Contraceptive Options
Focus on Combined Hormonal Vaginal Ring
After the completion of this program, participants will be able to:

• Discuss the landscape of contraceptive availability and usage in Canada including challenges with patient adherence
• Promote awareness of non-daily contraceptive options
• Understand the physiology of the vagina as a drug delivery system
• Be able to effectively counsel patients on the use and advantages of the vaginal contraceptive ring
LANDSCAPE OF CONTRACEPTIVE AVAILABILITY AND USAGE IN CANADA
Why Another Contraceptive Method?

CHOICE
Higher Continuation Rates When Women Are Given A Choice of Contraceptive

Unintended Pregnancy

- Among Danish-born women with unintended pregnancy, 45% reported contraceptive use\(^1\)
- Among French women, 65% of unintended pregnancies occurred in women reporting contraceptive use\(^2\)
  - 21% of these women reported using an oral contraceptive

<table>
<thead>
<tr>
<th>Reason for Missed Tablets</th>
<th>Percent of Women (n=176)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Took tablets late/forgot to take tablets</td>
<td>60.3</td>
</tr>
<tr>
<td>Illness, medication</td>
<td>10.6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7.7</td>
</tr>
<tr>
<td>No explanation, do not know</td>
<td>21.4</td>
</tr>
</tbody>
</table>

Teenage Pregnancy Rates in Canada

## Contraceptive Methods Used in Canada

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Contraceptives</td>
<td>44</td>
<td>32</td>
<td>38</td>
</tr>
<tr>
<td>Condom</td>
<td>54</td>
<td>21</td>
<td>32</td>
</tr>
<tr>
<td>Sterilization, male</td>
<td>7</td>
<td>15</td>
<td>32</td>
</tr>
<tr>
<td>Sterilization, female</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>12</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Injection (DMPA*)</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Intrauterine device</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rhythm</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

*DMPA was not available in Canada at the time of the 1998 survey

<table>
<thead>
<tr>
<th>Contraceptive Method</th>
<th>Percent who ever used method</th>
<th>Percent who discontinued due to dissatisfaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral contraceptives</td>
<td>84.5</td>
<td>29.2</td>
</tr>
<tr>
<td>Intrauterine device</td>
<td>6.0</td>
<td>36.4</td>
</tr>
<tr>
<td>Norplant</td>
<td>2.1</td>
<td>42.0</td>
</tr>
<tr>
<td>Injection (DMPA*)</td>
<td>17.1</td>
<td>42.3</td>
</tr>
</tbody>
</table>

*DMPA was not available in Canada at the time of the 1998 survey

## Contraceptive Use in Canada (n = 2751)

<table>
<thead>
<tr>
<th>Contraceptive Use</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never used</td>
<td>14.9%</td>
</tr>
<tr>
<td>Sometimes used</td>
<td>9.3%</td>
</tr>
<tr>
<td>Usually used</td>
<td>10.6%</td>
</tr>
<tr>
<td>Always used*</td>
<td>65.2%</td>
</tr>
</tbody>
</table>

*Women who had a hysterectomy or were using female or male sterilization were included in the “always used” group.

Oral Contraceptives Compliance


Active pills missed

% of women

Cycle 1

Cycle 2

Cycle 3

Diary

Electronic device
Annual Efficacy

NUMBER OF UNPLANNED PREGNANCIES PER 100 WOMEN-YEARS

1st-Line Contraceptive Options

- Oral contraceptive pill
- Contraceptive patch
- Contraceptive injection
- Contraceptive vaginal ring
- Intrauterine system (IUS)
- Intrauterine device (IUD)
- Condom
NON-DAILY CONTRACEPTIVE OPTIONS
Non-Daily Contraceptive Methods

CONTRACEPTIVE VAGINAL RING NUVARING®

CONTRACEPTIVE PATCH EVRA®

CONTRACEPTIVE INJECTION DMPA

COPPER IUD Nova T® and Flexi T®

LEVONORGESTREL INTRAUTERINE SYSTEM MIRENA®
The Vaginal Contraceptive Ring

United States: FDA approval October 2001
Available since 2002

Canada: Health Canada approval 2004
Available January 2005
Hormonal Vaginal Ring Characteristics

- **Hormonal content:**
  - 120 µg/day etonogestrel (ENG)
  - 15 µg/day ethinyl estradiol (EE)
- Flexible, transparent
- Monthly vaginal ring
- Outer diameter: 54 mm
- Thickness: 4 mm
- One ring per cycle 3 weeks ring-in; 1 week ring-free

¹NuvaRing® [package insert], Roseland, NJ, Organon USA, Inc, 2008
### Median follicular diameter, E2 and P concentrations (n=16)

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Estradiol (E2) (pmol/L)</th>
<th>Progesterone (nmol/L)</th>
<th>Follicular diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mulders & Dieben, Fertil Steril, 2001;75:865–70
Reserve of etonorgestrel /EE after 21 days (n=16)

### Contraceptive Efficacy: Pregnancy Prevention*

*These data are for the European study

<table>
<thead>
<tr>
<th></th>
<th>Pregnancies</th>
<th>Cycles (n)</th>
<th>Pearl Index</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intent to treat (method failure and user failure)</strong></td>
<td>6</td>
<td>12,109</td>
<td>0.65</td>
<td>0.24–1.41</td>
</tr>
<tr>
<td><strong>Per protocol population (method failure)</strong></td>
<td>3</td>
<td>9,880</td>
<td>0.40</td>
<td>0.08–1.16</td>
</tr>
</tbody>
</table>

Vaginal Contraceptive Ring: Tolerability vs. Combined Oral Contraceptive†

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall discontinuation rate</td>
<td>1.06</td>
<td>[0.81, 1.38]</td>
</tr>
<tr>
<td>Discontinuations due to adverse events</td>
<td>1.33</td>
<td>[0.89, 2.00]</td>
</tr>
<tr>
<td>Breakthrough bleeding (cycle 6)</td>
<td>0.22*</td>
<td>[0.05, 0.88]</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.89</td>
<td>[0.48, 1.63]</td>
</tr>
<tr>
<td>Headache</td>
<td>1.30</td>
<td>[0.80, 2.10]</td>
</tr>
<tr>
<td>Breast tenderness</td>
<td>0.43</td>
<td>[0.09, 2.01]</td>
</tr>
<tr>
<td>Breast pain</td>
<td>2.25</td>
<td>[0.99, 5.14]</td>
</tr>
<tr>
<td>Weight increase</td>
<td>0.93</td>
<td>[0.41, 2.13]</td>
</tr>
<tr>
<td>Acne</td>
<td>0.23*</td>
<td>[0.08, 0.63]</td>
</tr>
</tbody>
</table>

* p<0.05

† Levonorgestrel 150 ug + EE 30 ug

Vaginal Contraceptive Ring / COC Device-related Side Effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Odds Ratio</th>
<th>[95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukorrhea</td>
<td>6.42*</td>
<td>[2.71, 15.22]</td>
</tr>
<tr>
<td>Vaginitis</td>
<td>2.84*</td>
<td>[1.34, 6.01]</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>7.51</td>
<td>[0.78, 72.32]</td>
</tr>
<tr>
<td>Genital pruritus</td>
<td>4.58*</td>
<td>[1.14, 18.41]</td>
</tr>
</tbody>
</table>

† Levonorgestrel 150 ug + EE 30 ug

*p<0.05

Patient Telephone Call-back Rates for 3 Months After Initiation

- Percentage of patients who called back at least once
- Percentage of patients who called back more than once

COC users
Patch users
Vaginal ring users

Absolute Contraindications

- <6 weeks postpartum if breastfeeding
- Hypertension (SBP>160 or DBP>100)
- VTE (current/past)
- Ischemic heart disease
- History of CVA
- Complicated valvular heart disease
- Migraine headache with focal neurological symptoms
- Migraine without aura over age 35
- Breast cancer (current)
- Diabetes with end organ involvement
- Active viral hepatitis; Severe cirrhosis
- Liver tumor
- Smoker over age 35 (>15 cig/day)
- Known thrombophilia
- SLE with positive APLA
Putting the VTE Risk into Context

Non-pregnant / non-OC users (4.5)

OC Users (9.1)

Pregnancy (30)

per 10,000 women

Based on a representative survey of 48,525 German women using EURAS methodology (Dinger Contraception 2007)
# Vaginal Contraceptive Ring: Lipid Metabolism

## Median % change from baseline to cycle 6

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Vaginal Ring</th>
<th>30 EE/150 LNG</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.8</td>
<td>3.1</td>
<td>NS</td>
</tr>
<tr>
<td>HDL</td>
<td>1.5</td>
<td>-11.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDL</td>
<td>0.0</td>
<td>9.5</td>
<td>0.001</td>
</tr>
<tr>
<td>TG</td>
<td>23.8</td>
<td>8.6</td>
<td>NS</td>
</tr>
</tbody>
</table>
## Duration of Contraceptive Use and Window of Forgiveness

<table>
<thead>
<tr>
<th>Contraceptive method</th>
<th>Duration of use</th>
<th>Window of forgiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>COC</td>
<td>24 hours</td>
<td>12-24 hours</td>
</tr>
<tr>
<td>Patch</td>
<td>7 days</td>
<td>2 days</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>21 days</td>
<td>15 days</td>
</tr>
<tr>
<td>DMPA</td>
<td>12 weeks</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>5 years</td>
<td>6 months</td>
</tr>
<tr>
<td>MIRENA®</td>
<td>5 years</td>
<td>2 years</td>
</tr>
</tbody>
</table>
Compliance: Incidence of “Perfect Use”

* p=0.03; ** p=0.05
CVR: contraceptive vaginal ring; OCP: oral contraceptive pill

Other Advantages of Vaginal Ring

- Less frequent administration (once monthly)
- EE dose 15 μg/day*
- Vaginal administration
  - Rapid absorption, constant serum concentrations
  - Avoids gastrointestinal interference with absorption
  - Avoids hepatic first-pass metabolism
  - No interference with other drugs
- Proven cycle control
- Low rates of discontinuation due to adverse events
- High adherence
- Easily inserted by the woman
- Discreet / shift work

*not comparable to 15 μg oral contraceptive pill

Vaginal ring user acceptability
Ease of insertion and removal

Vaginal ring user acceptability

Sexual comfort

Non-contraceptive Benefits

• Oral contraceptives have recognized non-contraceptive benefits

• Assume vaginal contraceptive ring offers the same non-contraceptive benefits
  – Lack of evidence, except for endometriosis

Leyland et al. JOGC 2010; 244 (7):S1-S28.
Potential Barriers to Vaginal Contraception

- Insertion into vagina
- Coverage / access
- Does not provide protection against sexually-transmitted infections (nor do other combined hormonal contraceptives – only condoms provide STI protection)
Patient Counselling

• Address common patient questions:
  • Does it work?
  • Won’t it fall out?
  • Won’t I feel it?
  • Won’t my partner feel it during sex?
  • Won’t it cause infections?
Vaginal Contraceptive Ring: Insertion

• Can be inserted on any day of the cycle (even if patient has not finished bleeding)

• Back-up method recommended for the first 7 days if a Quick Start method is used

• Withdrawal bleed normally starts within 2-3 days of removing ring

• Withdrawal bleeding may continue beyond the ring-free week (usually spotting)

• Should be reinserted after 7 days regardless of spotting
Vaginal Contraceptive Ring: No Need to Remove During Intercourse
Missing the Vaginal Ring

Removal ≤ 3 hours

Insert the ring ASAP.
Keep it in until the scheduled ring removal day.

Delayed insertion ≥ 24 hours or removal for more than 3 hours

During week 1

1. Removal > 3 hours or unsure how long ring was removed

Insert the ring ASAP.
Keep it until the scheduled ring removal day.
Back-up contraception for 7 days.
Consider EC.*

EC = emergency contraception

* If unprotected intercourse within the last 5 days.
Missing the Vaginal Ring

Delayed insertion $\geq$ 24 hours or removal for more than 3 hours

During week 2 or 3

2. Removal < 72 hours (< 3 days)
   Insert the ring ASAP. Keep it until the scheduled ring removal day. Start a NEW CYCLE with a NEW RING with no HFI.

3. Removal $\geq$ 72 hours ($\geq$ 3 days)
   Insert the ring ASAP. Keep it until the scheduled ring removal day. Start a NEW CYCLE with a NEW RING with no HFI. Back-up contraception for 7 days. Consider EC.*

* If repeated or prolonged omission.
The RING
vaginal contraceptive ring

During which week of your contraception cycle was the ring forgotten, expelled, or removed early?

> Week 1
> Week 2 or Week 3
> Ring was worn longer than scheduled
THE VAGINA AS A DRUG DELIVERY SYSTEM
Anatomy of the Vagina

- Large surface area (60 cm$^2$) of squamous epithelium available for drug uptake
- Dense vascularity allows rapid, steady drug uptake
- Distensible vaginal wall due to collagen and elastin
- Lower 1/4 of vaginal is peripherally innervated making it highly sensitive to touch and temperature
- Upper part of vagina is innervated by the autonomous nervous system making it relatively insensitive to touch and temperature
Innervation of the Vagina/
Position of the Ring

Correct position

Incorrect position

The Ciba Collection of Medical Illustrations,
Vol. 2, Reproductive System
Vasculature of the Vagina

- **Arterial Supply**
  - Multiple sources
  - Uterine, pudendal
  - Hemorrhoidal

- **Venous Drainage**
  - Pudendal
  - Vaginal, uterine,
  - Vesical, rectosigmoid
Drugs Administered Vaginally

• Antimicrobials/antifungals
• Spermicides
• Reproductive Hormones:
  • Prometrium, progesterone, progesterone ring,
  • Premarin, Estring, Vagifem, Estrace
  • OCP, NuvaRing
• Prostaglandins: Misoprostol, Dinoprostone
• Sildenafil
• NSAIDS
Vaginal Drugs in Development

- Gyminox gel: Contraception, STI prevention
- Terbutaline gel: Dysmenorrhea, endometriosis
- Demegen gel: STI prevention
- Lidocaine Ring: Cervical analgesia
- Oxybutynin Ring: Hyperactive bladder
- Tenofovir gel: Prevent HIV transmission
- Antibody III-174 implant: Prevent/treat HSV II
User satisfaction with vaginal ring

The 3 most frequently mentioned responses were:

- Do not have to remember anything (43%)
- Easy to use (28%)
- Effective method (10%)

Pharmacokinetic Profile Differs Depending Upon Route of Administration


Number of days after first administration

EE (pg/mL)

Treatment:
- Observed vaginal ring (n=8)
- Observed patch (n=6)
- Observed LNG/EE OC (n=8)
• Many methods of contraception, including new delivery systems

• Non-daily contraceptive choices are available – choose one that best fits a woman’s needs and lifestyle

• The vagina is an effective drug delivery system for combined hormonal contraception
Websites for Additional Information

SOGC Trusted Resources:

• sogc.org
• sexualityandu.ca
• hpvinfo.ca
• endometriosisinfo.ca
• menopauseandu.ca