

DIALOGUES



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In This Issue

Advances in the Use of Intrauterine Contraception

Philip D. Darney, MD, MSc

Professor and Chief
Obstetrics, Gynecology and
Reproductive Sciences
San Francisco General Hospital
University of California,
San Francisco
San Francisco, California



Raquel D. Arias, MD

Associate Dean
Associate Professor
Department of Obstetrics and
Gynecology
Keck School of Medicine
University of Southern California
Los Angeles, California



An Update on the Vaginal Ring

Deborah M. Smith, MD, MPH

Clinical Associate Professor of
Obstetrics and Gynecology
Howard University College
of Medicine
Washington, DC



Susan J. Wysocki, RNC, NP, FAANP

President and CEO
National Association of Nurse
Practitioners in Women's Health
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Produced by:



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Estimated time for completion of activity: 1.5 hours

Release Date: July 2006

Termination Date: July 31, 2009

Available online at
www.usc.edu/cme

Advances in the Use of Intrauterine Contraception

Philip D. Darney, MD, MSc, and Raquel D. Arias, MD

Educational Objectives:

The health care provider should be able to:

- identify the expanded populations of eligible potential intrauterine contraceptive (IUC) users as a result of labeling changes and recent studies
- manage issues that commonly arise during IUC use
- increase awareness and acceptance of IUC use by dispelling misperceptions

Recent evidence-based labeling changes for the copper T 380A intrauterine contraceptive (IUC; ParaGard®) and studies of the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena®) indicate the potential for expanded use of these safe, highly effective, long-term, reversible contraceptive methods. Some previously expressed or implied limitations on copper IUC use have now been removed from labeling, greatly increasing the number of women eligible to use this form of contraception.¹ Labeled indications for copper IUC use now include¹:

- nulliparous and nulligravid women aged 16 and over, as well as parous women not in a mutually monogamous relationship (although such a relationship is encouraged in the user information)
- women with a history of sexually transmitted infections (STIs) or pelvic inflammatory disease (PID), who do not exhibit behavior suggestive of high risk for PID

These labeling changes reflect the results of studies showing that there is no increased risk of infertility after discontinuation of IUC use, even in nulligravida²⁻⁴; no increased risk of PID (except during the first 20 days following insertion), even with long-term use of IUCs⁵⁻¹⁰; and no difference in complications (eg, PID, expulsion, perforation) between parous and nulliparous IUC users.¹¹ Contrary to the findings of early IUC studies,^{12,13} a recent case-control study of 1985 women found that, among nulligravid women, previous use of a copper IUC is not associated with increased risk of tubal occlusion (Table 1); however, infection with *Chlamydia trachomatis* is associated with increased risk of tubal occlusion.² Moreover, a large body of

evidence has established that risk of infections among IUC users after the first 20 days following insertion is related to women's individual risk behaviors for acquiring STIs, not to IUC use.^{5-10,14} PID in IUC users is very uncommon after the first 20 days following insertion,^{5,7,10,15} when colonization of the endometrial cavity by vaginal bacteria transferred by insertion is no longer present. Therefore, since there is no increased risk of infection after the first 20 days after insertion, there is no increased risk of future infertility with IUC use.^{16,17}

The uterine spermicidal activity produced by the copper-bearing IUC and cervical barrier to sperm transport produced by the LNG-IUS prevent fertilization and produce the highly effective contraceptive action of IUCs.^{16,18} Despite evidence that use of IUCs is as effective in preventing pregnancy as female sterilization,^{6,16,19,20} the 2002 National Survey of Family Growth found that IUCs were currently used by only 1.3% of US women aged 15 to 44.²¹ Only 0.1% of women aged 15 to 19 and 1.1% of those aged 20 to 24 were currently using IUCs. In contrast, in the rest of the world, IUCs are the most widely used method of reversible contraception.²² Reasons for this persistent underutilization of IUCs in the United States include lingering misperceptions (discussed below).^{22,23} The increased number of women now considered eligible for IUC use, as reflected in the labeling changes for the copper IUC, may help to expand use of this safe and highly effective contraceptive method, particularly among nulliparous women.

The increased number of women now considered eligible for IUC use, as reflected in the labeling changes for the copper IUC, may help to expand use of this safe and highly effective contraceptive method, particularly among nulliparous women.

To date, there have been no changes in labeling for the LNG-IUS comparable with those for copper IUC labeling. Use in nulliparous women is not contraindicated in LNG-IUS labeling, but the recommended

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Table 1. History of Use of a Copper IUC and Risk of Tubal Occlusion*2

Previous Use of a Copper IUC	Infertile Women with Tubal Occlusion (n=358)		Infertile Controls (n=953)	Odds Ratio (95% CI)	Pregnant Controls (n=584)	
	no. (%)	no. (%)			no. (%)	Odds Ratio (95% CI)†
No	335 (93.6)	896 (94.0)	1.0	544 (93.2)	1.0	
Yes	23 (6.4)	57 (6.0)	1.0 (0.6–1.7)	40 (6.8)	0.9 (0.5–1.6)	
Duration of use						
≤6 mo	9 (2.5)	27 (2.8)	0.8 (0.4–1.8)	11 (1.9)	1.4 (0.6–3.6)	
7–12 mo	6 (1.7)	15 (1.6)	1.1 (0.4–2.8)	8 (1.4)	1.0 (0.3–3.0)	
≥13 mo	8 (2.2)	15 (1.6)	1.3 (0.6–3.2)	21 (3.6)	0.6 (0.3–1.4)	
IUC removed because of side effects						
Yes	11 (3.1)	33 (3.5)	0.8 (0.4–1.7)	13 (2.2)	1.4 (0.6–3.2)	
No	12 (3.4)	24 (2.5)	1.3 (0.6–2.7)	27 (4.6)	0.7 (0.3–1.4)	
Gynecologic problems during use						
Yes	16 (4.5)	41 (4.3)	1.0 (0.6–1.8)	21 (3.6)	1.2 (0.6–2.4)	
No	7 (2.0)	16 (1.7)	1.1 (0.4–2.6)	19 (3.3)	0.6 (0.2–1.4)	

*For infertile women, data represent the use of a copper intrauterine contraceptive (IUC) before the women suspected a fertility problem. In each analysis, the women with no previous use of a copper IUC served as the reference group. The ratios were adjusted for age, income, number of sexual partners, years of education, and history of sexual intercourse during the teenage years. CI denotes confidence interval.

†The odds ratios are for the comparison with the infertile women with tubal occlusion.

Adapted, with permission, from Hubacher D, Lara-Ricalde R, Taylor DJ, Guerra-Infante F, Guzman-Rodriguez R. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. *N Engl J Med.* 2001;345:561–567. Copyright © 2001 Massachusetts Medical Society. All rights reserved.

patient profile includes parity.²⁴ However, data from various studies indicate that the LNG-IUS is at least equivalent to copper IUCs with regard to safety (ie, no increased risks of PID, subsequent infertility, ectopic pregnancy) in both nulliparous and parous women, and some studies suggest decreased risk of PID with use of the LNG-IUS.^{6,11,17,25–29}

Table 2 summarizes recommendations of the World Health Organization (WHO) with regard to eligibility for initiating use of either IUC.^{29,30}

IUC Management

Although complications are infrequent with IUC use, clinicians should be familiar with appropriate management approaches to common issues.

Abnormal Pap Tests

Cervical dysplasia. IUCs do not cause cervical dysplasia. In a 7-year comparison of the 2 IUCs, incidence of Pap tests reported as grade III (severe dysplasia, high-grade squamous intraepithelial lesion) or higher was 0.3–0.4 per 100 woman-years and of Pap tests reported as grades IV and V (high-grade squamous intraepithelial lesion, atypical glandular cells) was 0.1 per 100 woman-years with either IUC.³¹ These rates are similar to overall rates of abnormal Pap tests in women aged 18 to 65 regardless of IUC use: in the United States, between 1996 and 2000, the rate of abnormal Pap tests (all classifications) was 2.3%.³² The presence of an IUC does not alter the standard development, management, or therapy (including loop electrosurgical excision procedure [LEEP]) of cervical dysplasia if it occurs. There is no biologically plausible reason to remove the IUC if cervical dysplasia is found on a Pap test.

Actinomyces-like organisms (ALOs). Regardless of IUC use or nonuse, *Actinomyces* is commonly present in the normal vagina and is part of the normal flora in the gastrointestinal tract.^{33,34} ALOs are a common finding in Pap tests of both IUC users and nonusers; however, this incidental finding represents colonization, not infection.³¹ The majority of the evidence suggests that ALO-positive Pap tests do not definitively predict actinomycotic PID.^{33,35,36} Women with ALO-positive Pap tests are almost always asymptomatic^{34,36}; in asymptomatic well women, antibiotic treatment and IUC removal are unnecessary.^{22,34–36} The only time IUC removal is recommended in the presence of ALO is when signs and symptoms of upper genital-tract infection (eg, uterine tenderness, pelvic mass, pelvic pain) are also present; in these rare instances, antibiotic treatment should be instituted and the IUC removed after treatment has been initiated.^{1,22,24,34}

Lower and Upper Genital-Tract Infections

Bacterial vaginosis (BV). Investigation has shown that the bacterial flora found on removed IUCs consist of common aerobic and anaerobic microorganisms.¹⁰ Appropriate treatment for BV is metronidazole (500 mg bid/7 days), but IUC removal is unnecessary.^{29,34,37}

Lower genital-tract infection with STIs (eg, chlamydia or gonorrhea). Women with chlamydia or gonorrhea pathogens in their cervixes are at increased risk for upper genital-tract infection whether or not they use IUCs.⁶ There is no increased risk of acquiring chlamydia with IUC use compared with nonuse, and there are few data regarding acquisition of gonorrhea during IUC use.⁶ WHO and other guidelines recommend treatment of the STI with appropriate antibiotics, with no need to remove the IUC if the woman wishes to continue use.^{29,34}

Table 2. World Health Organization Eligibility Criteria for Initiating Use of Intrauterine Contraception^{29,30}

Rating Scale:

- 1 = Can use the method. No restriction on use.
- 2 = Can use the method. Advantages generally outweigh theoretical or proven risks. If method is chosen, more than usual follow-up may be needed.
- 3 = Should not use the method unless clinician makes clinical judgment that the patient can safely use it. Theoretical or proven risks usually outweigh the advantages of method. Method of last choice, for which regular monitoring may be needed.
- 4 = Should not use the method. Condition represents an unacceptable health risk if method is used.

Condition	Copper IUC	LNG-IUS
Obesity (BMI >30 kg/m ²)	1	1
Multiple risk factors for CVD	1	2
Hypertension		
Controlled	1	1
Uncontrolled	1	1 (systolic 140-159 or diastolic 90-99) 2 (systolic ≥160 or diastolic ≥100)
Ischemic heart disease (past/current)	1	2
Stroke history	1	2
Diabetes		
No vascular disease/non-insulin	1	2
With vascular disease	1	2
Known thrombogenic mutations (eg, factor V Leiden)	1	2
History of DVT/PE	1	2
Current DVT/PE	1	3
Breast cancer		
Current	1	4
No cancer for 5 years	1	3
Smoking		
Age <35 years	1	1
Age >35 years	1	1
Nonmigraine headaches	1	1
Migraines aged ≥35 years, no aura	1	2
Migraine with aura, any age	1	2
Drug interactions		
Rifampicin	1	1
Griseofulvin	1	1
Antiretroviral (ARV)		
Clinically well on ARV	2	2
Not clinically well on ARV	3	3
Other antibiotics	1	1
Certain anticonvulsants: barbiturates, carbamazepine, oxcarbazepine, phenytoin, primidone, topiramate	1	1

Copper IUC=copper T380A intrauterine contraceptive; LNG-IUS=levonorgestrel-releasing intrauterine system; BMI=body mass index; CVD=cardiovascular disease; DVT=deep vein thrombosis; PE=pulmonary embolism.

Adapted, with permission, from Ziemann M, Arias R. Nonhormonal contraception in women with medical conditions. *Female Patient*. 2005;(suppl):8-12.³⁰

Upper genital-tract infection. Some^{6,26,38} but not all³¹ studies have found slightly lower rates of cervicitis, endometritis, and upper genital-tract infection among LNG-IUS users than in copper IUC users, but the rates were low with all IUC types. If PID does occur in an IUC user, treatment according to Centers for Disease Control and Prevention guidelines is the same as in a nonuser. IUC removal is unnecessary if the woman is fully informed and wishes to continue use.^{6,29} Although copper IUC labeling states that most clinicians remove the IUC¹ and LNG-IUS labeling states that removal after

initiation of antibiotic therapy is usually appropriate,²⁴ available evidence indicates no difference in effect of treatment whether the IUC is kept in place or removed.^{6,29}

String Issues

Monthly checking of IUC strings by the user is recommended in labeling to assure that the IUC is still placed correctly; however, many women do not do so and have no adverse consequences. If strings seem longer than usual, are "missing" to the touch, or if a hard part of the IUC can be felt, the strings may have become twisted, or pregnancy, partial expulsion, or perforation may have occurred. Effective backup contraception should be used until the clinician's examination can be performed. In many cases, a cytobrush twisted within the cervix can establish whether strings are curled in the cervical canal. If not, pregnancy should be ruled out. Once pregnancy is ruled out, a sonogram or an abdominal flat-plate x-ray, including the upper peritoneal cavity, can determine whether the IUC is present. Although the LNG-IUS is less likely to cause an inflammatory reaction in the peritoneal cavity than the copper IUC, which has the potential to produce a profound inflammatory response in peritoneal tissue, we recommend removal—preferably by laparoscopy—of all intraperitoneal IUCs.

Long IUC strings (eg, 4-5 cm, cut just to the level of the introitus) are usually not a problem to the user or her sex partner. If penile discomfort occurs, it is likely a result of too-short strings. The simple remedy is to cut off the strings entirely, which does not pose a problem for continuing IUC use; for example, the strings are usually removed during LEEP without adverse consequences.

Pregnancy During IUC Use

IUCs provide highly effective protection against pregnancy overall, so pregnancy during IUC use is very rare. The gross cumulative pregnancy rates at 7 years of use are 1.4 per 100 women for the copper T 380A IUC and 1.1 per 100 women for the LNG-IUS.^{27,31} Among these uncommon pregnancies during IUC use, the overall rates of ectopic pregnancy were found to be extremely low (per 1000 woman-years of use, copper IUC, 0.5; LNG-IUS, 0.0), representing an 80% to 90% reduction in ectopic pregnancy risk compared with noncontraceptors.^{27,28,31} Although the *absolute* and *relative* risks of ectopic pregnancy are significantly reduced with IUC use compared with noncontraceptors, ectopic pregnancy must be ruled out in women who do become pregnant during IUC use because the *ratio* of ectopic to intrauterine pregnancy in this setting is increased.^{28,34} LNG-IUS labeling contraindicates use in women with a history of ectopic pregnancy or a condition that would predispose to ectopic pregnancy.²⁴ Such histories and conditions are not contraindications for the copper IUC¹ although the LNG-IUS reduces risk of ectopic pregnancy even more than does the copper IUC.

Whether or not a pregnant IUC user intends to continue an intrauterine pregnancy, the IUC should be removed as soon as possible, because the risks of spontaneous abortion, preterm delivery, and infection are increased among women who conceive with IUCs in place and whose IUCs remain in the uterus.^{16,35} Women who wish to continue the pregnancy should be informed that IUC removal itself carries a small risk of spontaneous abortion, but this risk is less than that associated with leaving the IUC in place.^{16,35} The risk of spontaneous abortion is not increased if the IUC is easily removed or expelled during the first trimester of pregnancy.^{16,34} Women who plan to continue their pregnancies should also be aware of the possibility of septic spontaneous abortion (ie, fever, heavy bleeding, pain, abnormal vaginal discharge) whether or not the IUC is removed.^{35,37}

If IUC strings are not visible in a pregnant woman, ultrasound may facilitate IUC identification and removal.³⁴ Leaving the IUC in place when it is not easily removable does not further increase the risk of septic spontaneous abortion.³⁴ If the IUC is left in place during pregnancy, however, the incidence of preterm labor and delivery is further increased.^{34,35} There is no evidence that risks of congenital anomalies or obstetrical complications at delivery are increased in pregnancies occurring with an IUC in place.³⁴

Noncontraceptive Uses of IUCs

The LNG-IUS has been used effectively in the prevention and/or treatment of menorrhagia, myomas, dysmenorrhea, and endometriosis.^{31,39-49} (See also "Management of Bleeding Disorders With Contraceptive Steroids," *Dialogues in Contraception*[®], Volume 9, Number 4.) Past and current use of copper IUCs has been found to reduce risk of endometrial cancer by 40% compared with never-users, with risk reduction persisting for more than 15 years after

IUC discontinuation.⁵⁰⁻⁵⁴ Although data are more limited, the LNG-IUS may also protect against endometrial cancer,^{44,55} as do combination oral contraceptives containing a progestin.⁵⁶ Studies have also suggested that risk of invasive cervical cancer among copper IUC users is reduced 40% compared with nonusers.^{57,58} Use of the LNG-IUS, which decreases the number of bleeding days and reduces the amount of menstrual blood loss, may be beneficial for perimenopausal women until menopause and as a noninvasive alternative for women experiencing heavy bleeding who are considering endometrial ablation or hysterectomy.^{59,60} Although not approved for this use in the United States, the LNG-IUS also may be used as a source of progestin during postmenopausal estrogen therapy.⁶¹⁻⁶⁶

The copper IUC, inserted as emergency contraception (EC) up to 7 days after unprotected intercourse, is highly effective (99%) in preventing pregnancy.⁶⁷⁻⁷⁰ Because of the relatively high cost of the copper IUC compared with hormonal EC (Plan B®), use of the copper IUC for EC is most appropriate when the woman wants to continue use of the IUC as her ongoing method of contraception.^{68,69} The LNG-IUS should not be used for EC as it has not been studied for this indication.

Dispelling Misperceptions About IUCs

IUCs are not abortifacients. The IUC's mechanism of action is spermicidal, not abortifacient.⁷¹⁻⁷³ In one study, no normally dividing zygotes were found in the tubal flushings of postcoital midcycle IUC users, while in postcoital midcycle women not using contraception, normally dividing zygotes were recovered from the oviducts of half the women.¹⁸

IUC use does not increase risk of ectopic pregnancy. Contrary to a widespread misperception, current or previous use of either IUC does not increase risk of ectopic pregnancy compared with nonuse.

IUC use does not increase risk of ectopic pregnancy. Contrary to a widespread misperception, current or previous use of either IUC does not increase risk of ectopic pregnancy compared with nonuse^{27,28,31}; in fact, IUC use protects against the occurrence of ectopic pregnancy compared with noncontraceptors.²⁸ Both intrauterine and ectopic pregnancy rates with IUC use are significantly lower than those in noncontraceptors; however, if pregnancy does occur during IUC use, the likelihood of an ectopic pregnancy is about 5%.^{27,28,31} Following discontinuation of IUC use, the risk of subsequent ectopic pregnancy is not increased compared with never-users, even in women with previous ectopic pregnancies.^{16,34}

IUC use does not increase risk of PID or infertility. There is no increased risk of infection or PID in IUC users compared with nonusers after the first 20 days following insertion and therefore no increased risk of future infertility.^{5,15,16}

There is no increased risk of infection or PID in IUC users compared with nonusers after the first 20 days following insertion and therefore no increased risk of future infertility.

IUC prescribing does not increase risk of clinician liability. Misperceptions like the ones discussed above have led some to believe that clinicians who provide IUCs are at increased risk for legal liability. In fact, litigation involving the currently available IUCs is extremely rare.⁷⁴ Thorough counseling and informed consent are recommended for all women selecting any form of contraception.

Many women are appropriate candidates for IUC use. Growing evidence and the recent labeling changes for the copper IUC indicate that the potential IUC user population is much greater than previously believed (Table 2).^{29,30} Studies have found that women who have no current PID and do not engage in sexual behaviors that increase STI risk are appropriate candidates for IUC use, regardless of age, parity, or history of ectopic pregnancy.^{11,29} Furthermore, in the absence of intrauterine or vaginal infection, copper IUC insertion can be performed at any time during the menstrual cycle

(if pregnancy can be ruled out) and during menses and lactation; product labeling states that insertion immediately following delivery or first-trimester abortion may increase risk of expulsion.^{1,75-79} Product labeling for the LNG-IUS states that insertion should occur within 7 days of the onset of menstruation or immediately after first-trimester abortion, and that insertion immediately postpartum may increase risk of expulsion and perforation.²⁴

Summary

IUCs are extremely effective, safe, long-term, rapidly reversible contraceptives that are greatly underutilized in the United States due to misperceptions. As effective as sterilization in preventing pregnancy, IUCs can be used safely by many more women than previously believed, specifically including nulliparous and young women. By informing women of the evidence-based facts about the copper IUC and the LNG-IUS, clinicians can assist appropriate candidates for IUC use to benefit from highly effective contraception independent of user activity.

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An Update on the Vaginal Ring

Deborah M. Smith, MD, MPH, and Susan J. Wysocki, RNC, NP, FAANP

Educational Objectives:

The health care provider should be able to:

- describe recent information regarding various aspects of vaginal ring use
- counsel appropriate potential candidates for combination hormonal contraception about the vaginal ring as an acceptable nondaily option

Introduced to the United States in 2001, the vaginal contraceptive ring (NuvaRing®) is a flexible, 1-size ring of ethylene vinylacetate copolymer, which releases 15 mcg of ethinyl estradiol (EE) and 120 mcg of etonogestrel (ENG; the active metabolite of desogestrel) daily.^{1,2} The vaginal ring is intended to be worn continuously for 3 weeks, then removed for 1 week to allow scheduled withdrawal bleeding before replacement with a new vaginal ring to begin the next cycle.¹ Contraceptive steroids are absorbed through the vaginal epithelium, thus acting systemically to prevent ovulation.¹ Contraceptive effectiveness is high, with pregnancies occurring during use at a rate of 1.18 (confidence interval [CI], 0.73–1.80) per 100 woman-years of use.³ Cycle control is very good, with uncommon (average 5.5% per cycle over cycles 1 to 13) instances of breakthrough bleeding (primarily spotting).³

Recent Vaginal Ring Studies

In the 5 years since the vaginal ring's approval in the United States, a number of studies have been published. To update clinicians, various aspects of vaginal ring use are addressed in this article.

Pharmacokinetics

An open-label, randomized study compared EE pharmacokinetics (PK) in users of 3 combination hormonal contraceptives: the monthly vaginal ring (NuvaRing®, which releases 15 mcg EE/day), the weekly transdermal patch (ORTHO EVRA®, which releases 20 mcg EE/day), and a daily combination oral contraceptive (COC; 30 mcg EE/150 mcg levonorgestrel [LNG]; equivalent to Leven®, Nordette®, Levora®, Seasonale®).⁴ Analysis of the mean EE area under the curve (AUC) over 21 days of treatment found that EE exposure with the vaginal ring was 3.4 times lower than with the patch and 2.1 times lower than with the COC (10.6±2.5, 35.8±5.5, 21.9±2.9, respectively; $p < .05$). While use of estrogen-containing contraceptives is associated with increased risk of thrombotic events, it is not known whether there are differences in risk of serious adverse events (eg, venous thrombosis and embolism [VTE]) based on differences in PK profiles of various contraceptives.^{5,6} No epidemiologic data are yet available regarding clinical risk of VTE with use of the vaginal ring. As with all estrogen-containing contraceptives, women with contraindications to estrogen use (eg, current or past thromboembolic disorders, severe hypertension, personal history of breast cancer, smoking over age 35) should not use the vaginal ring.¹

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After the vaginal ring is inserted, serum levels of EE and ENG rise rapidly, reach maximum concentrations within 1 week, and remain constant throughout the recommended 3-week duration of ring use or longer.^{7,8} The level of ENG, which provides the contraceptive activity, has been found to remain at a sufficient level to inhibit ovulation completely for at least 4 weeks of continuous use of one vaginal ring,^{1,7,8} potentially providing an additional several days of effective protection against pregnancy by each vaginal ring.

Weight and Efficacy

A recent retrospective secondary analysis of data regarding vaginal ring users in phase III clinical trials examined the possible effect of baseline body weight on contraceptive efficacy.⁹ In the intent-to-treat ($n=3259$) population, 27 pregnancies occurred (0.83%); in the per-protocol ($n=2788$) population, 12 pregnancies (0.43%) occurred over the 1-year study period. The baseline weight range for all women in whom pregnancies occurred was 48 to 85.3 kg (106–188 pounds). The numbers of pregnancies per cycle were evenly distributed over the baseline weight deciles (range 0–4 pregnancies per decile) of this range. Among the 41 women in the study population who had baseline weights of 89.9 kg (198 pounds) or greater, no pregnancies occurred, suggesting that use of the vaginal ring is not associated with an increased pregnancy rate among heavier women.⁹

Quick Starting the Ring

Product labeling states that, for first use of the vaginal ring, it should be inserted on the first day of the woman's menses if she has not used hormonal contraception in the preceding cycle or—if she is changing from another combination hormonal method or a progestin-only OC—on any day (but no later than the day following the usual hormone-free interval) if she has been using the previous method consistently and correctly.¹ When a woman is switching from use of the levonorgestrel-releasing intrauterine system (LNG-IUS; Mirena®), vaginal ring insertion should occur on (or anytime before) the day of LNG-IUS removal; if she has been using depot medroxyprogesterone acetate (DMPA; Depo-Provera®), vaginal ring insertion should occur on (or anytime before) the day when the next injection would be due. An off-label alternative method of vaginal ring insertion is called Quick Start. Immediate initiation of vaginal ring use during the clinician visit in which it is prescribed, irrespective of the woman's menstrual cycle day, without waiting for a Sunday start, menses start, or return visit, can provide quicker onset of contraceptive protection and requires less time for method initiation counseling.¹⁰ Before implementation of this off-label approach, pregnancy should be ruled out through history and a sensitive urine pregnancy test if appropriate. Women initiating vaginal ring use through Quick Start should be counseled to use backup contraception (eg, condoms) for the first 7 days of method use and should be provided with emergency contraception (EC) to use in case of unprotected coitus or unscheduled ring removal. Most vaginal ring users in a study of Quick Start reported either no change (42.3%) or a good change (43.5%) in their bleeding patterns from baseline.¹⁰

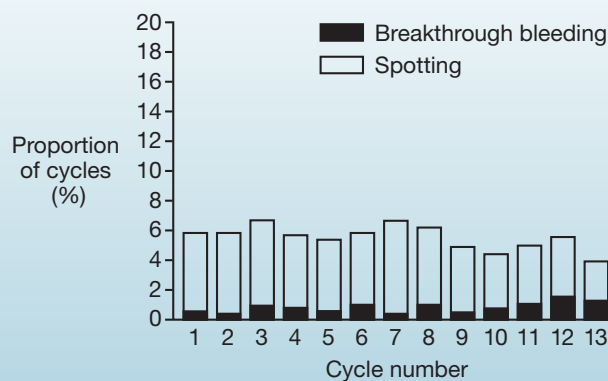
Bleeding Patterns

When the vaginal ring is removed to allow scheduled withdrawal bleeding, bleeding usually (98.5% of cycles)³ starts 2 to 3 days after the ring is removed.¹ The mean duration of withdrawal bleeding ranges from 4.5 to 5.2 days.³ In two large-scale ($N=2322$), noncomparative 1-year clinical trials, breakthrough bleeding (primarily spotting) occurred in an overall average of 5.5% of women per cycle (average 4.4% in European study, average 7.0% in North American study) (Figure).³ In studies comparing cycle control in vaginal ring users and COC users, incidences of breakthrough bleeding/spotting were lower with the vaginal ring than with the COCs.^{10–12} In a 6-cycle study ($N=264$), for example, the incidence of breakthrough bleeding/spotting with the vaginal ring was 1.1% to 5.0% per cycle compared with 5.4% to 38.8% per cycle with the COC (150 mcg LNG/30 mcg EE).¹¹ In a 1-year study ($N=716$), breakthrough bleeding/spotting occurred in 3.6% to 6.2% of vaginal ring users per cycle compared with 4.7% to 10.4% of COC (3 mg drospirenone/30 mcg EE; Yasmin®) users per cycle.¹²

Extended Use

Like users of other combination hormonal methods, vaginal ring users who wish to modify the occurrence of scheduled withdrawal bleeding may benefit from extended or continuous use, although these regimens are not indicated in labeling.¹³ In a trial of 3 extended regimens (49-day cycle, 91-day cycle, 364-day cycle; each vaginal ring worn for 21 days and replaced no later than Day 24) compared with a 28-day cycle (21 days of vaginal ring use, followed by a ring-free week) of vaginal ring use, the

Figure. Incidence of breakthrough bleeding and spotting over 13 cycles of vaginal ring use (per-protocol population*).



*Per-protocol population: n=2015; 16,912 treatment cycles.

Adapted, with permission, from Dieben TO, Roumen FJ, Apter D. Efficacy, cycle control, and user acceptability of a novel combined contraceptive vaginal ring. *Obstet Gynecol.* 2002;100:585-593.³

number of scheduled bleeding days was reduced with postponement of the ring-free week, but the number of unscheduled breakthrough bleeding/spotting days increased, compared with the conventional regimen. Of the longer regimens, the frequency of breakthrough bleeding/spotting was lowest with the 49-day cycle. Some women may prefer to tolerate breakthrough spotting if it is accompanied by a reduction in scheduled withdrawal bleeding.¹³

Acceptability

Studies have reported high levels of user acceptability and satisfaction with the vaginal ring.^{12,14-16} In a 13-cycle study of user acceptability, 96% (n=1492) of study completers reported themselves "very satisfied" or "satisfied" with the vaginal ring; 94% of study completers said they would recommend the method to others.¹⁴ Studies examining sex partner acceptability of the vaginal ring found high levels (>90%) of satisfaction (ie, "never/rarely minding partner's ring use") among men as reported by the women; more than 65% of vaginal ring users reported that their partners never or rarely felt the ring during sexual intercourse.^{14,15}

Counseling About Vaginal Ring Use

Women considering contraceptive selection should be made aware of the vaginal ring as an option for eligible candidates (eg, those without contraindications to estrogen). The convenience of using a nondaily combination hormonal contraceptive method that requires user action only twice each month should be explained. An actual vaginal ring should be shown to women so that they are familiar with its size, structure, and consistency. Counseling about the vaginal ring should focus on the convenience of its use. Most women are experienced in using medicated vaginal products or tampons and should not find ring insertion difficult. However, women who state their discomfort with the idea of vaginal insertion may be reluctant to consider vaginal ring use.¹⁷ Such women may be encouraged by learning that one assessment of vaginal ring user satisfaction found that women who had reported discomfort in touching their genitals at baseline were more likely to be highly satisfied than less satisfied with the vaginal ring after 3 months of use.¹⁶ Initial insertion of the vaginal ring in the presence of the clinician (ie, using the Quick Start approach) may also help overcome any hesitation about use of the method.¹⁶

Although it is not necessary to remove the vaginal ring from the vagina, if desired, a woman may remove it for up to 3 hours for purposes of sexual intercourse or other reasons. Clinicians should emphasize to vaginal ring users that, if the ring has been out of the vagina for more than 3 continuous hours for any reason (eg, accidental expulsion, purposeful removal), backup contraception (ie, condoms or spermicides) should be used until the vaginal ring has been used continuously for 7 days.¹ If the ring is left out of the vagina for more than 3 hours during weeks 1 and 2 of a cycle, the same

ring should be reinserted as soon as possible. During week 3 of the cycle, the old ring should be discarded; a new ring can then be inserted immediately, thus starting the next 3-week use period, or withdrawal bleeding can be allowed before a new ring is inserted (no later than 7 days from the time the previous ring was removed or expelled).¹ Emergency contraception may be used if unprotected coitus occurred while or after the ring was out of the vagina for more than 3 hours.

Women should be made aware of the importance of promptly replacing the vaginal ring after the ring-free week of each cycle; if the ring-free interval is extended beyond 1 week, ovulation could occur in some women, compromising their protection against pregnancy.^{1,18} If extension of the ring-free interval occurs, backup contraception must be used until the new ring has been used continuously for 7 days.¹

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The contraceptive efficacy of the vaginal ring does not appear to be compromised by concomitant use of tampons,¹⁹ spermicides,²⁰ or antimycotic medications for the treatment of vaginitis.²¹ Like other hormonal contraceptives, the vaginal ring does not protect against sexually transmitted infections (STIs). Use of condoms is recommended for vaginal ring users who are at risk of STIs.

In counseling women about potential use of the vaginal ring, clinicians can dispel some misperceptions about this contraceptive method by explaining the available evidence. For example, some clinicians and women believe that expulsion of the vaginal ring occurs frequently. However, a retrospective analysis of clinical trial data reported that, overall, expulsion occurred in only 0.5% of 33,462 cycles of vaginal ring use.²² The rate of expulsion decreased from 1.1% at cycle 1 to 0% at cycle 13. Nonetheless, unnoticed expulsion—especially during sexual intercourse—may occur; women should be reminded to check for the presence of the vaginal ring in such circumstances.

Some women erroneously believe that use of all hormonal contraceptives, including the vaginal ring, causes weight gain. In a 3-cycle comparison of weight change with vaginal ring or COC use, there was minimal measured change in weight with either method (mean weight gain, 3 pounds in 3 months; CI, 1.9-3.6).²³ More than 60% of participants completing the study (n=161) maintained their weight within 3 pounds or lost weight (maximum loss, 11 pounds). Study participants' self-reported weights were not correlated with measured weight changes, a finding common to many studies and one that may account for the misperception that use of hormonal contraception increases weight.²³

No adverse changes in cervical cytology, vaginal flora, or endometrial histology have been found to occur with use of the vaginal ring.^{3,24-28}

Summary

The vaginal ring is a convenient, nondaily, rapidly reversible, low estrogen-dose, combination hormonal method with high contraceptive effectiveness and good cycle control. Inserted once monthly, the vaginal ring offers appropriate candidates another effective option that should be discussed during contraceptive selection counseling.

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Questions and Answers

Andrew M. Kaunitz, MD, Ronald T. Burkman, MD, Deborah M. Smith, MD, MPH and Carolyn L. Westhoff, MD, MSc

Q. In a woman with inactive or stable mild systemic lupus erythematosus (SLE) in remission, which contraceptive methods are appropriate?

A. Andrew M. Kaunitz, MD: Effective contraception is of particular importance in women with SLE because of the high maternal, fetal, and neonatal morbidity associated with this condition.¹ In addition, combination (estrogen/progestin) hormonal contraceptives offer important potential noncontraceptive benefits to women with SLE, including possible prevention of glucocorticoid-induced osteoporosis.^{2,3} Findings from 2 large randomized trials support the safety of combination oral contraceptives (COCs) in women with inactive or stable SLE who do not have anticardiolipin antibodies.^{4,5} One of these studies⁴ also found that use of intrauterine contraception (IUC) appeared safe in this patient population. In addition to the presence of anticardiolipin antibodies, the presence of antiphospholipid antibodies or a history of nephritis or vascular disease should be considered contraindications to the use of combination hormonal methods in women with SLE.⁶ Some experts suggest that the presence of lupus anticoagulant should also be considered a contraindication to use of combination hormonal contraceptives. In women with SLE who are inappropriate candidates for estrogen-containing hormonal contraceptives, progestin-only methods and IUCs appear to offer safe alternatives.

Q. Which contraceptive methods are appropriate for women with one or more known thrombophilic risk factors (eg, factor V Leiden) but no personal history of thrombotic events?

A. Ronald T. Burkman, MD: Routine testing for thrombophilic factors is not appropriate before contraceptive selection unless a family history of thrombophilia is present. Most women with thrombophilias will not develop venous thrombosis or embolism (VTE) even with use of estrogen-containing hormonal contraception.⁷ Women with no personal history of thromboembolism often have thrombophilia testing because of a strong family history of thrombotic events; when they test positive, it is important to remember that screening tests for coagulation disorders have poor positive predictive value for clinical events and may exclude many women who could safely benefit from combination hormonal contraceptive use.⁷⁻⁹ Although the overall increased absolute risk of VTE with use of estrogen-containing contraceptives is low (3 to 5 cases per 10,000 woman-years of use,^{10,11}) women with known inherited or acquired thrombophilias should avoid estrogen-containing contraceptives to prevent further

increasing their risk of thrombosis. The World Health Organization's medical eligibility criteria for contraceptive use classifies known thrombogenic mutations as category 4, conditions that represent an unacceptable health risk if estrogen-containing contraceptives are used.¹² Use of progestin-only contraceptives or IUCs is appropriate in such women.

Q. A recent journal article suggests that COC use reduces sexual desire. What do you tell women who are concerned about this possibility, which was reported in consumer media?

A. Deborah M. Smith, MD, MPH: The article in question¹³ found that, among women with sexual dysfunction who were currently using or had previously used COCs, levels of sex hormone-binding globulin (SHBG) were elevated compared with never-users. The participants in this retrospective study were limited to women who had reported themselves to the investigating facility as experiencing sexual dysfunction, thus limiting the applicability of the findings. Moreover, the mechanisms of sexual dysfunction, including the possible role of increased SHBG levels with combination hormonal contraceptive use (which binds circulating testosterone), have not been clearly determined in controlled trials.¹⁴ Research regarding the effects of hormonal contraception is limited and findings are inconclusive. Although some studies have suggested an association between COC use and sexual dysfunction, including decreased desire,¹⁵ others have found no consistent difference in the effect on sexual desire between COC users and users of nonhormonal methods or placebo.^{16,17} Overall, the studies suggest that most women do not experience decreased libido during COC use, while some studies have reported an increase in libido during use, and some have reported no change.¹⁷ For a more comprehensive discussion, see "Hormonal Contraceptives and Libido" in *Dialogues in Contraception*[®], Volume 9, Number 2, Summer 2005.

Q. In a woman who tests positive for human papillomavirus (HPV) with cervical intraepithelial neoplasia (CIN) 1 or atypical squamous cells of unknown significance (ASCUS), will hormonal contraceptive use increase her risk of disease progression?

A. Carolyn L. Westhoff, MD, MSc: A recent, large (N=5060), 2-year, prospective, randomized trial evaluated the effect of current and former use of various hormonal contraceptives (oral contraceptives [OCs],

injectable contraceptives [depot medroxyprogesterone acetate (DMPA); Depo-Provera[®]], levonorgestrel implants [Norplant[®]], pregnancy, and parity on risk of CIN 3 among oncogenic (<CIN 2) HPV-positive women with minimally abnormal Pap smears over a 2-year period.¹⁸ OC use was not associated with progression to CIN 2 or CIN 3 compared with oncogenic HPV-positive OC never-users. Of the other contraceptive methods and other variables evaluated, only current DMPA use was associated with slightly elevated risk of CIN 2 or CIN 3 in oncogenic HPV-positive women compared with never-users. The findings of this research indicate that HPV-positive status should not restrict use of hormonal contraception.

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