

Combined hormonal contraceptives CHC Session IV

Vaginal Ring CVR – Transdermal Patch CTP

Advanced slide kit complementing the
WHO training tool www.fpctraining.org

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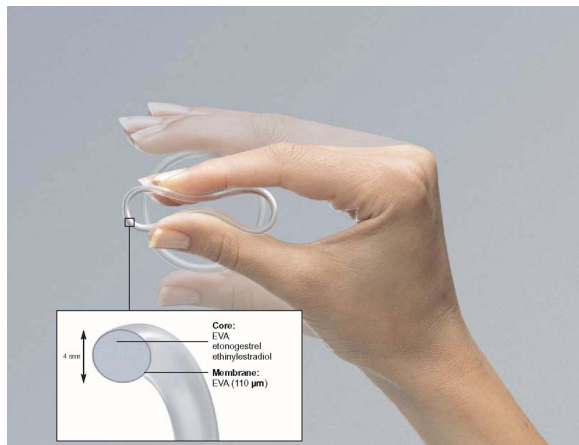
To enable teachers to understand and explain:

- 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

Description and formulation

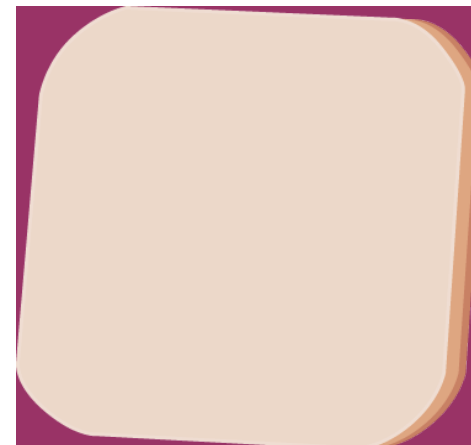
Vaginal ring

- Flexible, soft, latex-free ring, 54 mm in diameter, 4 mm in cross-section
- Contains 2.7 mg EE and 11.7 mg ENG



Transdermal patch

- Matrix system, 20 cm², 3 layers
- Middle layer contains 0.60 mg EE and 6 mg NGMN (EU)



Alternatives (or in development)

Vaginal ring

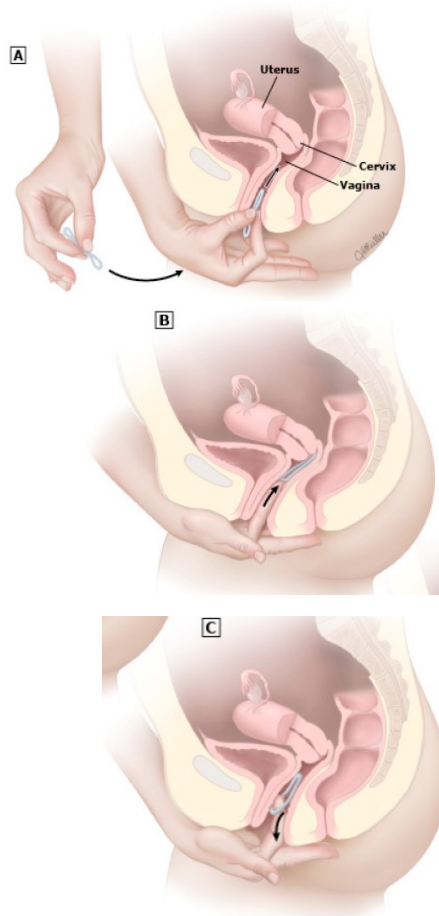
- Generics of Nuvaring
- Ornibel (EE/ENG)
- E₂/ENG rings
- E₂/NOMAC rings
- SA/EE ring (Annovera)

Transdermal patch

- EE/GSD patch
- EE/LNG patch
- LNG only patch

Application

Vaginal ring



Transdermal patch

- Clean, dry, intact healthy skin
- Not on the breast
- Each time different site
- No lotions or occlusive dressings



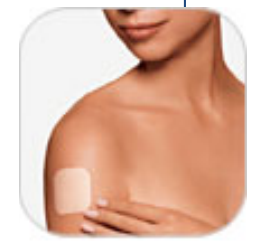
buttocks



abdomen



upper torso
(front and back
except on your breasts)



upper outer arm

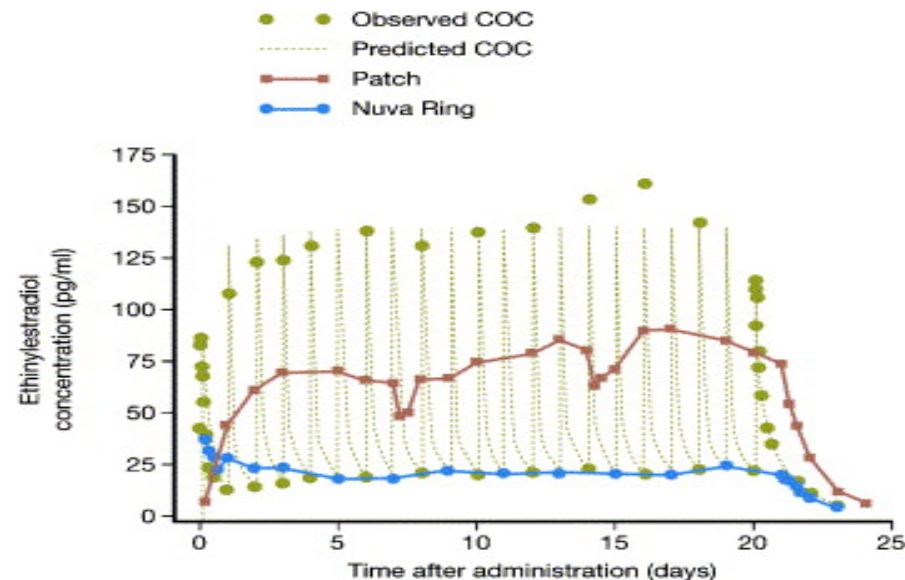
Pharmacokinetics

Vaginal ring

- Daily release 15 μg EE and 120 μg ENG
- Systemic EE exposure low (3.4x lower than patch) (2.1x lower than 30 mcg pill)

Transdermal patch

- Daily release 35 μg EE and 200 μg NGMN
- Overall EE concentration \approx 50 mcg EE pill



Regimen of use

Vaginal ring

- Start cycle day 1-5
- 3 weeks in, 1 week out
- Omitting hormone-free week possible
- Extended use: unscheduled bleeding

Transdermal patch

- Start cycle day 1-5
- Once a week for 3 weeks, 1 week out
- Switch of patch change day in patch-free week
- Omitting hormone-free week not advised
- Extended use: headache, nausea, mastodynia, thrombosis

Similarities: ring, patch and pill

- Combined hormonal method
- Systemic working mechanism
- Medical eligibility criteria (WHO)
- Postpartum use (breastfeeding and non-breastfeeding)
- Effectiveness
- Non-contraceptive benefits and risks
- General contraindications
- Metabolic effects
- Initiation, switching and back-up
- Return of ovulation
- Follow-up

Advantages ring and patch > pill

- No enzymatic degradation in the gastrointestinal tract
- No first-pass hepatic metabolism
- Lower hormone doses needed
- No daily peak and troughs of plasma hormone levels
- No need for daily self-administration
- No daily user compliance
- No difficulty swallowing pills

Contraceptive failure rates

Method	% of women experiencing an unintended pregnancy within first year	
	Typical use	Perfect use
No method	85	85
Spermicides	28	18
Condom male	18	2
Diaphragm	12	6
Combined pill	9	0.3
Evra Patch	9	0.3
NuvaRing	9	0.3
Progestin –only pill	9	0.3
Depo-Provera	6	0.2
Implanon	0.05	0.05
IUD Copper T380Ag*	0.3	0.3
IUD Mirena (LNG)*	0.2	0.2
Female sterilisation	0.5	0.5
Male sterilisation	0.15	0.1

*Source I.Sivin, Contraception 1990,; Vol.42NO 4.; adapted from Trussel Contraception 2011

➤ Patch is less effective in women with body weight ≥ 90 kg!

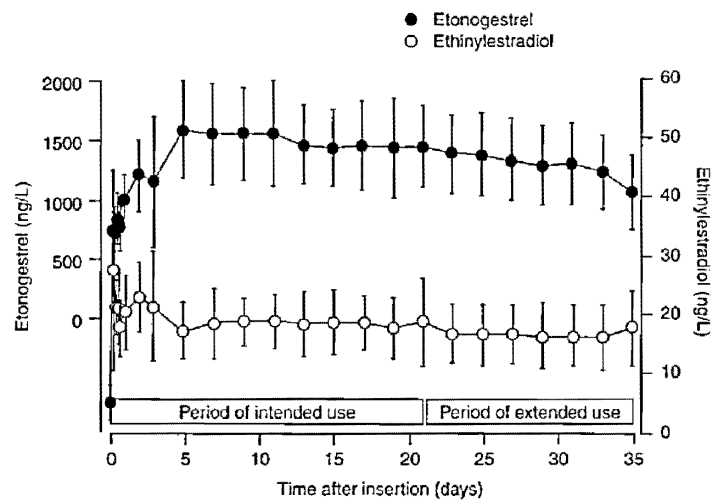
Dosing errors ring and patch

- Extension of ring- or patch-free week
- Unscheduled removal ring or detachment patch
 - apply new device asap
 - keep originally scheduled day
 - ≤ 48 h: no additional contraception
 - > 48 h:
 - ✓ 7 days additional contraception
 - ✓ If unprotected sex took place
 - During previous 5 days in hormone-free interval
 - Any day in week 1
 - Consider emergency contraception
 - Any day in week 3
 - Omit the ring- or patch-free week

Differences between ring and patch

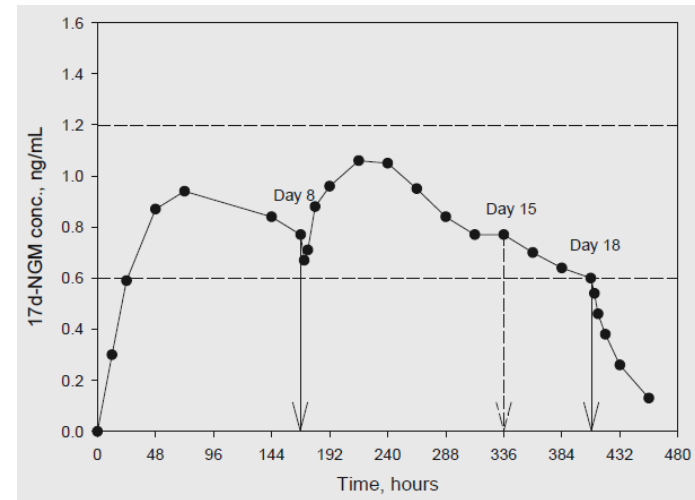
Rules for forgotten removal

Vaginal ring



- Up to 35 days: no additional contraception
 - <28 days, ring-free week possible
 - 28-35 days: no ring-free week possible

Transdermal patch



- Up to 2 days: no additional contraception
- > 2days
 - Additional contraception or avoid sex for 7 days, eventually EC
 - Keep same patch change day

Concurrent use

Vaginal ring

- EE and ENG levels not altered by
 - Spermicide (nonoxynol-9)
 - Tampons
 - Antibiotics (amoxicillin, doxycyclin)
- EE and ENG levels increased by
 - Miconazole

Transdermal patch

- EE and NGMN levels not altered by
 - Tetracycline

Cycle control compared with the 30 μ g EE pill

Vaginal ring

- **Equivalent or superior**
 - Less frequent spotting and breakthrough bleeding
 - Prolonged or frequent bleeding is less likely
 - Early or late withdrawal bleeding is less likely
 - Improved cycle control after switching from pill or patch
 - Superior cycle control in women with dysfunctional uterine bleeding

Transdermal patch

- **Equivalent or inferior**
 - Unscheduled bleeding common in first two cycles
 - After two cycles, similar pattern spotting and breakthrough bleeding
 - At six months, unscheduled bleeding declines and remains stable

Acceptability compared with pill

Vaginal ring

- Satisfaction 84%-96%
 - Easy to use
 - Once-a-month
 - Remains effective if removal and reinsertion are not in time
 - Low systematic hormone levels
 - Rapidly effective
 - Reversible
- Improved psychosexual function in most RCTs

Transdermal patch

- Satisfaction higher than with the pill (OR 1.35: CI 1.09-1.68)

Compliance compared with pill

Vaginal ring

- Adherence: 80%-90%
- Discontinuation rate: 28%-35%
- Side effects as reason: 11%-30%
- Randomised controlled trials
 - ring users less likely to discontinue (12% vs 22%)
 - no difference
 - using „quick start“: ring users less likely to discontinue (11% vs 16%)

Transdermal patch

- Adherence superior to the pill: 89% vs 79% (OR 2.05; CI 1.83-2.29)
- Discontinuation rate higher (58% vs pill 47%) (OR 1.59; CI 1.26-2.00)
- Side effects as reason higher (OR 2.28; CI 1.61-3.25)

Side effects compared with the pill

Vaginal ring

- Systemic side effects generally similar
- Breast tenderness and nausea less frequent
- Less acne compared with EE/LNG pill
- No differences in headache or weight gain

Transdermal patch

- Systemic side effects generally similar
- Breast tenderness (first two cycles), nausea, vomiting, and dysmenorrhea more frequent
- Less moodiness
- No differences in headache or weight gain

Device-related problems

Vaginal ring

- Local vaginal symptoms
 - Vaginitis
 - Vaginal wetness
 - Vaginal discharge (17%)
 - No increased bacterial vaginosis
- Device related events
 - Europe 4.1%, 4.7%, 6.6%,
- Expulsion rates
 - Switzerland 1.7%
 - The Netherlands 6.0% (negative relation with ease of insertion)
 - USA 9% - 20%
 - Africa 14%
 - Counsel women to check
- During intercourse
 - (13%-16% remove ring)
 - Reinsert within 3 hours

Transdermal patch

- Application site reactions
 - Skin reactions 14%-20%
 - Treatment limiting 2.6%
- Replacement for
 - Complete detachment 1.8%
 - Partial detachment 2.9%

Acceptability 'ring vs patch': RCT

- Continuation 3 cycles
 - per protocol population: 94.6% vs 88.2%, $p=.03$
 - Intention-to-treat population: 91.6% vs 83.7%, $p=.03$
- Reason for discontinuation
 - Ring: discomfort, adverse effects
 - Patch: adverse effects, skin irritation, problems with adherence
- Plan to continue method after 3 cycles: 71.0% vs 26.5%, $p<.001$
- Adverse effects:
 - Ring: frequent vaginal discharge, bothersome with sex to user or partners
 - Patch: longer periods, increased dysmenorrhea, frequent nausea, frequent mood swings, frequent skin rash
- Device-related problems 'at least once during any 3 week use period'
 - Ring was 'expelled' 20.4% vs patch 'fell off' 46.0%, $p<.001$
- Satisfaction: 78% vs 39%, $p<.001$

Same VTE risk for ring and patch

Statement of the European Medical Agency 2013

Risk of developing a blood clot (VTE) in a year

Women not using a combined hormonal pill/patch/ring and are not pregnant	About 2 out of 10,000 women
Women using a CHC containing levonorgestrel, norethisterone or norgestimate	About 5-7 out of 10,000 women
Women using a CHC containing etonogestrel or norelgestromin	About 6-12 out of 10,000 women
Women using a CHC containing drospirenone, gestodene or desogestrel	About 9-12 out of 10,000 women
Women using a CHC containing chlormadinone, dienogest or nomegestrol	Not yet known*



Arterial thromboembolism

Vaginal ring

- No significant difference compared with multiple types of pills

Transdermal patch

- No significant difference compared with NGM pills

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

Contraindications:

- Dermatological problems
- Overweight women
- Diabetic women

Extended regimen not advised