Long-Acting Reversible Contraceptives

Intrauterine Devices and the Contraceptive Implant

Eve Espey, MD, MPH, and Tony Ogburn, MD

The provision of effective contraception is fundamental to the practice of women's health care. The most effective methods of reversible contraception are the so-called long-acting reversible contraceptives, intrauterine devices and implants. These methods have multiple advantages over other reversible methods. Most importantly, once in place, they do not require maintenance and their duration of action is long, ranging from 3 to 10 years. Despite the advantages of long-acting reversible contraceptive methods, they are infrequently used in the United States. Short-acting methods, specifically oral contraceptives and condoms, are by far the most commonly used reversible methods. A shift from the use of short-acting methods to long-acting reversible contraceptive methods could help reduce the high rate of unintended pregnancy in the United States. In this review of long-acting reversible contraceptive methods, we discuss the intrauterine devices and the contraceptive implant available in the United States, and we describe candidates for each method, noncontraceptive benefits, and management of complications.

(Obstet Gynecol 2011;117:705–19)
DOI: 10.1097/AOG.0b013e31820ce2f0

Long-acting reversible contraceptive is the name given to methods with long duration of action and without the need for active adherence once initiated. Long-acting reversible contraceptive methods available in the United States include two intrauterine devices (IUDs) and a contraceptive implant (Fig. 1). A less commonly used term, but more descriptive, is that of forgettable contraceptives, which are defined as those methods requiring attention no more often than every 3 years and including IUDs, implants, and sterilization.[1] In contrast to other user-dependent methods, including pills, patch, ring, condoms, and injections, long-acting reversible contraceptive methods only require intervention to discontinue. They are characterized by low failure and high continuation rates, earning them a position at the top tier of contraceptive methods, side by side with sterilization.[2]

Long-acting reversible contraceptive methods hold great promise in the United States and globally to reduce unintended pregnancy. In the United States, oral contraceptives and condoms are the most commonly used reversible contraceptive methods.[3] The effectiveness of these methods is limited by their relatively high failure and low continuation rates in typical use.[4] Many unintended pregnancies occur in women who use methods inconsistently, incorrectly or both, problems obviated with the use of long-acting reversible contraceptives (Fig. 2). In developed countries where long-acting reversible contraceptive methods comprise a larger proportion of the method mix, unintended pregnancy rates are often lower.[5] The Institute of Medicine has called for an increase in long-acting reversible contraceptive use among young women as a national priority.[6] The past decade has seen an encouraging increase in the use of IUDs in the United States; in 2002, only 2% of reproductive-aged U.S. women used an IUD compared with 5.5% in

From the Department of Obstetrics and Gynecology, University of New Mexico, Albuquerque, New Mexico.

Continuing medical education for this article is available at http://links.lww.com/AOG/A228.

Corresponding author: Eve Espey, MD, MPH, Professor, Department of Obstetrics and Gynecology, University of New Mexico, Albuquerque, NM 87131; e-mail: eespey@salud.unm.edu.

Financial Disclosure
The authors did not report any potential conflicts of interest.

ISSN: 0029-7844/11

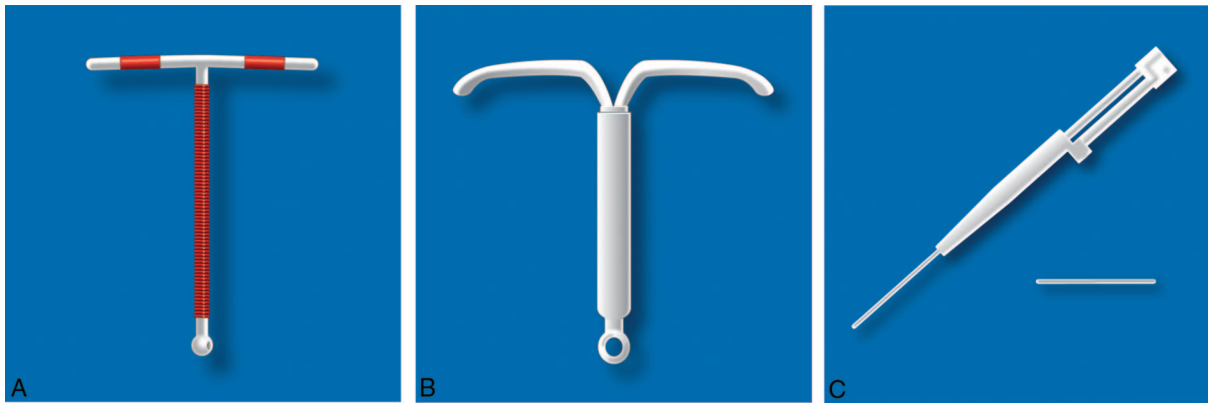

Fig. 1. Intrauterine devices and implant available in the United States. **A**. Copper intrauterine device (IUD). **B**. Levonorgestrel-releasing IUD. **C**. Etonogestrel implant. Illustration by John Yanson.

Espey. Long-Acting Reversible Contraceptives. Obstet Gynecol 2011.

2008.[3] A single-rod contraceptive implant, the etonogestrel implant, was approved by the U.S. Food and Drug Administration (FDA) in July 2006 and has been marketed in the United States since the autumn of that year. Its prevalence of use is as yet unknown.

Despite the good news about increased use of long-acting reversible contraceptive methods, the persistent and unacceptably high rate of unintended pregnancy in the United States remains a challenge,

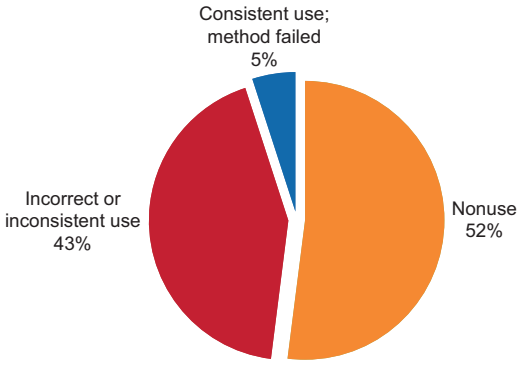

Fig. 2. Long-acting reversible contraceptive potential for preventing unintended pregnancy. The causes of unintended pregnancies by method use during month of conception. Long-acting reversible contraceptive methods could affect the 43% of women in the category of inconsistent or incorrect use. Source: Guttmacher Institute, Community health centers and family planning. Improving contraceptive use. *In Brief* 2008 Series, No. 1. New York (NY): Guttmacher; 2008. Available at: http://www.guttmacher.org/pubs/2008/05/09/ImprovingContraceptiveUse.pdf. Retrieved November 30, 2010.

Espey. Long-Acting Reversible Contraceptives. Obstet Gynecol 2011.

hovering at approximately 50% of all pregnancies for the past two decades.[7] Although many factors could help reduce unintended pregnancy, the factor that clinicians can directly affect is that of helping women improve contraceptive use. A philosophical shift—one in which unintended pregnancy is considered a public health emergency, requiring urgent and vigorous action—could prompt increased discussions of contraception at every visit, expedited appointments for women desiring contraception, efforts to further reduce barriers to contraception initiation and continuation, and, simply, to increase use of long-acting reversible contraceptive methods.

Long-Acting Reversible Contraceptive Methods

The copper IUD (Cu-T380A), the levonorgestrel intrauterine system, and the etonogestrel implant are the three long-acting reversible contraceptive methods currently marketed in the United States. The Cu-T380A is a T-shaped plastic device with 380 mm of copper wire wrapped around the stem and arms. It is FDA-approved for up to 10 years of continuous use. The levonorgestrel intrauterine system has a similarly shaped polyethylene frame medicated with a reservoir of 52 mg of levonorgestrel, of which 20 micrograms is released daily through the rate-limiting membrane. The levonorgestrel intrauterine system is approved for up to 5 years of use. The etonogestrel implant is a 4-cm-long × 2-mm-diameter single-rod device. It contains 68 mg of the progestin etonogestrel, the biologically active metabolite of desogestrel, embedded in a solid core of ethylene vinyl acetate, which is released at a rate of 60–70 micrograms/day in the first few weeks after insertion and

25–30 micrograms/day by the end of the third year of use. It is approved for up to 3 years of use and is placed using a prepackaged sterile inserter that is preloaded with the device.

Both IUDs and implants have a checkered history in the United States. After safety concerns and litigation surrounded IUDs in the 1980s, a virtual hiatus in IUD use occurred until the approval of the Cu-T380A in 1989 and the approval of the levonorgestrel intrauterine system in 2000. Much reassuring safety data have accumulated on these intrauterine methods over the past two decades. The six-rod contraceptive implant, Norplant (Wyeth Pharmaceuticals), was available in the United States from 1991 until 2002, when its manufacturer discontinued production, nominally because of problems with the supply of product components. Despite high efficacy and excellent continuation rates, difficult Norplant removals led to litigation against the manufacturer and may have been a factor contributing to its discontinuation. The current etonogestrel implant, marketed worldwide since 1998 and in the United States since 2006, is also supported by a large body of safety data.[8–10] A new version of the etonogestrel implant, with an improved inserter and a radiopaque device for easier detection, is currently undergoing study.[11]

Overall, IUDs and the contraceptive implant have many advantages and few disadvantages (Table 1). Several evidence-based clinical guidelines are available to assist clinicians in the "nuts and bolts" of long-acting reversible contraceptive use, including the identification of appropriate candidates and the management of complications or unique medical circumstances. The American College of Obstetricians and Gynecologists has published both Committee Opinions[12,13] and Practice Bulletins[14–16] addressing long-acting reversible contraceptive methods. The Society of Family Planning publishes evidence-based guidelines, available on their web site (Societyfp.org), on topics of interest or controversy in family planning, including the use of IUDs in nulliparous women. Most recently, the Centers for Disease Control and Prevention released its comprehensive U.S. medical eligibility criteria (MEC) for contraceptive use in 2010.[10] The MEC criteria are useful for decision-making about appropriate contraceptives for women with specific characteristics or medical conditions using a 4-point rating scale: Category 1 is given for a condition for which there is no restriction for the use of the contraceptive method; Category 2 is given for a condition for which the advantages of using the method generally outweigh the theoretical or proven risks; Category 3 is given for a condition for which the theoretical or proven risks usually outweigh the advantages of using the method; and Category 4 is given for a condition that represents an unacceptable health risk if the

Table 1. Comparison of Characteristics of the Copper Intrauterine Device, the Levonogestrel Intrauterine System, and the Etonogestrel Implant

	Copper	Levonorgestrel Intrauterine System	Contraceptive Implant
Pregnancy	0.2[43]	0.3[42]	0.1%[9,65,75]
U.S. Food and Drug Administration-approved duration of effectiveness	Up to 10 y	Up to 5 y	Up to 3 y
Mechanism of action	Spermicidal[85,86] Inhibition of sperm and ovum migration[85,86]	Spermicidal[85,86] Inhibition of sperm and ovum migration[85,86] Thickening of cervical mucus[85,86]	Inhibition of ovulation[87,88] Thickening of cervical mucus[87,88] Thinning of endometrium[87,88]
Onset of effectiveness	Immediate	Immediate	24–48 h[87]
Return to fertility after removal	Immediate*	Immediate*	Immediate*[89]
When to initiate	Any time during the cycle* Immediately after dilatation and curettage for abortion or spontaneous abortion Immediately postpartum	Any time during the cycle* Immediately after dilatation and curettage for abortion or spontaneous abortion Immediately postpartum	Any time during the cycle* Immediately after dilatation and curettage for abortion or spontaneous abortion Immediately postpartum
Retail cost	$440	$703	$625.04

* Ovulation returns within 10 days to 2 weeks.[90]

contraceptive method is used. Table 2 is an excerpt from the summary chart of U.S. MEC for contraceptive use in 2010, listing those conditions for which use of an IUD or implant are considered a category 3 or 4.

IUDS

Candidates for IUDs

Most women are good candidates for IUD use. A major and persistent obstacle to extending use of IUDs to more women is the application of restrictive criteria to define those women for whom the method is suitable. Parous monogamous women traditionally have been considered the only ideal candidates, whereas data support an extended spectrum of appropriate candidates. This spectrum comprises women seeking effective and long-term contraception and includes the following types of women.

Nulliparous Women

Data are reassuring that IUDs are effective, acceptable, and have excellent continuation rates in nulliparous women, although evidence is limited given the exclusion of nulliparous women from many studies.[17] Available data suggest that the IUD does not increase the risk of pelvic inflammatory disease (PID) in nulliparous women beyond the small increased risk present for all women in the first 20 days after IUD insertion.[18,19] Additionally, the IUD does not appear to cause tubal infertility.[20] Despite these reassuring studies, many clinicians continue to limit IUD use. Although the package insert for the levonorgestrel intrauterine system discourages clinicians from using the device in nulliparous women, such language was removed from the package insert for the Cu-T380A in 2005. The same data submitted to the FDA to modify the package insert for the Cu-T380A would apply to the levonorgestrel intrauterine system, but the

Table 2. Conditions for Which Intrauterine Devices and the Contraceptive Implant Are Usually Not or Never Not Recommended (Category 3 or 4)

			Levonorgestrel-Releasing Intrauterine Device		Copper Intrauterine Device	
Condition	Subcondition	Implant	Initiation	Continuation	Initiation	Continuation
Anatomic abnormalities	Distorted uterine cavity			4		4
	Other abnormalities			2		2
Breast cancer*	Current	4		4		1
	Previous (no evidence of current disease for 5 y)	3		3		1
Cervical cancer	Awaiting treatment	2	4	2	4	2
Cirrhosis	Mild (compensated)	1		1		1
	Severe (decompensated)*	3		3		1
Endometrial cancer*		1	4	2	4	2
Gestational trophoblastic disease	Decreasing or undetectable β-hCG levels	1		3		3
	Persistently elevated β-hCG levels or malignant disease*	1		4		4
Human immunodeficiency virus	High risk or human immunodeficiency-infected*	1	2	2	2	2
	Acquired immune deficiency syndrome (see drug interactions)*‡	1†	3	2†	3	2†

Category 1, No restriction (method can be used); Category 2, Advantages generally outweigh theoretical or proven risks; Category 3, Theoretical or proven risks usually outweigh the advantages; Category 4, Unacceptable health risk (method not to be used).

* Condition that exposes woman to increased risk as a result of unintended pregnancy.

† Please see the complete guidance for a clarification to this classification. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr59e0528a1.htm.

‡ Please refer to the U.S. medical eligibility criteria guidance related to drug interactions. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/rr59e0528a1.htm.

Modified from Centers for Disease Control and Prevention. Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. Available at http://www.cdc.gov/reproductivehealth/unintendedpregnancy/Docs/USMEC-Color-final.doc. Retrieved November 30, 2010.

manufacturer has not requested an update. Although the levonorgestrel intrauterine system for nulliparous women is an off-label use, nulliparous women may be considered good candidates for its use.[17] The U.S. MEC gives IUD use in nulliparous women a Category 2 rating for both the CuT380A and the levonorgestrel intrauterine system, indicating that the advantages generally outweigh the theoretical or proven risks.

Clinicians and patients may have concerns that IUD insertion may be more painful or difficult in nulliparous women. Although nulliparous women may experience more pain, overall pain scores for IUD insertion are low for both nulliparous and multiparous women,[21] and insertion can be approached similarly for both. The few studies that have examined the use of preinsertion misoprostol do not consistently show differences in ease of insertion but do confirm that insertion is successful in the majority of nulliparous women whether or not misoprostol is used.[22,23]

Adolescent Women

Adolescent pregnancy is a major public health problem. Rates are high, the majority of adolescent pregnancies are unintended, and many end in abortion.[7] For adolescents who do not choose abortion, the effect of young motherhood may be profound. The typical adolescent pattern of episodic, sporadic sexual activity puts teenagers at particularly high risk for inconsistent contraceptive usage and discontinuation of short-term methods. Increased use of long-acting reversible contraceptive methods by adolescents may assist in decreasing rates of unintended pregnancy. Adolescents are also at higher risk for sexually transmitted disease and should be counseled about using both a highly effective contraceptive method and condoms.

Although less evidence is available regarding IUD use by adolescents, the available evidence is reassuring[23] and the stakes are high, particularly for those teenagers who already have had a child and have a significant risk of rapid repeat pregnancy. In a recent study of attitudes and beliefs of teenagers at a family planning clinic appointment, 55% had not heard of IUDs.[24] Those who had heard of IUDs from a health care provider were almost three times as likely to be interested in using it. These findings reinforce the idea that physicians may create demand for IUDs simply by including it in routine contraceptive counseling. The U.S. MEC gives IUD use in adolescent women a Category 2 rating, finding that the advantages generally outweigh the theoretical or proven risks.

Use in Women Immediately After Uterine Aspiration for Miscarriage or Abortion

Contraceptive counseling and method initiation are often neglected for women experiencing a miscarriage, even though half of those pregnancies are unintended. In addition, approximately half of women who have had an elective abortion have had a previous abortion.[25] No-show rates for follow-up visits are high and can lead to a missed opportunity for providing effective contraception. Immediate postaspiration IUD insertion has several advantages, including patient motivation and convenience, and is supported by evidence.[26] Women who undergo immediate insertion of an IUD after a first trimester uterine aspiration are no more likely to expel the IUD or experience other complications than women with interval insertion.[27] In a prospective comparative study, women who received an IUD immediately after abortion were three times less likely to have a repeat abortion within the next 3 years than women who received another contraceptive method.[28] Studies in other countries show similar reductions in repeat abortion.[29,30] The U.S. MEC gives immediate IUD insertion after first trimester uterine aspiration a category 1 rating, indicating that there is no restriction for IUD use in this clinical situation.

Women Immediately Postpartum

Considerable evidence supports the practice of IUD insertion within 10 minutes of delivery of the placenta.[31] Although uncommon in the United States, immediate postplacental delivery IUD insertion is routine in several countries, including Mexico and Egypt.[32] The IUD may be placed manually, with a ring forceps or with the standard inserter. Ultrasound guidance may be helpful, particularly during the learning phase, in ensuring fundal placement of the IUD. Immediate postplacental delivery insertion has several benefits similar to those of postaspiration IUD insertion. Motivation is often high and the hospital setting is convenient for both patient and provider. Although the IUD expulsion rate for postplacental delivery insertion may be up to twice as high as that with interval insertion, the benefits of immediate-acting contraception may outweigh the disadvantage of an increased expulsion rate.[31] No-show rates for postpartum visits may be high, patients may become pregnant before the visit, and insurance coverage may be lost by 6 weeks, underlining the advantage of immediate provision of contraception.[33]

As with all hormonal methods, questions arise about the compatibility of breastfeeding and use of the

levonorgestrel intrauterine system. No trials have examined this scenario. The U.S. MEC gives a Category 1 rating to immediate postpartum insertion of a Cu-T380A, indicating no restriction on its use, and a Category 2 rating for the levonorgestrel intrauterine system, indicating that the advantages generally outweigh the theoretical or proven risks. Those involved in preparing the U.S. MEC have identified the effect of hormonal contraceptives on lactation as a high priority area for additional research.[34]

Women With Coexisting Medical Problems

IUDs are often the ideal contraceptive choice for women with medical problems, particularly those for whom estrogen is contraindicated. The U.S. MEC gives IUDs a rate of 1 or 2 points for a variety of conditions, including smoking, obesity, seizure disorders, and gallbladder disease.[10,15]

Women Seeking Emergency Contraception

The copper IUD is underutilized as a method for emergency contraception, despite its high effectiveness. A recent prospective cohort study documented no pregnancies in 1,963 women with insertion of a copper IUD within 120 hours of unprotected intercourse. Continuation rates for long-term contraception were high, at 94 per 100 woman-years, among this sample of Chinese women.[35]

Clinicians could have a major role in increasing the use of IUDs, restrictive criteria remain the norm. Although IUD use has increased over the past several years, a survey of obstetrician-gynecologists found that 20% of respondents had not inserted an IUD in the past year; however, of those who had, most (79%) reported inserting 10 or fewer.[36] In a survey of family planning clinicians in California, 40% did not offer IUDs to contraceptive patients.[37] Although many clinicians cite lack of patient demand as a reason for not providing more IUDs, a recent study demonstrated a large uptake of long-acting reversible contraceptive methods when such methods were included in counseling and made available without financial obstacles. In a sample of 2,500 women, 67% chose either an IUD (56%) or the single-rod contraceptive implant (11%).[38]

Noncontraceptive Benefits of IUDs

Noncontraceptive benefits of IUDs are becoming increasingly well-known, particularly those accruing to the levonorgestrel intrauterine system. Some say that with a speculum and a levonorgestrel intrauterine system, you can run a gynecology clinic. The levonorgestrel intrauterine system is FDA-approved for the indications of contraception and heavy bleeding, and evidence for its usefulness in other gynecologic conditions, such as leiomyomas, adenomyosis, endometriosis, and as the progestin component of hormone therapy, is accumulating. Additionally, the Cu-T380A has been shown to have a protective effect against endometrial cancer,[39] and preliminary case series data suggest that the levonorgestrel intrauterine system may be effective in treating endometrial hyperplasia.[40] Several reviews and meta-analyses outline the noncontraceptive benefits of IUDs.[39,41,16]

Heavy Menstrual Bleeding

Strong evidence confirms the utility of the levonorgestrel intrauterine system for treatment of heavy vaginal bleeding. In levonorgestrel intrauterine system users with no symptoms of menorrhagia, prospective studies have documented an increase in hemoglobin ranging from 0.5 to 1.6 g/dL, as well as a decrease in dysmenorrhea.[42] In women who have menorrhagia, use of a levonorgestrel intrauterine system is often therapeutic. Results pooled from numerous heterogeneous prospective studies show a decrease in measured menstrual blood loss estimated at 74% to 97%, and the number of bleeding days was reduced by 50%.[41] Satisfaction rates with the levonorgestrel intrauterine system were high in these studies (72%–94%), and overall continuation rates were excellent (65%–88%). A Cochrane review concludes that use of the levonorgestrel intrauterine system is associated with high patient satisfaction and willingness to continue the method, but with more progestogenic side effects than surgery.[43] A single, small, randomized trial (N=39) compared the levonorgestrel intrauterine system with combined oral contraceptive pills, the most common first-line therapy for heavy bleeding, and found reductions in bleeding with both but a greater reduction in the levonorgestrel intrauterine system group.[44] Meta-analyses suggest that 50%–60% of women may avoid hysterectomy with use of an levonorgestrel intrauterine system. Although some ultimately undergo hysterectomy when the levonorgestrel intrauterine system is not successful in controlling bleeding, a trial of the levonorgestrel intrauterine system remains more cost-effective than immediate surgery.[45] The levonorgestrel intrauterine system compares favorably with surgery in improving quality of life in women with heavy bleeding.[43] Surgery, particularly hysterectomy, is more effective at reducing bleeding but is associated with more serious complications.[46]

Uterine Leiomyomas

Several small studies suggest that the levonorgestrel intrauterine system may improve menorrhagia in women with leiomyomas. A systematic review of 11 trials in which women with leiomyomas used the levonorgestrel intrauterine system found that menstrual bleeding decreased and that hemoglobin and hematocrit increased among continuing users.[47] The evidence for these findings is fair, based on the noncomparative study design and small number of women studied. In women with menorrhagia and leiomyomas that do not distort the uterine cavity, particularly those who wish to avoid surgery, clinicians may recommend a trial of the levonorgestrel intrauterine system as an alternative to ablation or hysterectomy. Users of either the levonorgestrel intrauterine system or the Cu-T380A who subsequently have leiomyomas diagnosed may continue to use the IUD. The U.S. MEC gives a 2-point rating for both levonorgestrel intrauterine system and Cu-T380A IUD use in women with uterine leiomyomas, indicating that the advantages generally outweigh theoretical or proven risks.

Endometriosis

Two randomized controlled trials and three observational studies with small numbers of women have examined the effect of the levonorgestrel intrauterine system on pain in women with varying degrees of endometriosis.[41] Results suggest reductions in dysmenorrhea and pelvic pain, pointing to the need for larger studies. Although the data are scant, women who desire contraception and have pain from endometriosis may be reasonable candidates for a trial of the levonorgestrel intrauterine system.

Progestin Component of Hormone Therapy

A number of randomized controlled trials, as well as cohort and observational studies, have examined the use of the levonorgestrel intrauterine system as the progestin component of combined hormone therapy and its utility in protecting the endometrium from hyperplasia during use of exogenous estrogen.[41] The levonorgestrel intrauterine system is protective against uterine cancer in the setting of hormone therapy. In these heterogeneous studies, endometrial suppression was confirmed by histology, ultrasound measurement of the endometrium, or both. Additionally, use of the levonorgestrel intrauterine system reduces number of bleeding and spotting days compared with oral progestin. In the United Kingdom, the levonorgestrel intrauterine system is licensed to provide endometrial protection for women using estrogen therapy.

IUD Complications

Perforation of the Uterus

The rate of uterine perforation at the time of IUD insertion is estimated at 0.8 to 2.2 per 1,000 IUD insertions.[42] Although perforations of the IUD into the abdominal cavity may be diagnosed soon after placement, they also can be diagnosed years later, for example, as an incidental finding on an abdominal X-ray. Most commonly, perforations are initially suspected when the strings are missing on speculum or bimanual examination. In reviews of IUD perforations from national registries, severe pain at insertion and unexpected pregnancy were both associated with IUD perforation.[48] Missing strings should prompt a search for the location of the IUD. If ultrasonography fails to reveal the IUD, then an abdominal X-ray should be obtained to exclude IUD expulsion and confirm a diagnosis of IUD perforation. The levonorgestrel intrauterine system may be more difficult to visualize with ultrasonography than the Cu-T380A. Placement of a sound in the uterus during the X-ray may facilitate localization of the IUD.

Once the IUD is known to be in the abdomen, it should be removed. Although some investigators consider removal optional,[49] the World Health Organization and other authorities recommend it.[2] Concerns with retained intra-abdominal IUDs include adhesion formation, infection, rare cases of injury to intra-abdominal organs, and patient anxiety. The majority of intra-abdominal IUDs may be removed laparoscopically and are often found encased in omentum or in the pouch of Douglas. A careful search with the laparoscope will often reveal a tell-tale string or a small amount of exposed plastic that leads the operator to localize the device (Fig. 3). In challenging cases in which the IUD cannot be visualized, intraoperative fluoroscopy or X-ray may be helpful. In a recent series of 10 intra-abdominal IUDs, eight were removed laparoscopically and two required laparotomy.[50] Although perforation is rare, it is often viewed as a major complication and may dissuade providers from offering IUD insertion. The number of unintended pregnancies and abortions prevented by use of IUDs outweighs the disadvantage of the unusual IUD perforation.

IUD and Pregnancy

Despite the high efficacy of IUDs, clinicians who routinely place IUDs may face the challenge of the

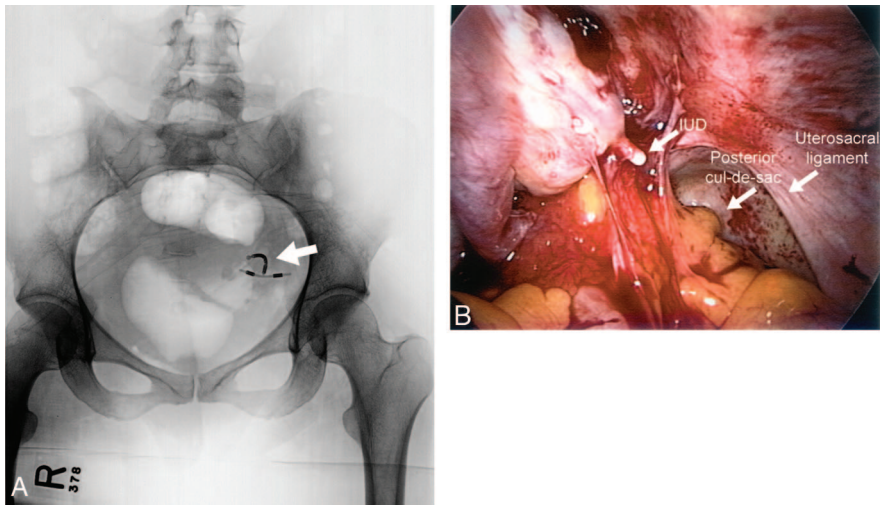

Fig. 3. A missing intrauterine device (IUD) identified by abdominal X-ray **(A)** and laparoscopy **(B)** was located in the cul-de-sac. **A.** X-ray showing IUD. **B.** Laparoscopic view of the IUD. Posterior cul-de-sac and uterosacral ligament are also shown. Photographs courtesy of Dr. Stephanie Teal.

Espey. Long-Acting Reversible Contraceptives. Obstet Gynecol 2011.

woman who becomes pregnant with an IUD in place. Women should be counseled to seek medical attention immediately if they suspect they have become pregnant while using the IUD, given the risk of ectopic pregnancy. Although it is a misconception that IUDs increase the risk of ectopic pregnancy, it is true that the small percentage of women who become pregnant while using an IUD are more likely to have an ectopic pregnancy.[51,52] In a woman using an IUD with a positive pregnancy test result, the clinician's first responsibility is to determine whether the pregnancy is intrauterine. Women with an ectopic pregnancy may be treated medically or surgically, as indicated. Although the IUD, if appropriately placed, need not be removed and may continue to provide contraception, many women in this situation request IUD removal, finding it difficult to trust a method that was unsuccessful.

Women with a viable intrauterine pregnancy may desire induced abortion. The IUD should be removed, and medical or surgical abortion may be offered depending on the individual clinical scenario. In women who desire to continue the pregnancy, removal of the IUD when strings are visible is recommended by both the FDA and World Health Organization,[53,54] although these recommendations are based on scant data. Complications associated with a retained IUD in pregnancy include septic abortion and preterm labor, whereas complications associated with removing the IUD include miscarriage.[55]

PID

Despite the small increased risk of PID in the first 20 days after IUD insertion, PID remains unusual at any time period.[19] Optimal treatment for the woman in whom PID develops with an IUD in place is unclear. Limited evidence suggests that the degree of inflammation seen in women diagnosed with PID, either with or without an IUD in place, is similar. A small study suggests no differences in outcomes in women diagnosed with PID, treated with antibiotics, and randomized to IUD retention compared with removal.[19] Decisions about IUD removal compared with retention in this setting are often based on the severity of the illness, the response to antibiotic therapy, and the woman's parity.

IUD Insertion Protocol

Cumbersome IUD insertion protocols requiring several visits can pose a roadblock to women seeking an IUD. Consistent with the approach of reducing barriers to contraception and initiating the method promptly once chosen, an IUD insertion may be accomplished during a single visit. Assuming pregnancy may be reasonably excluded, an IUD may be placed on any day of the woman's cycle. If difficulty is encountered during insertion, an oral narcotic or paracervical block may be administered. Women at high risk for sexually transmitted diseases should be screened according to evidence-based guidelines.[56,57] Such screening may be performed at the time of IUD insertion, and insertion need not be delayed until results are obtained. If the *Chlamydia* or gonorrhea test results are positive, then the woman may be treated for the sexually transmitted disease per standard protocol. There is no evidence that the IUD should be removed before or during treatment.[58,59]

CONTRACEPTIVE IMPLANT

Candidates for the Contraceptive Implant

The etonogestrel implant is an appropriate contraceptive option for most women, with a U.S. MEC Category 1 for women of all ages and parity. Contraindications are rare (Table 2).

Adolescent Women

The implant may be a particularly attractive option for adolescents. Past experience with Norplant suggests that implants are an acceptable and effective contraceptive for many teenagers. A study of postpartum teenagers reported that implant users were more likely to continue the method at 2 years than either oral contraceptive or depot medroxyprogesterone acetate (DMPA) users.[60] The average interval between the index pregnancy and a repeat pregnancy was 24.8 months for implant users compared with 18.1 months for oral contraceptive or DMPA users. The study underscored the need for prompt, effective contraception for adolescents, because 47% of teenage mothers in the study resumed intercourse within 6 weeks of delivery. In another study of adolescent mothers involved in a comprehensive pregnancy prevention program, the only factor correlated with an increased interval of time to repeat pregnancy was initiation of a contraceptive implant.[61]

Since the FDA placed a black box warning on DMPA because of its effects on bone mineral density, concerns have arisen about the effect of other progestin-only methods on bone mineral density, especially in young women. Bone mineral density is only a surrogate marker, and conclusions about actual fracture risk should not be drawn based on the effect of contraceptives on bone mineral density. However, it is reassuring that an examination of bone mineral density in users of the implant compared with users of a copper IUD demonstrated no differences in bone mineral density of the lumbar spine, the proximal femur, or the distal radius.[62] In addition, estradiol levels were similar in both groups. The U.S. MEC gives use of the implant a category 1 rating for use in adolescents, indicating no restrictions on its use.

Obese Women

Concerns have been raised that overweight and obesity may have a negative impact on the effectiveness of hormonal contraceptives. Little evidence is available to guide decision-making about use of the etonogestrel implant in obese women because most trials have excluded women weighing more than 130% of ideal body weight.[9,63] In a study that included women of all weights, 19.4% were defined by body mass index as overweight and 8.9% were obese. No pregnancies occurred in overweight or obese women using the implant.[64] In a postmarketing analysis, the few reported pregnancies were equally distributed across all weight categories.[65] The typical use effectiveness of the implant is so high that even if pregnancy rates in obese women were two-times to three-times higher than those in normal-weight women, the implant would remain highly effective. A study is currently registered with ClinicalTrials.gov investigating the pharmacokinetics of the implant in obese women. Lacking further research, the implant should be offered to obese women with appropriate counseling about the lack of definitive data proving effectiveness.

Postpartum and Breastfeeding Women

Insertion of the implant before hospital discharge has the same advantages as immediate postpartum IUD insertion. A recent study of postpartum women using the implant reported no deleterious effects on measures, including blood pressure, blood count, lipid profile, and inflammatory markers.[66] The U.S. MEC gives the implant a category 1 rating for postpartum women who are not breastfeeding. In breastfeeding women, limited data indicate that use of the implant does not affect breastfeeding outcomes. A study of lactating women randomized to the implant compared with a copper IUD, both initiated at least 4 weeks postpartum, found no differences in milk composition or quantity.[67] The same study patients and their infants were followed-up for up to 3 years and no differences were noted in the duration of breastfeeding, infant weight and body length, biparietal diameter, or psychomotor development.[68] In another study, exclusively breastfeeding women were randomized to implant insertion or DMPA, both administered at 24–48 hours postpartum. They were followed-up for up to 12 weeks and no differences were found in breastfeeding continuation between the two groups.[66] The U.S. MEC gives a category 2 rating to use of the implant by breastfeeding women.

Factors that may influence immediate compared with delayed implant insertion include insurance coverage and access to care with a provider trained to insert the implant.

Noncontraceptive Benefits

The contraceptive implant is approved by the FDA only for use as a contraceptive. However, as with

other hormonal contraceptives, noncontraceptive benefits add to the appeal of the method. Hormonal methods such as GnRh agonists, DPMA, and Norplant have been successfully used to treat pelvic pain syndromes. Current studies, although limited in number, are encouraging that the etonogestrel implant may provide another option for treatment of pain syndromes. In a study of 315 patients, rates of dysmenorrhea decreased from 59% at baseline to 21% with treatment.[69] Of the 187 patients with dysmenorrhea at baseline, 81% reported improvement and only 10% reported an increase in symptoms.

A pilot study comparing the etonogestrel implant to DMPA in women with laparoscopically proven endometriosis reported that both methods were associated with decreased pain scores. In the etonogestrel implant group, pain intensity scores decreased by 68% compared with 53% in the DMPA group.[70] A case series of five women with severe pain from endometriosis reported that four of the five had excellent relief of symptoms with the implant.[71] A randomized trial of 23 women with pelvic pain and pelvic congestion syndrome compared treatment with the etonogestrel implant to no treatment. Women with the implant had significantly lower pain scores at 1 year, decreased severity of dysmenorrhea, less monthly blood loss, and fewer days of pain than untreated controls.[72]

Insertion and Removal

Providers must complete a 3-hour, FDA-mandated training session before beginning implant insertions. The training session includes an overview of the method as well as hands-on training with a simulated arm and placebo devices. Training must be coordinated by a representative of the company distributing the implant. Since 2006, the company has changed owners twice, leading to disruptions in the availability of training.

Information on training sessions is available at http://www.implanon-usa.com. The training requirements are cumbersome but aim to encourage appropriate counseling and prevent deep insertions that can make removals difficult.

Insertion and removal of the implant are simple procedures with few complications.[73] A study of 330 patients at 16 U.S. sites reported an average insertion time of less than 1 minute and removal time of 3.6 minutes.[74] In a summary of international trials, 1% of women experienced insertion complications, none of which was major.[9] Complications included hematoma and slight bleeding at the insertion site. In the same summary, 1.7% of women experienced removal complications and none was major.[9] Removal complications were most commonly associated with fibrous scarring or deep location of the implant. Wrapping the upper arm with compressive gauze for 24 hours may limit the minor common side effect of bruising.

Nonpalpable Implants

The most likely cause of pregnancy in implant users is noninsertion of the device. Although contraceptive trials showed no pregnancies in implant users, postmarketing analysis of actual implant performance documented a pregnancy rate of approximately 1 per 1,000 implants.[65,75] The most common reason for pregnancy was noninsertion of the implant:[65] although the woman had undergone the insertion procedure, either no implant or a placebo implant was placed. Noninsertion was confirmed by the absence of detectable etonogestrel levels and accounted for 50.3% of reported pregnancies. Before insertion, the implant should be visualized in the inserter and care should be taken to hold the inserter in an upright position once the needle guard is removed and before placing the implant in the arm. Holding the inserter upright prevents the implant from inadvertently falling out. The implant should be palpated in its position under the skin of the arm both by the woman and by the clinician immediately after insertion. If the implant is not palpable, further evaluation, typically ultrasonography, should be undertaken to ascertain whether and where it was actually inserted.

The device must be palpated before initiating an attempt at removal. Most nonpalpable devices are the result of deep insertion; migration of the implant from the site of initial insertion may occur with deep insertion. Localization of a nonpalpable implant is approached with ultrasonography, using a 10–14 MHz transducer. Transducers typically used in obstetrics are only 3.5–5.0 MHz and do not consistently provide an adequate image.[76] Providers should relay the clinical history of deep implantation to the consulting radiologist and ensure that the radiologist has the appropriate equipment and expertise to locate nonpalpable implants. In the event that palpation or ultrasonography does not localize the implant, magnetic resonance imaging may be helpful. The currently available implant is not radio-opaque and will not be seen on X-ray or computed tomography scanning. If imaging fails to localize the implant, then etonogestrel levels should be obtained to verify that

the implant is in the woman's body. Only the manufacturer can obtain an etonogestrel level. Consultation with the manufacturer is recommended to help ascertain if a woman is an appropriate candidate for an etonogestrel level and how to obtain and run the sample (http://www.implanon-usa.com).

Removal of deep implants in the radiology suite has been accomplished with a sterile set-up and the use of lidocaine as an anesthetic. The ultrasonographer or radiologist locates the implant with an ultrasound transducer wrapped in a sterile cover; it may be helpful to mark the site with a sterile pen to identify the appropriate location for the incision. Ultrasonography can identify the hemostat and guide it to the implant. After removal and application of a steri-strip, a bandage may limit bruising of the arm. Deeply placed implants should be removed by providers familiar with the anatomy of the upper arm.

Side Effects of the Contraceptive Implant

The most common side effect of the etonogestrel implant is unpredictable bleeding. An integrated analysis of 11 international trials including 942 women and 24,679 cycles reported that 11.3% of patients discontinued the etonogestrel implant prematurely because of bleeding abnormalities.[8] On average, the number of days of bleeding per 90-day reference period was 17.5. Infrequent bleeding (33.6%) or amenorrhea (22.6%) characterized more than one-half of all 90-day reference periods, whereas approximately one-quarter of the women reported prolonged (16.9%) or frequent (6.1%) bleeding. Patients with a more favorable bleeding pattern in the first 90 days after insertion tended to continue with a favorable pattern throughout the entire duration of use. More than half of those patients with an initial unfavorable pattern experienced an improved pattern over time. Overall, the number of bleeding days in implant users was similar to the number of bleeding days in a woman's natural cycle, but the pattern of bleeding was less predictable.

A study of 1,183 women reported an unfavorable bleeding pattern in almost one-third of women. Approximately 15% experienced prolonged bleeding and 16% experienced menometrorrhagia. Bleeding was the most common reason for implant removal.[77] Thorough counseling of patients before placement of the etonogestrel implant may decrease removal because of bleeding.

If an implant user presents with bleeding irregularities, she may be offered several options. Reassurance that more than half of patients with unfavorable bleeding patterns in the first 90 days of use will experience an improved pattern within the next 3–6 months may influence women to continue the implant. Alternatively, women may achieve at least temporarily improved bleeding patterns when treated with 1–3 months of continuous combination oral contraceptives. Although the improvement may occur simply with the passage of time and may not be attributable to the combination oral contraceptives, the end result may be continuation of the implant. A study of implant users who experienced an acute bleeding episode randomized women to various combinations of mifepristone, doxycycline, and ethinyl estradiol compared with placebo. The study found that mifepristone combined with either doxycycline or ethinyl estradiol was more effective than placebo in terminating an acute bleeding episode but did not improve subsequent bleeding patterns.[78] No clearly effective treatments have been identified to reduce irregular bleeding in women using progestin-only contraceptives.[79]

Other adverse events reported in trials of the implant included headache (15.3%), weight gain (11.8%), changes in acne (11.4%), breast pain (10.2%), and emotional lability (5.7%).[8] Because the studies were not randomized controlled trials, no cause-and-effect relationship has been established between the reported adverse effects and the implant. Overall, only 13.9% of patients discontinued the implant because of perceived adverse events other than irregular bleeding. The most common reasons for discontinuation were emotional lability (2.3%), weight increase (2.3%), acne (1.3%), headache (1.6%), and depression (1.0%).

In small short-term studies, the etonogestrel implant has no adverse effects on lipid metabolism and liver function. A case-control study of 18 women followed-up for 12 weeks found decreases in high-density lipoprotein, low-density lipoprotein, and cholesterol.[80] A comparison of the etonogestrel implant and Norplant reported increases in bilirubin with both methods, but levels remained within the normal range.[81] Another study found no changes in multiple parameters of liver function.[69]

Contraceptive Implant Insertion Protocol

As with IUDs, cumbersome insertion protocols can present barriers to etonogestrel implant placement. In most cases, the implant can be placed at a single visit when pregnancy can be reasonably excluded. Preventive services such as sexually transmitted disease screening and cervical cytology should be encouraged in appropriate patients but are not a prerequisite

for implant insertion. There is no requirement for a pelvic examination before placement of the etonogestrel implant.

Cost-Effectiveness of Long-Acting Reversible Contraceptive Methods

Studies from the United States and Europe consistently show that long-acting reversible contraceptive methods are the most cost-effective contraceptives after approximately 2 to 3 years of use.[82,83] A factor contributing to low uptake of long-acting reversible contraceptive may be the significant up-front cost associated with these methods. The cost of the devices varies depending on negotiated rates with different payers, but the current national retail price is approximately $700 for the levonorgestrel intrauterine system device alone (Table 2). In addition to the cost of the device, costs for the office visit and insertion procedure add to overall charges. Practices may be hesitant to stock the devices because of the high cost, but waiting to order a long-acting reversible contraceptive device until a patient chooses it represents another barrier and eliminates the convenience of same-day insertion. Some payers do not cover all long-acting reversible contraceptive methods and even with insurance coverage, high copays may deter patients from choosing these methods.

CONCLUSION

Although the determinants of unintended pregnancy are complex and multifactorial, the promotion of long-acting reversible contraceptive methods should be the cornerstone of a strategy to reduce such pregnancies, both in the United States and globally. The three long-acting reversible contraceptive methods available in the United States–the Cu-T380A, the levonorgestrel intrauterine system, and the contraceptive implant–are the most effective with typical use at preventing pregnancy, the most cost-effective, and are associated with the highest levels of satisfaction and continuation of all reversible methods. Traditionally, contraception counseling has included all methods presented in a neutral fashion. However, given the tremendous advantages of long-acting reversible contraceptives compared with other reversible methods, it is time to consider these methods as first-line and to counsel women and provide these methods accordingly. Women should be clearly and unequivocally informed that long-acting reversible contraceptives are the best contraceptive choice for most women.

REFERENCES

1. Grimes DA. Forgettable contraception. Contraception 2009; 80(6):497–9.
2. World Health Organization. Mechanism of action, safety and efficacy of intrauterine devices. Technical report series #753. Geneva: WHO; 1987.
3. Mosher WD, Jones J. Use of contraception in the United States: 1982–2008, Vital Health Stat 23 2010;1–44.
4. Trussell J. Contraceptive failure in the United States. Contraception 2004;70:89–96.
5. Trussell J, Wynn LL. Reducing unintended pregnancy in the United States. Contraception 2008;771:1–5.
6. Institute of Medicine. Initial national priorities for comparative effectiveness research. Washington (DC): The National Academies Press; 2009.
7. Finer LB, Henshaw SK. Disparities in rates of unintended pregnancy in the United States, 1994 and 2001. Perspect Sex Reprod Health 2006;38:90–6.
8. Mansour D, Korver T, Marintcheva-Petrova M, Fraser I. The effects of Implanon on menstrual bleeding patterns. Eur J Contraception Reprod Healthcare 2008;13(S1):13–28.
9. Darney P, Patel A, Rosen K, Shapiro LS, Kaunitz AM. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. Fertil Steril 2009; 91:1646–53.
10. Centers for Disease Control and Prevention. U.S. medical eligibility criteria for contraceptive use, 2010. MMWR Morb Mortal Wkly Rep 2010;59:52–63.
11. Mansour D, Mommers E, Teede H, Sollie-Eriksen B, Graesslin O, Ahrendt H, et al. Clinician satisfaction and insertion characteristics of a new applicator to insert radiopaque Implanon: an open-label, noncontrolled, multicenter trial. Contraception 2010;82:243–9.
12. Increasing use of contraceptive implants and intrauterine devices to reduce unintended pregnancy. ACOG Committee Opinion No. 450. American College of Obstetricians and Gynecologists. Available at: http://www.acog.org/publications/committee_opinions/co450.cfm. Retrieved August 10, 2010.
13. Intrauterine Device and Adolescents. ACOG Committee Opinion No. 392. American College of Obstetricians and Gynecologists. Available at: http://www.acog.org/publications/committee_opinions/co392.cfm. Retrieved August 10, 2010.
14. Intrauterine device. ACOG Practice Bulletin No. 59. American College of Obstetricians and Gynecologists. Available at: http://www.acog.org/publications/educational_bulletins/pb059.cfm. Retrieved August 10, 2010.
15. Use of hormonal contraception in women with coexisting medical conditions. ACOG Practice Bulletin No. 73. American College of Obstetricians and Gynecologists. Available at: http://www.acog.org/publications/educational_bulletins/pb073.cfm. Retrieved August 10, 2010.
16. Noncontraceptive uses of hormonal contraceptives. ACOG Practice Bulletin No. 110. American College of Obstetricians and Gynecologists. Available at: http://www.acog.org/publications/educational_bulletins/pb110.cfm. Retrieved August 10, 2010.
17. Lyus R, Lohr P, Prage S, Board of the Society of Family Planning. Use of the Mirena LNG-IUS and Paragard CuT380A intrauterine devices in nulliparous women. Contraception 2010;81:367–71.
18. Farley TM, Rosenberg MJ, Rowe PJ, Chen JH, Meirik O. Intrauterine devices and pelvic inflammatory disease: an international perspective. Lancet 1992;339:785–8.
19. Grimes DA. Intrauterine device and upper-genital-tract infection. Lancet 2000;16:356:1013–9.

20. Hubacher D, Lara-Ricalde R, Taylor DJ, Guerra-Infante F, Guzmán-Rodríguez R R. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. N Engl J Med 2001;345:561–7.

21. Hubacher D, Reyes V, Lillo S, Zepeda A, Chen PL, Croxatto H. Pain from copper intrauterine device insertion: randomized trial of prophylactic ibuprofen. Am J Obstet Gynecol 2006; 195:1272–7.

22. Sääv I, Aronsson A, Marions L, Stephansson O, Gemzell-Danielsson K. Cervical priming with sublingual misoprostol prior to insertion of an intrauterine device in nulliparous women: a randomized controlled trial. Hum Reprod 2007;22: 2647–52.

23. Allen RH, Bartz D, Grimes DA, Hubacher D, O'Brien P. Interventions for pain with intrauterine device insertion. Combination oral contraceptive. The Cochrane Database of Systemaatic Reviews 2009, Issue 3. Art. No.: CD007373.

24. Fleming KL, Sokoloff A, Raine TR. Attitudes and beliefs about the intrauterine device among teenagers and young women. Contraception 2010;82:178–82.

25. Gamble SB, Strauss LT, Parker WY, Cook DA, Zane SB, Hamdan S. Abortion surveillance–United States, 2005. MMWR Morb Mortal Wkly Rep 2008;57:1–32.

26. Grimes DA, Lopez LM, Schulz KF, Stanwood NL. Immediate postabortal insertion of intrauterine devices. Combination oral contraceptives. The Cochrane. Database of Systematic Reviews 2010, Issue 6. Art. No.: CD001777.

27. Creinin MD, Bednarek PH, Reeves MF, Cwiak CA, Espey E. Incomplete and failed abortion following immediate or delayed postaspiration IUD insertion. Contraception 2009;80: 203.

28. Goodman S, Hendlish SK, Reeves MF, Foster-Rosales A. Impact of immediate postabortal insertion of intrauterine contraception on repeat abortion. Contraception, 2008;78: 143–8.

29. Heikinheimo O, Gissler M, Suhonen S. Age, parity, history of abortion and contraceptive choices affect the risk of repeat abortion. Contraception 2008;78:149–54.

30. Roberts H, Silva M, Xu S. Post abortion contraception and its effect on repeat abortions in Auckland, New Zealand. Contraception 2010;82:260–5.

31. Grimes DA, Lopez LM, Schulz KF, Van Vliet HAAM, Stanwood NL. Immediate post-partum insertion of intrauterine devices. Combination oral contraceptives. The Cochrane Database of Systematic Reviews 2010, Issue 5. Art. No.: CD003036.

32. D'Arcangues C. Worldwide use of intrauterine devices for contraception. Contraception 2007;75:82–7.

33. Ogburn JA, Espey E, Stonehocker J. Barriers to intrauterine device insertion in postpartum women. Contraception 2005; 72:426–9.

34. Folger SG, Curtis KM, Tepper NK, Gaffield ME, Marchbanks PA. Guidance on medical eligibility criteria for contraceptive use: identification of research gaps. Contraception 2010;82: 113–8.

35. Wu S, Godfrey EM, Wojdyla D, Dong J, Cong J, Wang C, et al. Copper T380A intrauterine device for emergency contraception: a prospective, multicentre, cohort clinical trial. BJOG 2010;117:1205–10.

36. Stanwood NL, Garrett JM, Konrad TR. Obstetrician-gynecologists and the intrauterine device: a survey of attitudes and practice. Obstet Gynecol 2002;99:275–80.

37. Harper CC, Blum M, de Bocanegra HT, Darney PD, Speidel JJ, Policar M, et al. Challenges in translating evidence to practice: the provision of intrauterine contraception. Obstet Gynecol 2008;111:1359–69.

38. Secura GM, Allsworth JE, Madden T, Mullersman JL, Peipert JF. The Contraceptive CHOICE project: reducing barriers to long-acting reversible contraception. Am J Obstet Gynecol 2010;203:115.e1–7.

39. Hubacher D, Grimes D. Noncontraceptive health benefits of intrauterine devices: A systematic review, CME review article. Obstet Gynecol Surv 2002:57:120–8.

40. Buttini MJ, Jordan SJ, Webb PM. The effect of the levonorgestrel releasing intrauterine system on endometrial hyperplasia: an Australian study and systematic review. Aust N Z J Obstet Gynaecol 2009;49:316–22.

41. Varma R, Sinha D, Gupta JK. Non-contraceptive uses of levonorgestrel-releasing hormone system (LNG-IUS)–a systematic enquiry and overview. Eur J Obstet Gynecol Reprod Biol 2006;125:9–28.

42. Sivin I, Stern J. Health during prolonged use of levonorgestrel 20 micrograms/d and the copper TCu 380Ag intrauterine contraceptive device: a multicenter study. International Committee for Contraception Research (ICCR). Fertil Steril 1994; 61:70–7.

43. Lethaby A, Cooke I, Rees MC. Progesterone or progestogen-releasing intrauterine systems for heavy menstrual bleeding. Combination oral contraceptives. The Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD002126.

44. Endrikat J, Shapiro H, Lukkari-Lax E, Kunz M, Schmidt W, Fortier M. A Canadian, multicentre study comparing the efficacy of a levonorgestrel-releasing intrauterine system to an oral contraceptive in women with idiopathic menorrhagia. J Obstet Gynaecol Can 2009;31:340–7.

45. Hurskainen R, Teperi J, Rissanen P, Aalto AM, Grenman S, Kivelä A, et al. Clinical outcomes and costs with the levonorgestrel-releasing intrauterine system or hysterectomy for treatment of menorrhagia: Randomized trial 5-year follow-up. JAMA 2004;291:1456–1463.

46. Marjoribanks J Lethaby A, Farquhar C. Surgery compared with medical therapy for heavy menstrual bleeding. Combination oral contraceptives.The Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD003855.

47. Zapata LB, Whiteman MK, Tepper NK, Jamieson DJ, Marchbanks PA, Curtis KM. Intrauterine device use among women with uterine fibroids: a systematic review. Contraception 2010; 82:41–55.

48. Andersson K, Ryde-Blomqvist E, Lindell K, Odlind V, Milsom I. Perforations with intrauterine devices. Report from a Swedish survey. Contraception 1998;57:251–5.

49. Markovitch O, Klein Z, Gidoni Y, Holzinger M, Beyth Y. Extrauterine mislocated IUD: is surgical removal mandatory? Contraception 2002;66:105–8.

50. Ozgun MT, Batukan C, Serin IS, Ozcelik B, Basbug M, Dolanbay M. Surgical management of intra-abdominal mislocated intrauterine devices. Contraception 2007;75:96–100.

51. Xiong X, Buekens P, Wollast E. IUD use and the risk of ectopic pregnancy: a meta-analysis of case-control studies. Contraception 1995;52:23–34.

52. Furlong LA. Ectopic pregnancy risk when contraception fails. A review. J Reprod Med 2002;47:881–5.

53. Food and Drug Administration. Second report on intrauterine contraceptive devices. Washington (DC): Food and Drug Administraction; 1978.

54. Selected practice recommendations for contraceptive use. 2nd ed. Geneva (Switzerland); 2004. Available at: http://whqlibdoc.who.int/publications/2004/9241562846.pdf. Retrieved August 1, 2010.

55. Ganer H, Levy A, Ohel I, Sheiner E. Pregnancy outcome in women with an intrauterine device. Am J Obstet Gynecol 2009;201:381.e1–5.

56. U.S. Preventive Services Task Force. Screening for chlamydial infection: U.S. Prevnetive Services Task Force recommendation statement. Ann Intern Med 2007;147:128–34.

57. U.S. Preventive Services Task Force. Screening for gonorrhea: recommendation statement. Ann Fam Med 2005;3:263–7.

58. Skjeldestad FE, Halvorsen LE, Kahn H, Nordbø SA, Saake K. IUD users in Norway are at low risk for genital C. trachomatis infection. Contraception 1996;54:209–12.

59. Faúndes A, Telles E, Cristofoletti ML, Faúndes D, Castro S, Hardy E. The risk of inadvertent intrauterine device insertion in women carriers of endocervical Chlamydia trachomatis. Contraception 1998;58:105–9.

60. Lewis LN, Doherty DA, Hickey M, Skinner SR. Implanon as a contraceptive choice for teenage mothers: a comparison of contraceptive choices, acceptability and repeat pregnancy. Contraception 2010;81:421–6.

61. Stevens-Simon C, Kelly L, Kulick R. A village would be nice but … it takes a long-acting contraceptive to prevent repeat adolescent pregnancies. Am J Prev Med 2001;21:60–5.

62. Beerthuizen R, van Beek A, Massai R, Mäkäräinen L, Hout J, Bennink HC. Bone mineral density during long-term use of the progestagen contraceptive implant Implanon compared to a non-hormonal method of contraception. Hum Reprod 2000; 15:118–22.

63. Croxatto HB, Urbancsek J, Massai R, Coelingh Bennink H, van Beek A. A multicentre efficacy and safety study of the single contraceptive implant Implanon. Hum Reprod 1999;14: 976–81.

64. Otero Flores J, Balderas M, Bonilla C, Vazquez-Estrada L. Clinical experience and acceptability of the etonogestrel subdermal contraceptive implant. Int J Gynecol Obstet 2005;90: 228–33.

65. Graesslin O, Korver T. The contraceptive efficacy of Implanon: A review of clinical trials and marketing experience. Eur J Contraception Reprod Health Care 2008;13(S1): 4–12.

66. Brito MB, Ferriani RA, Quintana SM, Yazlle ME, Silva de Sá MF, Vieira CS. Safety of the etonogestrel-releasing implant during the immediate postpartum period: a pilot study. Contraception 2009;80:519–26.

67. Reinprayoon D, Taneepanichskul S, Bunyavejchevin S, Thaithumyanon P, Punnahitananda S, Tosukhowong P, et al. Effects of the etonogestrel-releasing contraceptive implant (Implanon) on parameters of breastfeeding compared to those of an intrauterine device. Contraception 2000;62:239–46.

68. Taneepanichskul S, Reinprayoon D, Thaithumyanon P, Praisuwanna P, Tosukhowong P, Dieben T. Effects of the etonogestrel-releasing implant Implanon and a nonmedicated intrauterine device on the growth of breast-fed infants. Contraception 2006;73:368–71.

69. Funk S, Miller MM, Mishell Dr Jr, Archer DF, Poindexter A, Schmidt J, et al. Safety and efficacy of Implanon, a single-rod implantable contraceptive containing etonogestrel. Contraception 2005;71:319–26.

70. Walch K, Unfried G, Huber J, Kurz C, van Trotsenburg M, Pernicka E, et al. Implanon compared with medroxyprogesterone acetate: effects on pain scores in patients with symptomatic endometriosis–a pilot study. Contraception 2009;79:29–34.

71. Yisa SB, Okenwa AA, Husemeyer RP. Treatment of pelvic endometriosis with etonogestrel subdermal implant (Implanon). J Fam Plann Reprod Health Care 2005;31:67–70.

72. Shokeir T, Amr M, Abdelshaheed M. The efficacy of Implanon for the treatment of chronic pelvic pain associated with pelvic congestion: 1-year randomized controlled pilot study. Arch Gynecol Obstet 2009;280:437–43.

73. Power J, French R, Cowan F. Subdermal implantable contraceptives compared with other forms of reversible contraceptives or other implants as effective methods for preventing pregnancy. Combination oral contraceptives. The Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD001326.

74. Levine JP, Sinofsky FE, Christ MF, Implanon US Study Group. Assessment of Implanon insertion and removal. Contraception 2008;78:409–17.

75. Harrison-Woolrych M, Hill R. Unintended pregnancies with the etonogestrel implant (Implanon): a case series from postmarketing experience in Australia. Contraception 2005;71: 306–8.

76. Shulman LP, Gabriel H. Management and localization strategies for the nonpalpable Implanon rod. Contraception 2006; 73:325–30.

77. Bitzer J, Tschudin S, Alder J. Acceptability and side-effects of Implanon in Switzerland: a retrospective study by the Implanon Swiss Study Group. Eur J Contraception Reprod Health Care 2004;9:278–84.

78. Weisberg E, Hickey M, Plmer D, O'Connor V, Salamonsen L, Findlay J, et al. A randomized controlled trial of treatment options for troublesome uterine bleeding in Implanon users. Hum Reprod 2009;25:1852–61.

79. Abdel-Aleem H, d'Arcangues C, Vogelsong KM, Gulmezoglu AM. Treatment of vaginal bleeding irregularities induced by progestin only contraceptives. Combination oral contraceptives. The Cochrane Database Systematic Reviews 2007, Issue 2. Art. No.: CD003449. DOI: 10.1002/14651858.CD003449.pub3.

80. Merki-Feld G, Imthurn B, Seifert B. Effects of the progestgen-only contraceptive implant Implanon on cardiovascular risk factors. Clin Endocrinol. 2008;68:355–60.

81. Biswas A, Biswas S, Viegas OA. Effect of etonogestrel subdermal contraceptive implant (Implanon) on liver function tests–a randomized comparative study with Norplant implants. Contraception 2004;70:379–82.

82. Trussell J, Lalla AM, Doan QV, Reyes E, Pinto L, Gricar J. Cost effectiveness of contraceptives in the United States. Contraception 2009;79:5–14.

83. Mavranezouli I, LARC Guideline Development Group. The cost-effectiveness of long-acting reversible contraceptive methods in the UK: analysis based on a decision-analytic model developed for a National Institute for Health and Clinical Excellence (NICE) clinical practice guideline. Hum Reprod 2008;23:1338–45.

84. Guttmacher Institute, Community Health Centers and Family Planning. Improving contraceptive use. *In Brief*, 2008 Series, No. 1. New York (NY): Guttmacher, 2008. Available at: http://www.guttmacher.org/pubs/2008/05/09/ImprovingContraceptiveUse.pdf. Retrieved November 30, 2010.

85. Rivera R, Yacobson I, Grimes D. The mechanism of action of hormonal contraceptives and intrauterine contraceptive devices. Am J Obstet Gynecol 1999;181:1263–9.

86. Stanford JB, Mikolajczyk RT. Mechanisms of action of intrauterine devices: update and estimation of postfertilization effects. Am J Obstet Gynecol 2002;187:1699–708.

87. Davies G, Feng L, Newton J, Van Beek A, Coelingh-Bennink J. Release characteristics, ovarian activity and menstrual bleeding pattern with a single contraceptive implant releasing 3-ketodesogestrel. Contraception 1993;47:251–61.

88. Croxatto H. Mechanisms that explain the contraceptive action of progestin implants for women. Contraception 2002;65:21–7.

89. Makarainen L, Van Beek A, Tuomivaara L, Asplund B, Coelingh Bennink H. Ovarian function during the use of a single contraceptive implant: Implanon compared with Norplant. Fertil Steril. 1998;69:714–21.

90. Vessey MP, Lawless M, McPherson K, Yeates D. Fertility after stopping use of intrauterine contraceptive device. Br Med J 1983;286:106.