Combined hormonal contraceptives
CHC Session IV
Vaginal Ring CVR – Transdermal Patch CTP

Advanced slide kit complementing the WHO training tool www.fptraining.org
To enable teachers to understand and explain:

- Description and formulation; Application
- Pharmacokinetics; Regimen of use
- Similarities ring, patch and pill; Advantages ring and patch > pill
- Contraceptive failure rates
- Dosing errors; Extended use
- Concurrent use
- Cycle control; Acceptability; Compliance; Side effects compared with pill
- Device-related problems; Acceptability ring vs patch
- Venous and arterial thromboembolism
- Counselling
The contraceptive vaginal ring is a flexible, soft, latex-free device measuring 54 mm in diameter, and 4 mm in cross-section. It contains 2.7 mg of ethinylestradiol and 11.7 mg of etonogestrel, which is the 3 keto-metabolite of desogestrel, a third generation progestin.

The transdermal contraceptive patch is a matrix system measuring 20 square cm, and composed of three layers. The middle layer is medicated and contains two hormones, 0.60 mg of ethinylestradiol and 6 mg of norelgestromin, the primary active metabolite of norgestimate, a second generation progestin.
• After pressing the sides together, the ring is inserted into the vagina as high as possible, where it sits above the urogenital diaphragm and surrounds the cervix, although the position of the ring does not affect contraceptive efficacy. The ring can easily be removed by hooking a finger in it.

• The patch is applied to clean, dry, intact healthy skin of the buttock, abdomen, upper torso or upper outer arm, but not to the breast, as it might cause breast tenderness due to high local estrogen concentration. A different site is used each time a new patch is applied. Lotions and occlusive dressings should not be used at patch application sites.


- The ring releases 15 µg EE and 120 µg ENG daily, and the patch 35 µg of EE and 200 µg of norelgestromin.
- As a result, and calculated in this randomized study, systemic exposure to EE with the vaginal ring is 3.4 times lower than with the patch, and 2.1 times lower than with a 30 µg pill, whereas the overall EE concentration in patch users is comparable to that of a 50 µg EE pill.
Use of the CVR and the CTP
The ring and the patch should be initiated within five days after the start of the menstrual bleeding.
Each ring remains in the vagina for three weeks, and is then removed for one week. The patch is changed once a week for three weeks, followed by one patch-free week. The patch should always be changed on the same day of the week, which is known as the ‘Patch change day’. If a woman wants to switch to a new patch change day, she has to do that in the patch-free week.

Women who desire fewer days of withdrawal bleeding and are willing to tolerate some unscheduled bleeding, can safely use an extended ring regimen for up to one year, whereby the ring is changed every three weeks. Omitting the hormone-free week is also possible for the patch, but we advise to avoid this practice, given the possible incremental EE serum levels when patches are used continuously, resulting in increased risk of side effects such as headache, nausea, breast discomfort and thrombosis.
There are quite a number of similarities between the ring, the patch and the pill.

- The three methods have a similar systemic contraceptive working mechanism, such as inhibition of ovulation, thickening of the cervical mucus, decreasing of endometrial receptivity, and slowing of tubal motility.
- The WHO medical eligibility criteria for initiating and use are the same, in particular the postpartum use in breastfeeding and non-breastfeeding women.
- Effectiveness is similar, as are the general non-contraceptive benefits, risks and general contraindications, and the absence of clinically significant metabolic effects, such as changes in blood pressure, blood chemistries, lipid levels, carbohydrate metabolism, thyroid function, and hematological indices.
- Initiation, switching and need for a back-up method in case of extension of the hormone-free interval, or unscheduled non-use, are also essentially the same, and return of ovulation is equally rapid after stopping. Also follow-up rules are the same: in healthy women, no examinations or tests are essential or mandatory.
The ring and the patch offer several potential advantages to the pill:

- There is no enzymatic degradation in the gastrointestinal tract and no first-pass hepatic metabolism, resulting in lower doses to achieve therapeutic effects.
- Plasma hormone levels remain constant: there are no daily peaks and troughs.
- There is no need for daily self-administration, which might improve user compliance.
- The non-oral route of administration is useful for patients who have difficulty swallowing pills.

The pregnancy rate of the ring and the patch during the first year of use is equivalent to that of the pill: 9% for typical use, and 0.3% for correct use. However, phase III data suggest, that the patch may be less effective in women with body weight ≥90 kg. So the patch should preferably not be prescribed to obese women.
1. **WHO. Selected practice recommendations for contraceptive use • Third edition 2016**

- The principles of dosing errors with the ring and patch are similar to those of pill use.
- In case of extension of the ring- or patch-free week, or in case of unscheduled removal of the ring or detachment of the patch, a new ring or patch should be applied as soon as possible, and the woman should keep to the originally scheduled ring removal or patch change day.
- If this occurs within 48 h, no additional contraception is needed. If the interval is extended for more than 48 h, the woman should also use condoms or abstain from sex until she has used a ring or patch for 7 days in a row.
- If unprotected sexual intercourse occurred during the previous 5 days in the hormone-free interval, or on any day during the first week, the woman may wish to consider using EC.
- If sexual intercourse occurred during the third week, the woman should omit the ring- or patch-free week, and start a new ring or patch immediately.
3. WHO. Selected practice recommendations for contraceptive use • Third edition 2016

The rules for extended use of the ring and the patch are quite different. **RING**: If a woman forgets to remove the ring after three weeks, inhibition of ovulation is sufficiently maintained for another 2 weeks. So, if the same ring is used for up to 28 days, additional contraception is not needed. A hormone-free interval can be taken, if desired, but should not exceed 7 days. If the same ring is used for 28-35 days, insert a new ring and skip the hormone-free interval. In this situation no additional contraceptive protection is needed. **Patch**: If a woman forgets to change the patch after one week, there is only a two-day period of adequate contraceptive steroid levels. If users change the second or third patch within this window, there is no need for back-up contraception. After these two days, users will need back-up contraception or avoid sex for seven days and, in some instances, use emergency contraception. In all cases, the woman should keep the same patch change day.


- In ring users, serum EE and ENG levels are not altered by concurrent use of a spermicide (nonoxynol-9), nor by use of tampons. Also, concurrent use of antibiotics (amoxicillin and doxycyclin) does not alter these serum levels. On the contrary, concomitant vaginal use of the antifungal miconazole, has been shown to increase release of both steroids.

- In patch users, serum levels of EE and norelgestromin are not affected by concurrent use of tetracycline. However, it remains possible that efficacy of the patch may be affected by some other drugs.

- As we all know, cycle control is a benefit of all combined hormonal contraceptive methods.
- In several randomised controlled trials, it has been shown, that in ring users, cycle control is at least equivalent or even superior to that of the pill and the patch. Ring users are less likely than pill users to experience spotting and breakthrough bleeding, especially in the first few months of use. Also less likely among ring users are prolonged or frequent bleeding, and early or late withdrawal bleeding.
- An improvement in cycle control has also been demonstrated among women who switch from the pill or the patch to the vaginal ring, and in women with dysfunctional uterine bleeding.
- In patch users, unscheduled bleeding is a common side effect in the first two cycles of use. The pattern of breakthrough bleeding and spotting with the patch is similar to that reported in pill trials. By about six months, the frequency of such bleeding declines substantially and remains stable.
• Vaginal ring users are either as satisfied or more satisfied than pill users. 84% to 96% of ring users report being satisfied, as they find that the vaginal ring is easy to use, requires only once-a-month administration, remains effective if removal and reinsertion is not performed precisely on time, results in low systemic hormone levels, and is rapidly effective and reversible.

• Several randomized trials have reported improved psychological and sexual functioning among ring users as compared with pill users, but one randomized trial found that ring users reported more decreased libido compared to users of a levonorgestrel-containing pill (8.3 versus 0 percent).

• Only one patch RCT had satisfaction data, showing that patch users were more likely to be very satisfied with their method than pill users.
• Adherence with the vaginal ring regimen varies between different studies from 80 to 90% of cycles. Discontinuation of the ring occurs in 28 to 35% of women before one year, with most discontinuations occurring in the first three to four cycles. However, side effects were reported as reason for discontinuation in only 11 to 30% of the ring users.

• RCTs examining the continuation rate report different results. While one RCT found that ring users overall were less likely to discontinue than pill users (12 versus 22%), another RCT observed no difference. A RCT trial including 201 women using the “quick start” method, found, that ring users were less likely to discontinue than OC users (11% versus 16%).

• Adherence to the patch dosing regimen was shown to be superior to that for pills, in two adequate and well-controlled comparative trials (89% vs. 79%, respectively). However, discontinuation rates, and side effects as reason for discontinuation, were higher for patch users than for pill users.


• Systemic side effects from the vaginal ring and the patch are generally similar to those of oral contraceptives.
• However, estrogen-related side effects like breast tenderness and nausea, and also acne, are reported less often by vaginal ring users than pill users, a finding that is consistent across three trials comparing the ring with pills of varying ethinyl estradiol doses and different progestins.
• For trials comparing the patch to a pill, more breast symptoms during the first two cycles were reported, more nausea and vomiting, and more dysmenorrhea. About 85% of women experiencing breast symptoms described them as mild to moderate; the frequency declined markedly with continued use of the method. In one study, patch users reported less moodiness than pill users.
• No differences in headache or weight gain were seen across studies comparing ring users to pill users, or patch users to pill users.
• Problems related to the ring and patch methods are important.
• Ring users report more local vaginal symptoms such as vaginitis, vaginal wetness, and vaginal discharge (17%) than pill users. These symptoms, however, do not require treatment and do not appear to result in discontinuation of the ring. Use of the ring is not associated with a higher likelihood of bacterial vaginosis.
• In large efficacy studies, foreign body sensation was reported by 4% of women. In a Dutch daily practice study, 6% of women reported expulsion of the ring. In a ring-pill cross-over study, 9% reported ring slippage at least once weekly. So, ring expulsion may occur spontaneously, and women should be counselled to check for the presence of the ring after coitus, a strenuous effort (e.g., at defaecation), or tampon removal. If the ring accidentally falls out, it may be rinsed with cool or warm water, and reinserted into the vagina within three hours.
• Studies show that from 13-16% of users chose to remove the ring during intercourse. This interval of removal does not affect efficacy if the ring is reinserted within a three-hour time interval.
• In patch users, mild-to-moderate application site reactions were reported by 14-20% of women, and 2.6% of them stopped treatment for this reason. The patch adhered well with only 4.7% of all patches being replaced due to complete or partial detachment. Neither living in a warm, humid climate nor having a vigorous, athletic lifestyle increases the risk of detachment.
The acceptability of the ring and the patch were compared in a RCT during four consecutive cycles.

The percentage of women who completed three cycles was significantly higher for ring users in the per protocol population, and in the intent-to-treat population as well.

The most common reasons cited for ring discontinuation were discomfort with use and adverse effects. For patch discontinuation, reasons cited were adverse effects, skin irritation and problems with adherence.

Of the women who completed three cycles, significantly more ring users planned to continue use of their method.

Ring users were significantly more likely than patch users to experience frequent vaginal discharge, and that the device was bothersome during sex to them or their partners, whereas patch users were significantly more likely to experience longer periods, increased dysmenorrhea, frequent nausea, frequent mood swings, frequent skin rash.

Device-related problems were noted at least once during any 3-week use period more frequently with the patch: the patch fell off in 46.0% of women and the ring was expelled in 20.4% of women.

As a result, significantly more women stated they were satisfied with the ring than with the patch.

According to the EMAS statement 2013, the risk of VTE for the ring containing etonogestrel and the patch containing norelgestromin, is 6-12 per 10,000 women over a year, which is twofold the risk of a second generation pill.
A systematic review of primary research studies did not demonstrate an increased risk of arterial thromboembolism among women using the ring. Results from one prospective study revealed no significant difference as compared to a reference group of women using multiple types of pills.

- Two studies compared patch users to NGM pill users, and neither found a statistically significant difference in AMI or ischemic stroke.
Counselling aspects

Vaginal ring
• Highly effective, reversible, non-coitally-dependent
• No contraindications to estrogen or progestins
• Pill aversion, forgotten pill, gastrointestinal problems
• Adolescents, irregular lives
• Contraindications: genital problems
• Lower estrogen exposure
• Better cycle control
• Extended regimen possible

Transdermal patch
• Highly effective, reversible, non-coitally-dependent
• No contraindications to estrogen or progestins
• Pill aversion, forgotten pill, gastrointestinal problems
• Adolescents, irregular lives
• CI: dermatologic problems


• Candidates for the vaginal ring and the patch are women who desire highly effective, reversible, non-coitally-dependent contraception, who have no contraindications to taking estrogen or progestins. Also, women who do not want a pill, or who have gastrointestinal problems, or who forget to swallow a pill daily, are good candidates. For example, adolescents with their irregular lives.
• The ring is contraindicated in women with complaints of a pelvic organ prolapsed, or a genital touch taboo, the patch in women with dermatologic problems.
• In contrast to the patch, use of the ring may be advisable for women who want a lower estrogen exposure to the body, who want a better cycle control than experienced during pill use, or who want to use an extended regimen.