

# PHARMA

MODIFIED NO. 12

الكتاب: محمود جرادات وصهيب زعيتر

المدققين: إبراهيم الشوابكة

الككتوراة: يعقوب إرشيد





# **Oral Contraceptives**

Yacoub Irshaid, MD, PhD, ABCP Department of Pharmacology

#### Color code

Slides

Doctor

Additional info

**Important** 

#### **Lecture Topics:**

- 1. Introduction to Hormonal Contraception
- 2. Types of Combined Oral Contraceptives (COCs): Monophasic, biphasic, triphasic and tetraphasic (U.S. only)
- 3. Progestin-only Contraception: Mini pills, injectable (DMPA) and implants.
- 4. Estrogens and Progestins Used in Contraceptives
- 5. Mechanism of Action of COCs
- 6. Pharmacologic Effects on Body Systems
- 7. Therapeutic Uses
- 8. Adverse Effects: Mild, moderate and severe (contraindications)
- 9. Contraindications to Combined Oral Contraceptives
- 10. Oral Contraceptive Failure
- There are no more drugs to be memorized

### Hormonal Contraception (combinations or progesterone alone)

- A. Combinations of estrogens and progestins (given orally):
- 1. Monophasic forms: constant dosage of both components during the cycle. (This consistent dosing lasts for most of the month, followed by a hormone-free interval (usually 3-5 days) to allow for withdrawal bleeding, mimicking a natural menstrual period). The packaging of these contraceptives is often designed to guide the user. Tablets are usually arranged sequentially—tablet 1 is taken on day 1, tablet 2 on day 2, and so on. During the hormone-free days, some packs contain placebo pills to help maintain the habit of daily intake, while others may be empty or clearly marked as non-medicated.
- 2. Biphasic forms: dosage of one or both components is changed once during the cycle
- 3. Triphasic forms: dosage of one or both components is changed twice during the cycle.
- 4. Tetraphasic forms: in US

**TABLE 40-3** Some oral and implantable contraceptive agents in use.<sup>1</sup>

	Estrogen (mg	<b>j</b> )	Progestin (mg)	Progestin (mg)	
Monophasic combination tablets					
Alesse, Aviane, Lessinea, Levlite	Ethinyl estradiol	0.02	L-Norgestrel	0.1	
Levlen, Levora, Nordette, Portia	Ethinyl estradiol	0.03	L-Norgestrel	0.15	
Crysella, Lo-Ovral, Low-Ogestrel	Ethinyl estradiol	0.03	Norgestrel	0.30	
Yasmin	Ethinyl estradiol	0.03	Drospirenone	3.0	
Brevicon, Modicon, Necon 0.5/35, Nortrel 0.5/35	Ethinyl estradiol	0.035	Norethindrone	1.0	
Ortho-Cyclen, Sprintec	Ethinyl estradiol	0.035	Norgestimate	0.25	
Necon 1/35, Norinyl 1+, Nortrel 1/35, Ortho-Novum 1/35	Ethinyl estradiol	0.035	Norethindrone	1.0	
Ovcon-35	Ethinyl estradiol	0.035	Norethindrone	0.4	
Demulen 1/50, Zovia 1/50E	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					
Ortho-Novum 10/11, Necon 10/11					
Days 1–10	Ethinyl estradiol	0.035	Norethindrone	0.5	
Days 11–21	Ethinyl estradiol	0.035	Norethindrone	1.0	
Triphasic combination tablets					
Enpresse, 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	
Daily progestin tablets					
Nora-BE, Nor-QD, Ortho Micronor, Jolivette, Camila, Errin			Norethindrone	0.35	
Ovrette			D,L-Norgestrel	0.075	
Implantable progestin preparation					
Implanon			Etonogestrel (one tube	Etonogestrel (one tube of 68 mg)	

<sup>&</sup>lt;sup>1</sup>The estrogen-containing compounds are arranged in order of increasing content of estrogen. Other preparations are available. (Ethinyl estradiol and mestranol have similar potencies.)

### **Hormonal Contraception**

B. Progesterone alone - Continuous progestin therapy without concomitant administration of estrogen, orally or by implantation under the skin or intramuscular injection .

### **Hormonal Contraception**

#### • Estrogens:

Ethinyl estradiol (the most common estrogen), Mestranol.

#### • Progestins:

L-Norgestrel, Drospirenone, Norethindrone, Norgestimate, Ethynodiol diacetate.

The most common progestins are L-Norgestrel and Norethindrone.

Progestins are not all the same they differ from each other.

#### Some oral and implantable contraceptive agents

	Estrogen	mg	Progestin	mg
Monophasic	Ethinyl	0.02	L-Norgestrel	0.1
Combination	estradiol			
Tablets				
	Ethinyl	0.03	L-Norgestrel	0.15
	estradiol			
	Ethinyl	0.02	Norethindrone	1
	estradiol			
	Ethinyl	0.035	Norethindrone	1
	estradiol			
	Mestranol	0.05	Norethindrone	1
Biphasic				
Combination				
Tablets				
Days 1–21	Ethinyl	0.02	Desogestrel	0.15
	estradiol			
Days 22–27	Ethinyl	0.01	None	
	estradiol			
Days 1–10	Ethinyl	0.035	Norethindrone	0.5
	estradiol			
Days 11–21	Ethinyl	0.035	Norethindrone	1
	estradiol			
Triphasic				
Combination				
Tablets				
Days 1–6	Ethinyl	0.03	L-Norgestrel	0.05
	estradiol			
Days 7–11	Ethinyl	0.04	L-Norgestrel	0.075
	estradiol			
Days 12-21	Ethinyl	0.03	L-Norgestrel	0.125
	estradiol			

افهموا الجدول ما تحفظوه

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
4-Phasic Combination Tablet				
Days 1–2	Estradiol valerate	3	None	
Days 3–8	Estradiol valerate	2	Dienogest	2
Days 9–25	Estradiol valerate	2	Dienogest	3
Day 26–27	Estradiol valerate	1	None	
Daily Progestin Tablets	None	-	Norethindrone	0.35
Contraceptive Transdermal Patch (Apply 1 Patch per Week)	Ethinyl estradiol	0.02/24 h	Norgestromin	0.150/24 h
Implantable Progestin Preparation	None	-	Etonogestrel	(one tube of 68 mg)

Transdermal contraceptives are used when oral contraceptives are contraindicated or when there is poor patient compliance (Missing even one oral contraceptive pill can increase the risk of pregnancy).

For example, a monophasic pill might contain 0.02 mg of ethinyl estradiol and 1 mg of norethindrone in each tablet, taken daily for a set number of days (usually 21 days), followed by a hormone-free interval to induce withdrawal bleeding.

When discussing concentration, we focus on what each pill contains, not how it looks across the packaging. For example, a specific brand might provide 0.02 mg of ethinyl estradiol and 1 mg of norethindrone per tablet throughout the cycle—this uniform dosage is the key characteristic of a monophasic pill.

#### **Biphasic Pills:**

<u>Days 1 to 21</u>: The pills contain 0.02 mg of ethinyl estradiol and 0.15 mg of a progestin (e.g., desogestrel). <u>Days 22 to 27</u>: The pills contain only 0.01 mg of ethinyl estradiol with no progestin.

This change in hormone levels helps mimic natural hormonal fluctuations. Some packs have 21 pills, while others have 27 or 28, depending on the intended cycle length, which can vary among women. Withdrawal bleeding typically begins after the last active pill.

Hormonal contraceptives come in varying concentrations to suit different patients' hormonal sensitivities and medical histories. For instance:

One formulation may contain 0.035 mg of ethinyl estradiol and 0.5 mg of norethindrone.

Another may have the same estrogen dose but a different progestin concentration.

This variability allows physicians to tailor treatment. Some women may be sensitive to high estrogen or progesterone doses, experiencing side effects like mood changes, headaches, or breakthrough bleeding. That's why follow-up is essential.

That's why a woman should not walk into a pharmacy and simply request a contraceptive.

The dosage of oral contraceptives is adjusted primarily to reduce side effects, although it may also be modified to optimize effectiveness.

#### **Mechanism of Action:**

- Inhibition of ovulation (no fertilization = no pregnancy) by inhibiting pituitary function.
- •Changes in the environment required for Implantation such as cervical mucus (thick), endometrium, and motility and secretions of uterine tubes decrease the likelihood of conception and implantation.
- •Some individuals and groups in the U.S. consider combination oral contraceptives a form of abortion because they may prevent the implantation of a fertilized egg (zygote) into the endometrium.

نحن كمسلمين عندنا ضابط و هو نفخ الروح، في حديث ابن مسعود رضي الله عنه ، قال : حدثنا رسول الله صلى الله عليه وسلم وهو الصادق المصدوق قال : ( إن أحدكم يُجمع خلقه في بطن أمه أربعين يوما نطفة ، ثم يكون علقةً مثل ذلك ، ثم يكون مضغةً مثل ذلك ، ثم يُرسل إليه الملك فينفخ فيه الروح ، ويُؤمر بأربع كلمات : بكتب رزقه ، وأجله ، وعمله ، وشقي أم سعيد . فوالله الذي لا إله غيره ، إن أحدكم ليعمل بعمل أهل الجنة ، حتى ما يكون بينه وبينها إلا ذراع ، فيسبق عليه الكتاب فيعمل بعمل أهل النار ، وإن أحدكم ليعمل أهل النار حتى ما يكون بينه وبينها إلا ذراع ، فيسبق عليه الكتاب ، فيعمل بعمل أهل الجنة ) رواه البخاري ومسلم .

و تقرر الضابط في فتوى دائرة الإفتاء على ما يلي:

" إذا بلغ الجنين في بطن أمه أربعة أشهر أو جاوزها: فلا يجوز إسقاطه مهما كان تشوهه، إذا قرر الأطباء أن من الممكن استمرار حياته، إلا إذا ترتب على بقائه خطر محقق على حياة الأم.

وأماً إذا لم يبلغ الجنين أربعة أشهر، وثبت أنه مُشوَّه تشويها يجعل حياته غير مستقرة: فيجوز إسقاطه بموافقة الزوجين."

و الأصل بالإجهاض أنه ممنوع إلّا إذا دعت له الحاجة، و يكون وفق ضوابط شرعيّة معلومة عن الفقهاء.

\* و هنا أشير إلى ملاحظة مهمة، ألا و هي وجوب أن نعلم حكم الله في تعاملاتنا الطبية، حتى لا نقع فيما حرّم الله، لأن الجهل بمعلومة كهذه قد يؤدي بك إلى قتل نفس حرّم الله قتلها، أو إلى إيذاء تُسأل عنه أمام الله.

و بما أننا على أبواب المرحلة السريريّة، فانتظروا منّا ما يسرّكم في هذا الموضوع! 🔀

#### **Pharmacologic effects:**

#### 1. Ovary:

 Depression of ovarian function with chronic use, and the ovaries get smaller. This is reversible in most cases, it could be irreversible.

#### 2. Uterus:

 Hypertrophy of the cervix and polyp formation with chronic use, which may cause difficulty with cervical effacement if the patient becomes pregnant in the future.

- Cervical mucus becomes thick and less copious.
- Effects on endometrium are related to hormonal content.

#### 3. Breast:

- Enlargement under the effect of estrogen .
- **Suppression of lactation.** In women with contraindications to breastfeeding, lactation should be suppressed, as breastfeeding may harm the baby or lead to breast complications such as infection.
- Small amounts cross to breast milk.
- Some women can become pregnant while breastfeeding, and in some cases, menstruation may resume during the breastfeeding period.

#### 4. CNS:

- Low changes in mood, affect and behavior.
   Simple changes may not always be simple it depends on the patient's perception.
- Estrogens may be useful for premenstrual tension syndrome, postpartum depression and <u>climacteric depression</u>. See next Slide
- Progestins have central thermogenic action.

#### Climacteric Depression:

- "Climacteric" refers to the premenopausal phase, which is the period before a woman becomes menopausal.
- The type of depression seen here is different. We have two types of depression to consider:
- Major Depression This requires antidepressant treatment.
- Reactive Depression For example, if someone studies very hard for an undergraduate exam and receives a lower mark than expected, they might become depressed. This is considered abnormal and is classified as Reactive Depression.
- It's important to distinguish between the two. If you give **antidepressants** to someone with **reactive depression**, they may experience **all the adverse effects of the medication** unnecessarily.
- Why don't we worry as much about these side effects in **major depression**? They still occur, but the patient is often **too overwhelmed** by their depressive symptoms to notice or be **bothered** by the **adverse effects**.

- 5. Endocrine function:
- Estrogens increase plasma corticosteroid- binding globulin.
- Increase plasma renin activity That's why sodium and water retention occur, and aldosterone secretion.
- Increase thyroxine-binding globulin
- Estrogens increase plasma levels of SHBG → decrease plasma levels of free androgens.

#### 6. Blood:

- Serious thromboembolism. the most important one
- Estrogens increase clotting factors VII, VIII, IX, and X and decrease antithrombin III.
- Increase serum iron and total iron binding capacity.
- Some patients develop folic acid deficiency anemia.

It results from many factors, such as decreased absorption and relaxation of the gastrointestinal (GI) tract caused by oral contraceptives for example.

#### 7. Liver:

Estrogens reduce serum haptoglobins.

Haptoglobin is an acute phase protein capable of binding haemoglobin, thus preventing iron loss and renal damage. Haptoglobin also acts as an antioxidant

#### Cholestasis and cholelithiasis

- Cholestasis (intrahepatic bile obstruction estrogens cause precipitation and lead to stone formation) and Cholelithiasis (gallstone formation)
- These patients are more likely to develop **inflammation of the gallbladder** because they have both **cholestasis** and **cholelithiasis**.
- Any inflammation that occurs in the presence of foreign bodies requires removal of the foreign bodies.

#### 8. Lipid metabolism:

- Estrogens increase triglycerides, phospholipids, and HDL; while size of LDL particles is decreased. Triglycerides can increase, which is not a good thing, as they can contribute to pancreatitis. They are also involved in lipoprotein metabolism and can increase LDL. However, estrogen has a direct effect of reducing LDL and increasing HDL, which is protective against atherosclerosis. But:
- This effect may be modified by progestins.
- Progestins with androgenic properties and synthetic progestins diminish the beneficial effects of estrogens on lipoprotein metabolism, and lower HDL.

- So, if the overall effect on the lipid profile is not significantly negative, why do women who take oral contraceptives have a higher incidence of cardiovascular disease?
- It's because of thromboembolism, not atherosclerosis.

Go to the next slide

 The mechanism of increased cardiovascular disease in combined hormonal contraceptoion (CHC) users may be due to thromboembolic and thrombotic changes, rather than atherosclerosis.

If a woman already has abnormalities in her lipid profile, we deal with her as follow:

- Women with controlled (treated) dyslipidemia (abnormal levels of the lipids in the bloodstream ) can use low-dose CHCs, with periodic fasting lipid profiles. This means regular monitoring of the lipid profile — for example, monthly at first, and if the condition remains stable, we can extend the interval between checks and prescribe a lower dose.
- Women with uncontrolled and additional risk factors for cardiovascular disease like hypertension or smoke or DM should not take CHCs. 16

الدكتور علّق على موضوع التدخين و قال (عيب)، و يجدر الإشارة هنا و خصوصًا بعد ما خلّصنا البيسك و درسنا أمراض كثيرة و كان التدخين العامل الأول في كثير منها، فحريّ بنا أن نعالج أنفسنا من هذه الآفة - لمن أوقعوا أنفسهم بهذه البلوة - من جانبين:

الأول، أنه محرّم (أنت مسلم -> ربّنا أمر = سمعًا وطاعة). الثاني، أن مضرٌّ بالجسم و مهلكٌ للصحة، وأجسامنا وأموالنا ومن حولنا أمانة نُسأل عنها أمام الله.

لذا، اجعلوا الخطوة الأولى لكم بعد إنها البيسك إنكم تتركوا التدخين. 😀

- 9. Carbohydrate metabolism:
- Reduced rate of absorption of carbohydrate from GIT.
- Progesterone increases basal insulin levels and the rise in insulin induced by carbohydrate ingestion.
- Potent progestins may produce a reversible progressive decrease in carbohydrate tolerance over years.

- Progesterone increases insulin levels and basal insulin secretion.
   Despite this, potent progestins can cause carbohydrate intolerance how is that possible?
- It's because although insulin levels are increased, the tissues become less sensitive to insulin they develop insulin resistance.
- So, the increase in insulin is either a response to existing resistance or because the progestins themselves cause the resistance, leading the body to secrete more insulin.
- If someone has hyperglycemia, you need to determine the cause.
- You measure insulin levels (via C-peptide), and if it's high, you ask: How can insulin be high and the patient still have hyperglycemia?
- The answer is insulin resistance and progestins can cause this resistance.

- Therefore, nonsmoking women younger than 35 years with diabetes but no associated vascular disease can safely use CHCs. with observation
- Diabetic women with vascular disease (nephropathy, retinopathy, neuropathy, or other vascular disease) or diabetes of more than 20 years duration should not use CHCs.

#### 10. Cardiovascular system:

 Increase blood pressure, heart rate and slightly increase cardiac output.

#### 11. Effects on the skin:

- Increase skin pigmentation especially in women with dark complexions.
- Androgen-like progestins increase formation of sebum and may produce acne.

- The sequential agents and estrogens alone often decrease sebum production. So, if sebum production and acne occur, we can increase the estrogen component or use estrogen alone to help reduce these symptoms.
- Many patients may show suppression of sebum production, acne and hair growth because of suppression of ovarian androgens.
- You are essentially suppressing both estrogen and androgen production. In polycystic ovary syndrome (PCOS),
   there is hypersecretion of androgens, either due to increased production, increased sensitivity, or both.
- By inhibiting ovarian function, you reduce androgen levels, which is an important part of managing PCOS. This is not a cure for the underlying disease, but rather a treatment for the manifestations of the condition.

#### Therapeutic uses:

Next slide for explanation

- 1. Oral contraception:
- Failure rate of pregnancy ~ 0.5-1 per 100 women-years.

This means that women who take oral contraceptives for one year have a 1% chance of pregnancy — in other words, 1 out of every 100 women who take oral contraceptives for one year may still get pregnant. If the duration increases (e.g., five years), the failure rate won't still be 1% — it accumulates over time.

- Contraception failure has been observed in women missing one or more doses, those taking phenytoin or those taking antibiotics.
- 2. Endometriosis.

- Missing one or more doses increases the risk of pregnancy.
- Epileptic patients may become pregnant despite taking oral contraceptives because antiepileptic drugs increase the metabolism of estrogen through enzyme induction.
- Antibiotics, especially broad-spectrum or combination types, can also cause contraceptive failure. Here's why: The estrogen component of oral contraceptives is metabolized by conjugation. These conjugates are excreted in bile. Normally, gut bacteria hydrolyze the conjugates, releasing free estrogen that can be reabsorbed, helping maintain effective estrogen levels.
- These are three important causes of oral contraceptive failure you should know:
- 1- Missed doses
- 2- Enzyme-inducing drugs (like antiepileptics)
- 3- Broad-spectrum antibiotics

#### Regarding endometriosis:

- Oral contraceptives can be used to manage the symptoms of endometriosis, but they do not return ectopic endometrial tissue to its normal location.
  - They work by **reducing the symptoms**, such as **dysmenorrhea** (painful menstruation), and can help **regulate menstrual cycles**.
- Although oral contraceptives are primarily used for contraception, they are sometimes used to manage endometriosis symptoms as well.

#### **Adverse effects:**

- A. Mild: Mild conditions do not cause a contraindication.
- Nausea, mastalgia, breakthrough bleeding and edema (related to estrogen content of the pill).
- 2. Increased sedimentation rate (ESR) due to increased fibrinogen, there is no need to discontinue the drug.
- 3. Changes in serum proteins should be taken into account when evaluating endocrine functions. As we said, this is caused by increased protein binding of the drug, which reduces the free (active) fraction and therefore decreases the drug's effect.

4. Headache is often mild and transient, but migraine is made worse. This means that for patients with migraine, we do not give oral contraceptives, as they can worsen the condition.

#### 5. Failure of withdrawal bleeding (change prep).

If you give a patient an oral contraceptive preparation and **no withdrawal** bleeding occurs, this can be psychologically unacceptable for her. In such cases, you may need to change the preparation — there is likely a problem with the current one.

**Moderate** conditions — it **depends**; they **may or may not** be contraindications.

- B. Moderate: (may require discontinuance of oral contraception).
- 1. Breakthrough bleeding is common (25% of patients) with the use of progestational agents alone
- 2.Weight gain with combination agents containing androgen-like progestins. It's not due to water retention in this case, the weight gain is caused by muscle growth. There are progestins that cause weight gain through water retention, and estrogen can also lead to water retention. But in this case, the weight gain is due to increased muscle mass, not fluid retention.
- 3. Increased skin pigmentation exacerbated by vitamin B12 and folic acid deficiency. It is slowly reversible.

- 4. Acne with agents containing androgen-like progestins. Agents containing high estrogens improve acne.
- 5. Hirsutism may be aggravated by 19nortestosterone derivatives.
- 6. Ureteral dilation. Due to relaxation
- 7. Vaginal infections are more common and more difficult to treat. This happens because oral contraceptives change the secretions and the environment in the vagina and endometrium.

- 8. Amenorrhea occurs in some patients and persist for several years and is often associated with galactorrhea.
- This is specially true in women who had menstrual irregularities before taking oral contraceptives.
- These patients may have prolactinomas.
  - If galactorrhea occurs, you should investigate for prolactinomas — these are benign tumors that secrete prolactin. They should be removed, as they can cause infertility.

Severe conditions are an absolute contraindication.

- C. Severe (contraindications):
- 1. Venous thromboembolic disease.
- 2. Myocardial infarction.
- 3. Cerebrovascular disease.
- 4. Ischemic bowel disease.
- 5. Cholestatic jaundice (progestin, 17-alkyl substituted agents), cholecystitis and cholangitis.

- 6. Increased incidence of hepatic adenomas.
- 7. Depression (6%). high percent, 1% is considered a common adverse reaction.
- 8.Cervical infection with the human papillomavirus may increase incidence of cervical cancer. Here, we are referring to the use of combination oral contraceptives in the presence of a cervical infection not that the contraceptives cause the cervical infection. However, if a cervical infection is present, there are two neoplastic agents that can lead to neoplasm.

- Suitable in patients for whom estrogen administration is undesirable.
- Injection of <u>depot</u> medroxyprogesterone acetate (DMPA) every 3 months, which inhibits ovulation for 14 weeks.
- All users experience episodes of spotting and bleeding. unpredictable tendency
- Amenorrhea (lack of menses) is common.

 Not suitable for women planning a pregnancy because ovulation may be suppressed for 18 months after the last dose.

For **combined oral contraceptives**, when a family decides to have children, they can simply **stop taking them** and usually become **pregnant within 1–2 months**. However, in this case (referring to a different contraceptive method), **ovulation may be suppressed for up to 18 months on average**. So, for people who are planning to have children soon, **this method is not suitable**.

 Long-term DMPA reduces menstrual blood loss and is associated with a decreased risk of endometrial cancer. due to overstimulation of estrogen.

 Suppression of endogenous estrogens may be associated with a reduction in bone density and changes in plasma lipids and increased risk of atherosclerosis.

You suppress estrogen by inhibiting ovulation, even if you are giving supplemental estrogen in the oral contraceptive.

As a result, osteoporosis may occur, along with changes in plasma lipids and an increased risk of atherosclerosis.

 The progestin implants utilizes the subcutaneous implantation of capsules with an effect lasting up to 6 years. Using implantable progesterone

So we have three types of contraceptive methods:

- 1.Oral
- 2.Intramuscular (injected)

for 6 months means you've made the decision not to have children

40

- Associated with irregular bleeding rather than predictable menses. This is the major problem with progesterone — it's not well psychologically.
- May be associated with intracranial hypertension and papilledema.
- Adverse effects: headache, dizziness, bloating, weight gain, and reversible <u>reduction of glucose</u> tolerance due to insulin <u>resistance</u>.

و في ختام المرحلة الأساسية، بعض النصائح و التذكيرات لنا و لكم:

١) اشكروا الله أن بلّغكم هذه المرحلة، الكل تعب و قدّم لكن النوايا لم تكن واحدة، هناك من نوى بدراسته الحصول على العلامة فقط و منهم من نوى أن العلم عبادة و أن بذل الأسباب عبادة و أن التوكّل على الله عبادة و أن سدّ ثغور الأمة عبادة و أن ستر عورات المسلمين بأطباء يخشون الله عبادة، و أن تقوية شوكة الأمة علميًا عبادة، و أن إسعاد الوالدين و فخر هم بابنهم عبادة، و صبروا على مرارة التعلم و عقبات الطريق لله فنالوا بهذا الأجور الوفيرة من الله، و فرقٌ شاسع بين الأول و الثاني، فأخلصوا النوايا لله و استكثروا منها فهي نافعة لكم أيما نفع.

٢) اعلموا أنّ مهمّتكم عظيمة..

فعُظِّموا لها الخطى، استعينوا بالله على الضَّعف، استعيذوا بالله من الكسل، وسيروا للآخرة كأنَّكم تعيشون فيها، وتشتاقون لها، واعلموا أنّ هناك أُمّة، تقوم على أكتاف شبابها، عَلوا هُمومكم، وانظروا النَّجم ورافِقوا السَّماء، والله إنَّ فَتحًا يَلوح بالأُفُق، إن شاء الله.

#### أمّتنا بانتظارنا.



# امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!

٣) لا تكفروا نعمة الله عليكم، ربّنا أكرمنا بقضاء هذه السنوات الصعبة على خير، فاشكروا له و لا تجعلوا فرحكم بإنهائها كفران له و عصيان.

٤) الطريق طويل وما قطعنا إلّا الخطوة الأولى فقط، فاستعينوا بالله ولا تعجزوا و جدّدوا النوايا.

٥) من فريق طوفان الأقصى و لجان الدفعات، نسأل الله أن نكون وُفقنا لتقديم المساعدة على الوجه الذي يرضي الله تعالى عنّا خلال الأعوام الماضية، إن أحسنًا فمن الله و إن أسأنا فمن أنفسنا و الشيطان.

V2: slide 22/ we added the yellow sentence

لا تنسونا من دعواتكم، وققكم الله فيما هو آت و آتاكم علمًا و خشية.



# امسح الرمز و شاركنا بأفكارك لتحسين أدائنا!!