Progestin-only contraception (POC) Overview

An advanced slide kit complementing the WHO training tool is available from www.fptraining.org

Update July 2018
This session discusses the most commonly used POCs in Europe

- Desogestrel 75 µg pill (POP)
- Etonogestrel-releasing 3 year implant (Implant)
- Depot medroxyprogesterone acetate (DMPA)

Information about the levonorgestrel-releasing intrauterine system (LNG-IUS) will be given in the IUD/LNG-IUS sessions
Contents

- Progestin types
- Working mechanism
- Contraceptive efficacy and safety of POC
- Use in women with medical conditions
- Health benefits
- Adverse events: bleeding, breast tenderness, weight, acne, BMD

Antiandrogenic properties are used to treat hyperandrogenism. Risk of VTE is lowest with the second generation progestins.
POCs (pill, injectable and implant) act in different ways:

- The primary mechanism of action is to suppress ovulation. Progestins causes the hypothalamus and the pituitary gland to reduce production of the hormones that are necessary for ovulation. Without ovulation, there is no egg to be fertilised.

- Progestins also **thickens the cervical mucus**. The thickened mucus makes it more difficult for sperms to enter the uterine cavity. In the unlikely event that a woman does ovulate, this mucus barrier greatly reduces the chance that the egg will be fertilised.

- Ciliary action in the fallopian tubes is altered.
When we discuss with a women the efficacy of a contraceptive method we must consider typical use of the method, which means use in normal life by a typical user. In this slide we look at how effective contraceptive methods are as they are commonly used.

The slide shows the number of women who would get pregnant if 100 women used a method for 1 year. In 100 fertile women who were having sex without contraception, 85 would become pregnant. If the same 100 women were using an injectable, only six would become pregnant. If 100 women were using the COC, nine or 0.3 would become pregnant depending of the woman’s reliability to use a COC correctly.

Ref 3: The incidence rate of VTE in non-pregnant women not using hormonal contraception increased from 0.7 per 10,000 woman-years in women 15–19 years of age to 5.8 per 10,000 woman-years in women 45–49 years of age, or 8.3-fold in reproductive age women.

Ref 1: The risk of VTE is related to the dose of ethinylestradiol or estradiol. One of the main benefits of POC is the safety related to thromboembolic risk.

Ref 3: Although limited by the small number of cases and control subjects using the types of contraceptives under investigation, the data suggest that there is little or no increased risk of stroke, VTE or acute myocardial infarction associated with the use of oral or injectable progestogen-only or combined injectable contraceptives. However, further investigation into a possible adverse effect of POC used by women with very high blood pressure is indicated.

- Most users are young and healthy when they start contraception, but they are likely to be long-term users.
- Confident users are better users.
- POC is a very good option for contraception in high-risk women.
Health benefits of POC

- Reduction of heavy menstrual bleeding (HMB) (LNG-IUS, DMPA)
- Inhibition of growth of uterine fibroids (LNG-IUS, DMPA)
- Protection against iron-deficiency anaemia (LNG-IUS, DMPA)
- Reduction in sickle cell crises in women with sickle cell anaemia (DMPA)
- Decrease in endometrial cancer (DMPA)
- Reduction of dysmenorrhea and pain in women with endometriosis (POP, implant, LNG-IUS, DMPA)
- Minimal metabolic effects (POP, implant, LNG-IUS)
- Positive impact on catamenial epilepsy

Not all POC methods exert the same health benefits, as progestin dose and type vary between different formulations.
POC does not exert an effect on pre-existing pregnancy.

- Unexplained genital bleeding
- Pregnancy
- Severe liver disease
- Severe depression (be very careful, follow up)
- Breast cancer


Ref 2: A systematic review and mixed-treatment-comparison (MTC) meta-analysis were carried out of available data from randomised controlled trials (RCTs) to derive estimates of efficacy for eight classes of treatments for HMB (COC, danazol, endometrial ablation, LNG-IUS, placebo, progestins given for <2 weeks out of 4 during the menstrual cycle, progestins given for close to 3 weeks out of 4, and tranexamic acid. Thirty-four RCTs were identified, with follow-up from 1 to 36 months. Efficacy at 3 months of follow-up ranged from 87.5% for the LNG-IUS to 14.2% for progestins administered for <2 weeks out of 4 in a menstrual cycle.
Counselling is very important for the compliance of women for the progestin only methods; women who want a predictable bleeding pattern may not find POC acceptable.
<table>
<thead>
<tr>
<th>Method</th>
<th>Bleeding/spotting over time</th>
<th>Amenorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>POP</td>
<td>Decreasing</td>
<td>1st year 20%</td>
</tr>
<tr>
<td>Implant</td>
<td>Decreasing</td>
<td>1st year 19–25%</td>
</tr>
<tr>
<td>DMPA</td>
<td>Decreasing</td>
<td>1st year 47–60%</td>
</tr>
</tbody>
</table>
| LNG-IUS  | Decreasing                 | 1st year 43%  
|          |                            | 3rd year 57%   |

Frequency of frequent and prolonged bleeding decreases over time; therefore, reassurance is important if women find it troublesome.

Definitions of vaginal bleeding (reference period: 3 months).
1. Normal and regular blood loss: mainly related to the natural cycle or CHC use.
2. Unpredictable blood loss:
   • Frequent (more than five episodes of blood loss).
   • Prolonged (one or more episodes of blood loss lasting ≥14 days).
   • Spotting (small amount of blood loss, no need for sanitary protection).
   • Not frequent (less than three episodes of blood loss).
Treatment of subjective prolonged bleeding

- There are no options to improve bleeding pattern in the long term
- Treatment mainly aims to stop uncomfortable, prolonged bleeding especially in the early phase of POC use
- Support the woman to continue the method
Treatment of frequent and irregular bleeding with POC

If ultrasound is available you can check whether the endometrium is high or low. Fragile vessels in atrophic endometrium will respond better to estrogen treatment.

* Clinical experience.


Persistent unruptured follicles in POC users may cause estrogenic side effects

- Reason for breakthrough bleeding and breast tenderness in users of very-low-dose POC such as the LNG-IUS or POP can be unruptured follicle cysts which produce estradiol
- These cysts resolve spontaneously
- Reassure the patient

Ref 1: The Cochrane Database found little evidence of weight gain with progestin-only contraceptives. Some differences were noted when a POC was compared with no hormonal contraceptive. Actual mean weight gain was low for 6–12 months, i.e. less than 2 kg for most studies.

However, prospective studies demonstrate that in some DMPA and implant users, there can be a relevant increase in weight, which may lead to discontinuation.

Ref 1: The Cochrane Database found little evidence of weight gain with progestin-only contraceptives. Some differences were noted when a POC was compared with no hormonal contraceptive. Actual mean weight gain was low for 6–12 months, i.e. less than 2 kg for most studies.

However, prospective studies demonstrate that in some DMPA and implant users, there can be a relevant increase in weight, which may lead to discontinuation.
Acne, skin problems

A typical problem in adolescents, who are the biggest group of new contraceptive users
COCs decrease free testosterone levels by 40–50%, on average (Fotherby, 1994; Thorneycroft, 1999). This is partly due to reduced production of the androgen testosterone, achieved by the suppression of luteinising hormone, which causes decreased androgen synthesis. Androgen bioavailability is also reduced when COCs increase the level of the protein that binds free androgens (SHBG), which in turn, increases binding of testosterone. Second, testosterone has to be converted in the hair follicles and skin to dihydrotestosterone by the enzyme 5α-reductase to lead to acne (Cassidenti, 1991). COCs prevent the conversion of free testosterone to dihydrotestosterone. SHBG in circulation binds the free testosterone. If plasma levels of testosterone decrease, androgenic symptoms can improve. If we want to use a hormonal contraceptive to improve the androgenic signs it is very important use a CHC (CHC session3 ).


Take a good history and ask actively about depressive episodes. It is not prudent to start a POC or LNG-IUS in women with major depression. If there is no other choice, close follow-up is needed. A pill might be a better option to test tolerability.
Adverse event
BMD

- During the reproductive years maintenance of bone mineral density (BMD) is important to decrease fracture risk in later life
- Estrogen depletion can cause a decrease in BMD
- There is some concern that DMPA might have a negative impact on BMD by suppressing ovarian function
- Short-term studies do not indicate a negative effect of the POP or implant on BMD
There was a significant difference between DMPA users and non-users in the studies of Berenson et al. and Clark.

The Berenson study included 703 women aged 16–33 years (20 μg EE COC users, DPMA users and non-hormonal contraception [non-HC] users), who were followed for 36 months. DMPA users had the highest BMD loss at the spine during the first year, after which the loss slowed during the second and third years. At the femoral neck, BMD loss was slower during the first year, and increased during the second and third years. COC users had a slight BMD increase at the spine during the first 12 months, followed by a slow and gradual decrease in the second and third years, and had a slow and consistent decrease over time at the femoral neck. For total hip BMD, the changes were −3.5%, −0.3% and +1.6% among DMPA, COC and non-HC users, respectively, over the 3 years. Age was found to be an important determinant of BMD change by contraceptive method. Over 36 months, DMPA users 16–24 years old lost significantly more bone at the spine (4.2% vs 3.2%, \( p=0.006 \)) and femoral neck (6.0% vs 4.2%, \( p=0.001 \)) than those aged 25–33 years; however, COC users aged 16–24 years lost significantly less bone density at the spine (0.4% vs 0.8%, \( p=0.013 \)) than women 25–33 years of age. By contrast, non-HC users aged 16–24 years gained significantly more bone at the spine (3.3% vs 1.3%, \( p=0.001 \)) than those aged 25–33 years. The authors concluded that both DMPA and COC
containing 20 μg EE caused BMD loss. DMPA-related changes were found to be largely reversible at the spine regardless of the contraceptive method used after DMPA discontinuation and at the femoral neck if no hormonal contraception was used. However, use of a COC immediately after DMPA discontinuation may impede the ability to regain bone at the femoral neck, at least temporarily. This finding appears to have greatest relevance for white women who are at high risk of hip fracture after the menopause. Further studies are needed to confirm these findings and to determine whether they are robust across women of different races and ages.
Advantages
- High efficacy
- Efficacy not user-dependent (except POP)
- No increase in VTE or ATE risk (DMPA WHO2/3)
- Minimal metabolic effects
- No adverse effects of ethinylestradiol
- Safe in many medical conditions
- Improvement of HMB (DMPA, LNG-IUS)
- No negative impact on lactation
Disadvantages

- Unpredictable/prolonged bleeding
- Impact on body weight (POP?)
- Hormonal side effects (skin, mood, hair)
- Negative, but probably reversible, impact on bone density
- Return to fertility delayed with DMPA
- Impact on mood, especially in predisposed women