



What's New in Contraception?



By Denise Black, MD, FRCSC

Case

Jackie is a 32-year-old non-smoker who thinks she's completed her family, but is not entirely sure. Recently, she has noticed her menstrual periods are becoming increasingly heavy.

She presents to you requesting effective, reversible contraception, and possibly a reduction in menstrual bleeding.

Since the introduction of the oral contraceptive pill (OCP) in the early '60s, there hasn't been a lot of news in contraception. Estrogen doses have been lowered, new progestones introduced, and "phasing" popularised, but not much has been "new."

In 2002, this changed with three new and innovative advances in contraception that may revolutionise perspectives on contraception.

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In this article:

1. Review of three innovative products in contraception.
2. What are the side effects and risks of intrauterine and patch systems of contraception?
3. Who would benefit from the latest birth control products?

1. FREEDOM FOR TODAY'S WOMAN

Mirena™ is an intrauterine system, which acts by slowly releasing levonorgestrel into the uterus (Figure 1). This in turn induces endometrial atrophy and thickening of the cervical mucous. Ovulation inhibition is sporadic, and not the main contraceptive effect.¹ Although officially indicated only for contraception, the endometrial atrophy-inducing property of



Contraception

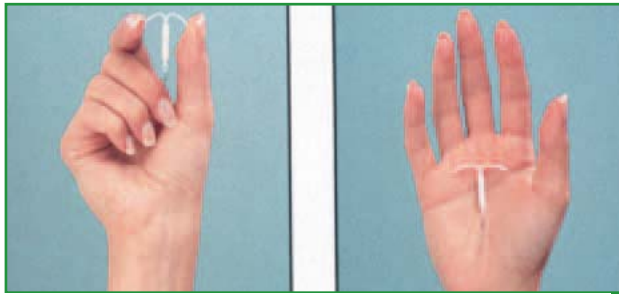


Figure 1. Mirena.

Mirena is rapidly making it a popular choice for non-surgical management of menorrhagia (Table 1).

Mirena is an extremely effective contraceptive; once in place, it is effective for five years. Studies on contraceptive efficacy have demonstrated a Pearl Index of 0.09, far superior to any other reversible form of contraception.²

Contraindications to Mirena include known or suspected pregnancy, current or recurrent cervicitis or pelvic inflammatory disease, undiagnosed uterine bleeding, fibroids or uterine anomalies which distort the uterine cavity, active liver disease, and hypersensitivity to levonorgestrel. It should not be used in patients who are immunosuppressed or

those with systemic septicemia or bacterial endocarditis. Antibiotic prophylaxis should be administered when inserting or removing Mirena in patients with congenital or valvular heart disease at risk of endocarditis.

Mirena is readily available in Canada. Costs will vary between provinces, but prices of \$300.00 to \$350 are considered average in Manitoba. Most, but not all, provincial formularies and third party plans will cover a percentage of the costs.

Mirena is not without side effects; in the first three months of use, irregular, unpredictable uterine bleeding is common. During the first cycle of use, the average number of days of bleeding and/or spotting was 16. This number dropped to nine by the third cycle, and four by the twelfth cycle.² During the first year of use, 16% of women experienced prolonged amenorrhea (> 90 days).² The spontaneous expulsion rate was 3.4% to 4.9%.² There is a statistically significant increase in the incidence of depression (2.9% versus 0 for Nova T Intrauterine Device™), but no increase in weight compared to Nova T users.² Mirena does not appear to interfere with lactation, and return to fertility after removal is rapid.³

In summary, Mirena is a highly effective, readily reversible contraceptive which requires only a single insertion for five years of protection. Although prolonged bleeding may occur in the first few months of use, over the long term, menstrual bleeding is greatly diminished.

2. NOT YOUR MOM'S BIRTH CONTROL

Evra™ employs the latest in patch technology delivering hormonal contraception in a transdermal system (Table 2). Each Evra patch contains 20 µg ethinyl estradiol and 150 µg norelgestromin, delivering continuous doses of these hormones for seven days. The system is used as a three weeks on, one week off plan, with patches needing to be changed once weekly. It works by inhibiting ovulation, inducing endometrial atrophy,

Table 1

Mirena™ Intrauterine System

Indication	Contraception
Secondary benefit	Reduced menstrual bleeding
Contraceptive efficacy	Pearl Index 0.09 preg/100 women years use
Contraindications	Pregnancy Undiagnosed vaginal bleeding Distorted uterine cavity Infection Immunosuppression Active liver disease
Cost	\$300.00 for five years
Notable side effects	Irregular bleeding for first 3-6 months Amenorrhea
Biggest advantage	5 years of worry-free contraception Reduced bleeding

Table 2
Evra Patch[®]

Indication	Contraception
Secondary benefit	Lighter periods
Contraceptive efficacy	Pearl Index 0.88 pregnancies /100 women years
Contraindications	Smokers over 35 History of venous thromboembolism/ thrombophilia Active liver disease Pregnancy Undiagnosed vaginal bleeding Estrogen sensitive malignancy Neurologic migraines/ transient ischemic attack Uncontrolled hypertension
Caution	Use in women \geq 90 kg
Cost	Close to OCP's
Notable side effects	Mastalgia
Biggest advantage	Once weekly dosing

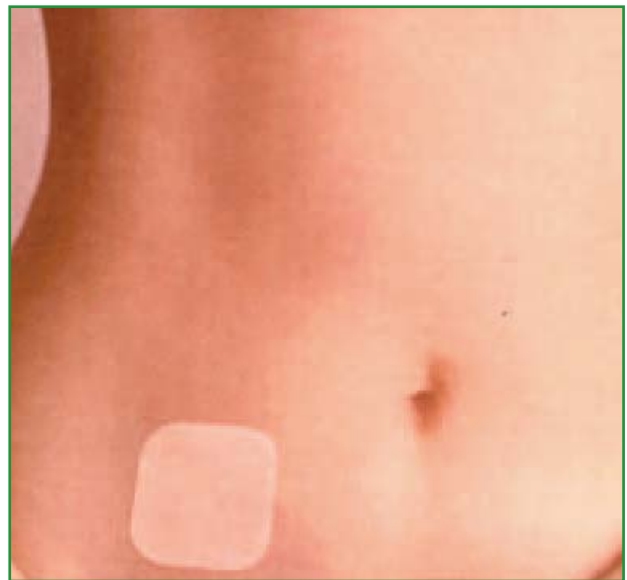


Figure 2. Evra Patch.

and causing thickening of the cervical mucous. Although the only current indication for use is contraception, it is reasonable to assume that the non-contraceptive benefits will be similar to those of OCPs.

Evra is highly efficacious. Combined efficacy data reveal a Pearl Index of 0.88 pregnancies/100 women years use over a total of 22,155 cycles.⁴ Perfect compliance is seen in 89% of cycles, significantly better than that of combined oral contraceptives (70% compliance).⁵

Contraindications to Evra are similar to those of combined oral contraceptives. An additional measure of caution should be taken when prescribing Evra to women who weigh more than 90 kg; the risk of con-

traceptive failure appears to be much higher in this group, with five of 83 subjects becoming pregnant.⁴

The most commonly observed side effects of Evra were breast discomfort (19% versus 6% for OCP users), headache (22% versus 22% for OCP users), application site reaction (20%), nausea (20% versus 18% for OCP users), and dysmenorrhea (13% versus 10% for OCP users).⁶ The breast discomfort usually resolves by cycle three.⁶ Breakthrough bleeding pat-

terns for women taking Evra were similar to those observed with combined oral contraceptives.

In large clinical trials, the incidence of complete and partial patch detachments was low. Complete detachment was seen in 1.8% of patch applications, with partial detachments occurring in 2.9% of applications. Application sites are preferably the lower abdomen, upper outer arm, buttocks or upper torso, but not

breasts (Figure 2).

Currently, there is an ongoing, large, multi-centred clinical trial evaluating patient acceptance of Evra. One of the most commonly asked questions is “Can the patch be worn in tanning salons?” The answer is yes, but the site should be rotated weekly to avoid an



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untanned “spot.” Upper outer arm application is recommended.

Evra has been approved for use in Canada, but due to supply problems, is available only through the study. It will become widely available possibly in the spring or early summer of 2003.

3. NOT YOUR DAILY VARIETY

NuvaRing™, an intravaginal hormone-releasing ring contraceptive, was launched in Europe in the spring of 2002 (Figure 3). NuvaRing is a flexible, plastic ring made of ethylene vinyl acetate which releases 15 µg of ethinyl estradiol and 120 µg of etonogestrel per day. This polymer allows uniform and highly consistent release of hormones. The system is placed intravaginally by the woman herself, as there is no “correct”

positioning. As long as it is inside the vagina and comfortable, it is correctly placed. It remains in the vagina for three weeks, is removed for a week for menstruation, and the next ring is then inserted (Table 3).

NuvaRing works by complete ovulation inhibition.⁷ Follicle-stimulating hormone, luteinising hormone, and progesterone levels throughout the duration of use demonstrated complete suppression of ovulation. Ovulation suppression was achieved after only three days of use, shorter than the seven days thought to be required for combined oral contraceptives.⁸ Ovulation was effectively inhibited for two further weeks if the NuvaRing was “accidentally” forgotten, indicating a margin of forgivability for prolonged use.⁷ Thickening of cervical mucous and endometrial thinning may also contribute to contraceptive efficacy.⁷

In contraceptive efficacy trials, the Pearl Index for



Contraception

NuvaRing users in North America was 1.27 pregnancies per 100 women years of use.⁹ Compliance was approximately 86% per cycle. A return to fertility after discontinuation was almost immediate.

Contraindications to NuvaRing are similar to those for combined OCPs. The only additional contraindication is hypersensitivity to any of the components of the system.

With NuvaRing, the incidence of adverse events is low. The most common treatment-related events were headache (5.8%), vaginitis (5.6%), leukorrhea (4.8%), and coital problems (4.4%). Only 2.6% of women experienced expulsion.⁹ The incidences of acne and nausea were lower than that observed with combined oral contraceptives.⁹ The incidence of clinically significant weight gain was less in NuvaRing users than those using combined OCPs.¹⁰ Breakthrough bleeding rates were low (5.5% of all cycles). Virtually all women (98.5%) experienced

scheduled menstruation.¹⁰

A commonly asked question with NuvaRing is whether sexual partners can feel the ring during inter-



Figure 3. NuvaRing.

Children's MOTRIN:^{*} On Duty For 8 Hours.

ibuprofen

Recommend the #1 selling pediatric ibuprofen.¹

- Works fast and lasts longer than acetaminophen for fever relief^{2,3}
- Safety profile demonstrated comparable to acetaminophen in a study of over 84,000 generally well children⁴
 - Excellent GI tolerability[†]
[†] Incidence 3 to 9%: nausea, epigastric pain, heartburn
 - No link with Reye's Syndrome found

Ibuprofen should not be administered to patients who are known to be hypersensitive to ASA or other NSAIDs, have systemic lupus erythematosus, acute peptic ulcer, gastrointestinal bleeding or are severely dehydrated. Please see prescribing information for warnings, precautions and contraindications.



Suspension Drops



Suspension Liquid



Chewables

Strong Relief That Lasts.

From The Makers of **Children's TYLENOL[®]**
acetaminophen



Contraception

Table 3

NuvaRing Vaginal Contraceptive

Indication:	Contraception
Secondary benefit	Lighter periods
Contraceptive efficacy	Pearl Index 1.27 pregnancies/100 women years
Contraindications	Smoker over age 35 History of venous thromboembolism/thrombophilia Active liver disease Pregnancy Undiagnosed vaginal bleeding Estrogen sensitive malignancy Neurologic migraines/transient ischemic attack Uncontrolled hypertension
Cost	Unknown
Notable side effects	Vaginitis/leukorrhea Partner feeling ring during coitus
Biggest advantage	Invisible, once monthly Patient controlled Lower systemic hormone levels

course, and whether they object. Acceptance of NuvaRing is high; although about 25% of male partners occasionally felt the ring, rarely or never did they object.¹¹ For those who object, removal of the ring for up to three hours did not affect efficacy.¹²

NuvaRing is currently available in Europe and

Take-home message

Canadian women now have expanded choices for effective, reversible, long-term contraception.

Jackie, our patient in question, would benefit from any of the three new therapies. Her goal is effective, reversible contraception with decreased menstrual flow. All of the new products will fill this dual need.

the U.S., but is still awaiting Health Protection Branch approval before it will be available for use in Canada. [CME](#)

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Interesting Web sites:
www.mirena.com
www.evra.com
www.nuvaring.com