 <p>You use Mini pills (which contain only progestin) with 4 types of females:</p> <ul style="list-style-type: none"> ✓ Lactating mothers ✓ Obese ✓ Smokers. ✓ Females > 35 years
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Combined Pills (COC) interactions

Medications that cause contraceptive failure

Impairing absorption:
Antibiotics that interfere with normal GI flora → **decrease** absorption → decrease its bioavailability e.g.: **Ampicillin**

CYT P450 Inducers:
Microsomal Enzyme Inducers → **Increase** catabolism of oral contraceptive e.g.: **Phenytoin, Phenobarbitone, Rifampin**

Medications that increase COC toxicity

Microsomal Enzyme Inhibitors:
↓ **metabolism** of oral contraceptive which will ↑ toxicity (e.g. **Acetaminophen, Erythromycin**).

Medications that are altered in clearance (↓) by COC

(e.g. **Warfarin, Cyclosporine, Theophylline**).

MINI PILLS, Progestin only pills (POP)

MINI Pills

Note

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

M.O.A

- **The main effect: increase cervical mucus, so no sperm penetration & therefore, no fertilization.**
 - make the endometrium thin → hard implantation
- Desogestrel is preferable more than old progestin generation in COC because it has no androgenic sequel

Uses

- Are alternative when oestrogen is contraindicated (e.g.: **during breast feeding, hypertension, cancer, smokers over the age of 35**).
- Should be taken every day, the same time, **all year round** (it has higher failure rate, if she miss the pill, pregnancy could happen)

P.K

I.M injection e.g. **medroxyprogesterone acetate** 150 mg every 3 months.
(it remains in the body for a long period of time, so it has long effect + should not be given to women who want to conceive because its effect)

Morning-After pill

Post Coital Contraception (**Emergency Contraception**)

Indications	<p>Contraception on instantaneous demand, 2ndry to unprotected sexual intercourse</p> <p>❖ <u>When desirability for avoiding pregnancy is obvious :</u></p> <ul style="list-style-type: none"> • Unsuccessful withdrawal before ejaculation • Torn, leaking condom • Missed pills • Exposure to teratogen e.g. Live vaccine ((لأنه هنا قد يحصل تشوه للجنين)) • Rape
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Methods of Use

Composition	Method of Administration	Timing of 1 st dose After Intercourse	Reported Efficacy
Ethinyl estradiol + Levonorgestrel	2 tablets twice with 12 hrs in between*	0** - 72hrs	75%
High-dose only Ethinyl estradiol	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	100% - 85 Very effective

Summary

Estrogen:

Ethinyl estradiol or Mestranol

Progestins

Levonorgestrel or Norgestimate

Has **No** systemic androgenic effect

Combined Pills COC

MOA	<ul style="list-style-type: none"> Inhibit ovulation by suppressing the release of FSH and LH → no action on the ovary → ovulation is prevented. Increase viscosity of the cervical mucus making it so viscous → no sperm pass
Monthly pills	For 25 Days at the same time : Start on the 5th day and end at 26th followed by 7 free days
Seasonal pills	<ul style="list-style-type: none"> ➤ Continuously for 84 days ➤ She will have 4 periods a year ➤ Good for perimenopausal with vasomotor symptoms ➤ Help with period migraine ➤ Could cause spotting during early use.

MINI Pills

(Progestin only)

MOA	Increase cervical mucus → no sperm penetration → no fertilization.
Indications	<ul style="list-style-type: none"> Are alternative when oestrogen is contraindicated Taken every day, the same time, all year round as I.M injection

Post Coital Contraception (Emergency Contraception)

indications	<p><u>When desirability for avoiding pregnancy is obvious:</u></p> <p>1-Unsuccessful withdrawal before ejaculation 2-Missed pills 3-Torn, leaking condom 4-Exposure to teratogens 5-Rape</p>
Methods of use	<p><u>Ethinyl estradiol + Levonorgestrel:</u> ↻ 2 tablets twice with 12 hrs in between</p> <p><u>High-dose only Ethinyl estradiol:</u> ↻ Twice daily for 5 days</p> <p><u>High dose only levonorgestrel:</u> ↻ Twice daily for 5 days</p> <p><u>Mifepristone ± Misoprostol:</u> ↻ A single dose, Very effective</p>

Quiz

Q1: What is the main mechanism of action of progesterone only pills?

- A. Increase cervical mucus
- B. Spermicidal
- C. Inhibit ovulation
- D. Makes sperm immotile

Q2: Which of the following is a progesterone only pill?

- A. Ethinyl estradiol
- B. Levonorgestrel
- C. Misoprostol
- D. Norethindrone

Q3: Which of the following morning-after pills is given as a single dose?

- A. Ethinyl estradiol
- B. Amitriptyline
- C. Misoprostol
- D. Norethindrone

Q4: Which of the following is not an indication for a morning-after pill?

- A. Rape
- B. Paracetamol intake
- C. Recent Live vaccine
- D. Torn condom

Q5: Which of the following is a spermicidal?

- A. Condom
- B. Cervical cap
- C. Diaphragm
- D. Certain jells

Q6: Which of the following is a major concern as an adverse effect related to Estrogen?

- A. Menstrual irregularities
- B. Cardiovascular problems
- C. Headache
- D. Hirsutism

Q7: You use mini pills which contain only progestin with all of the following except?

- A. Obese female
- B. Lactating female
- C. Female > 35 years
- D. Thrombophlebitis

Q8: Which of the following increase combined pills toxicity by inhibiting microsomal enzymes?

- A. Erythromycin
- B. Warfarin
- C. Theophylline
- D. Ampicillin

Q9: Which of the following is an adverse effect related to Progestin?

- A. Impaired glucose tolerance
- B. Cardiovascular problems
- C. Headache
- D. Hirsutism

Answers:
1) A
2) D
3) C
4) B
5) D
6) B
7) D
8) A
9) D



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*Thanks for those who
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References:

- ★ Team 436
- ★ Doctors' slides and notes



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