Published in final edited form as:

Postgrad Med. 2009 July ; 121(4): 18–25. doi:10.3810/pgm.2009.07.2025.

Reversible Contraception Update: The Importance of Long-Acting Reversible Contraception

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Abstract

The past several years have seen an expansion in contraception options. Emerging data support the use of long-acting reversible contraception (LARC) such as the intrauterine device and subdermal implant as the most effective methods of contraception with the highest continuation rates and very high levels of patient satisfaction. In addition, the appropriate target population for the use of the intrauterine device now includes nulliparous women and adolescents. When a patient considers initiating a new contraceptive method, it is important to consider the characteristics of each method, including the side effects, effectiveness, and patient acceptability. Additionally, medical comorbidities must also be evaluated prior to choosing a method. In this article, we provide a brief overview of available reversible contraceptive methods, with an emphasis on LARC.

Keywords

contraception; intrauterine device; intrauterine contraceptives; family planning; long-acting reversible contraception; adolescent contraception

Introduction

The World Health Organization characterizes contraceptive methods from the highest efficacy (intrauterine contraceptives [IUCs], implants, and sterilization) to moderate efficacy (combined hormonal methods and progesterone-only methods) to least effective such as barrier methods and fertility awareness.¹ In this article, we provide a brief overview of available contraceptive methods, with an emphasis on long-acting reversible contraception (LARC).

Long-Acting Reversible Contraception

Long-acting reversible contraception methods include contraceptive implants and IUC. These methods are highly effective, rivaling sterilization procedures, and last for ≥ 3 years (Table 1).

Contraceptive Implants

The available subdermal implant Implanon[®] is a single-rod measuring 4 cm that releases 68 μ g of etonogestrel per day. Implanon[®] provides 3 years of contraception with very high

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Conflict of Interest Statement: Jeffrey F. Peipert, MD, PhD discloses conflicts of interest with Barr-Duramed and Organon/Schering-Plough. Renee E. Mestad, MD, and Jessica Kenerson, MD, MPH disclose no conflicts of interest.

efficacy (failure rate < 0.1%). The single rod is inserted into the subcuticular tissue of the inner upper arm under local anesthesia (Figure 1). This method prevents pregnancy primarily by inhibiting ovulation and causing endometrial atrophy. Implanon® may also work by inhibiting sperm penetration through the cervix by thickening cervical mucus. Advantages of the implant include its high effectiveness and ease of use. Contraindications to the implant include pregnancy, undiagnosed abnormal vaginal bleeding, breast cancer, active liver disease, and allergies to any components of the device.

One inconvenient side effect of the single-rod implant is unpredictable and irregular bleeding. Other potential side effects include headaches, weight gain, and mood changes. Patients may experience temporary bruising and soreness at the site immediately after insertion. The subdermal implant is an excellent method for women desiring long-term, reversible contraception and who are willing to tolerate unpredictable bleeding.

Insertion difficulties experienced with the 6-rod subdermal implant that is no longer available in the United States (Norplant) have been addressed. Medical providers must complete an approved training course before the manufacturer will supply Implanon®.

Levonorgestrel-Releasing Intrauterine System (Mirena®)

The levonorgestrel-releasing intrauterine system (LNG-IUS) is a T-shaped frame made of polyethylene that releases levonorgestrel at a rate of 20 µg/day. The system provides 5 years of reliable contraception,² with a 0.2% failure rate in the first year.³ Progestin thickens cervical mucus, inhibits sperm capacitation and motility, causes endometrial atrophy, and can suppress ovulation in some women.⁴ Advantages of the LNG-IUS include high effectiveness and ease of use. Additionally, this method is not contraindicated for use in most patients with medical comorbidities and in women who cannot use estrogen-containing contraceptives. It can also be used with most medications. Noncontraceptive health benefits include decreased risk of ectopic pregnancy, decreased risk of endometrial cancer, decreased menstrual blood loss, and decreased dysmenorrhea.

Contraindications to the LNG-IUS include pregnancy, pelvic inflammatory disease ([PID]: current or within the past 3 months), cervicitis, current positive test for *Neisseria gonorrhoeae* or *Chlamydia trachomatis*, puerperal or postabortion sepsis (current or within the past 3 months), undiagnosed abnormal vaginal bleeding, genital tract malignancy, known uterine anomalies incompatible with insertion, known pelvic tuberculosis, allergies to the components, breast cancer within 5 years, or active liver disease.⁵ Appropriate candidates include both nulliparous and parous women, even young women and adolescents.⁶

Adverse events with insertion and use include uterine perforation, expulsion, bleeding, and cramping. Both IUCs increase the risk of miscarriage, infection, and preterm birth if the device is left in place during pregnancy. Other concerns include high initial cost, spontaneous expulsion, amenorrhea (a benefit to some), and mild discomfort with placement.

Copper T380A IUC or ParaGard®

The copper T380A IUC is a polyethylene T-shaped frame with copper wire wrapped around the 2 arms and the stem of the “T” (Figure 2). This method is highly effective for at least 10 years, with a failure rate of 0.6% to 0.8% in the first year.³ The copper appears to decrease the ability of sperm to fertilize the ovum.

Contraindications to the copper IUC are similar to the LNG-IUS with the addition of allergies to the components of the IUC, including copper. Breast cancer and liver disease are

not contraindications, and this method is ideal for women who want to avoid hormones. Appropriate candidates include both nulliparous and parous women and can be used in young and adolescent women.⁶

Adverse events are also similar to the LNG-IUS. Amenorrhea is not a concern with the copper IUC. Intermenstrual bleeding and cramping are common for the first several months after insertion of both the LNG-IUS and the copper IUC. Increased menstrual flow is common with the copper IUC. Increased bleeding and cramping usually subside after several months of use. Some clinicians recommend a course of nonsteroidal anti-inflammatory medications for patients complaining of persistent bleeding and cramping. The patient should call her provider for severe, unresponsive pelvic pain, persistent heavy vaginal bleeding, signs of infection (eg, fever, chills, etc.), or if device strings are not palpable. If strings are not palpable, the patient should use alternate contraception until examined by provider. Ultrasound and/or radiography are indicated to evaluate for uterine perforation or expulsion.

Combination Hormonal Contraception

Combination Oral Contraceptives (COCs)

Oral contraceptives are one of the most commonly used methods of contraception in the world. Most formulations contain either 20, 30, or 35 µg of ethinyl estradiol, and a progestin. Monophasic pills contain a consistent dose of estrogen and progestin. Multiphasic pills contain varying doses of estrogen and progestin. Traditionally, each package includes 21 active pills and 7 placebo pills. However, there is no scientific reason to support this regimen; it was developed to “mimic” the normal menstrual cycle. Newer brands package a variety of pill combinations that allow for withdrawal menstrual bleeding at different time intervals. Examples include the following: 24 days of active pills and 4 days of placebo pills; 84 days of active pills, with 7 days of placebo or a low-dose estrogen pill; or 21 days of active pills with 2 days of placebo pills and 5 days of a low dose of estrogen. Recently, COCs without placebo pills were also made available.

Failure rate with perfect use of COCs is 0.3%; however, failure rate with typical use increases to 8% to 9%.³ Higher failure rates among obese women have been noted in some studies. These women may benefit from decreased pill-free intervals rather than higher doses.⁷ Combination oral contraceptives prevent pregnancy by thickening cervical mucus and suppressing ovulation.

Noncontraceptive benefits of COCs include 1) possible prevention of ovarian cysts and hemoperitoneum caused by ruptured ovarian cysts in anticoagulated women; 2) treatment of dysmenorrhea; 3) treatment of menorrhagia and subsequent anemia; 4) improvement of acne; 5) reduced risk of benign breast disease; and 6) reduced risk of endometrial and ovarian cancer.

Contraindications to COCs include smoking over the age of 34, uncontrolled hypertension, vascular disease, history of deep vein thrombosis or pulmonary embolism, prolonged immobilization with major surgery, known thrombogenic mutation, current or history of heart disease, history of cerebrovascular accident, complicated valvular heart disease, migraine with aura, current breast cancer or within 5 years of treatment, diabetes with end-organ or vascular damage or > 20 years duration, active viral hepatitis, severe liver cirrhosis, and benign or malignant liver tumors.⁶ Combined oral contraceptives are an option for healthy perimenopausal women, patients with well-controlled hypertension who are < 35 years of age, women with lupus who do not have antiphospholipid antibodies, and

anticoagulated women.⁸ A number of medications are known to decrease serum steroid levels (Table 2).⁷ Combination oral contraceptives decrease the serum level of amprenavir.

The risk of venous thromboembolism (VTE) ranges from 0.5 to 9.7/10 000 women and increases with age.⁹ This risk decreases as estrogen dose decreases. Combination oral contraceptives do not appear to be associated with an increased risk of breast cancer among women using the lower doses distributed since the 1980s.¹⁰ Minor adverse events include nausea, breast tenderness, headache, vaginal spotting or bleeding outside the placebo interval, or decreased libido. Most of these adverse events resolve after 2 to 3 months of use.

Pregnancy must be ruled out prior to initiating COCs. One method of initiation is the Quick Start method. The patient takes the first pill the same day as the office visit. If the patient had recent intercourse without contraception, the clinician should recommend emergency contraception (EC) and begin the pills the next day. The patient should abstain from intercourse or use condoms for 7 days. If she is concerned about pregnancy, a urine pregnancy test should be offered in 2 to 3 weeks. Combination oral contraceptives are not teratogenic. The patient may also start COCs the first day of her next menses.

Contraceptive Vaginal Ring (CVR)

The CVR is a flexible, transparent ring that releases 120 µg of etonogestrel and 15 µg of ethinyl estradiol each day (Figure 3). There is a 0.3% risk of pregnancy in the first year with perfect use and an 8% to 9% risk with typical use.³ The ring acts primarily by ovulation suppression. The CVR offers a constant dose of hormone and distributes a lower dose of estrogen than COCs or the patch. The CVR increases vaginal *Lactobacillus*, which is an important component of the natural vaginal flora. Appropriate candidates include women who can use COCs but have difficulty remembering to take a pill daily. Women who travel frequently, have an erratic daily schedule, or often change work shifts should consider the vaginal ring.

Contraindications and adverse events with the CVR are similar to those of COCs. Drug interactions are possibly similar to those of COCs. Some women do not like the increase of physiological vaginal discharge. After infection is ruled out, patients may be reassured that increased discharge is secondary to an increase of normal flora that protects against genital infections.

To use CVR, the patient squeezes the ring and slides it into her vagina. It does not need to fit around her cervix. It can remain in the vagina 3 to 4 weeks (3 weeks if she wants a withdrawal period and 4 weeks if she does not). A new ring should be placed at the completion of each 4-week cycle. The CVR may remain in the vagina during intercourse or be removed for up to 3 hours. If removal is longer than 3 hours, the patient should use a back-up method of contraception for 7 days. The ring may be initiated using the same schedule described for starting COCs.

Transdermal Patch

The transdermal patch is a thin, beige, 20-cm² patch that releases 150 µg of norelgestromin and 20 µg of ethinyl estradiol daily. There is a 0.3% failure rate with perfect use and an 8% to 9% failure rate with typical use.³ Pregnancy is prevented through suppression of ovulation.

Contraindications and adverse events for the patch are similar to those of COCs. Pharmacokinetic data indicate higher serum levels of estrogen than with 35-µg COCs. Studies evaluating whether the patch is associated with an increased risk of VTE compared with COCs are conflicted. Some show a modest increased risk. Others have found the risk of

VTE between the 2 contraceptives is similar.¹¹ Skin reactions are the main side effect. Any woman without any contraindications who has difficulty remembering a daily pill can consider the patch. Women with erratic schedules or who travel are good candidates. It is easy to use and does not require a daily reminder. The patch provides a consistent hormonal dose.

The patient may begin use of the patch using the same protocol as that for COCs. The patch may be placed on the upper arm, upper back, hip, or buttocks. It should not be placed on the breast because unilateral breast pain may develop. The patient should clean the area with alcohol prior to placement to improve adhesion.

Progesterone-Only Contraception

Contraceptive Injection (Depo-medroxyprogesterone acetate [DMPA])

The DMPA injection is an aqueous suspension of 17-acetoxy-6-methylprogesterone. The intramuscular dose is 150 mg, and the subcutaneous dose is 104 mg. Both are given every 12 weeks, have an ideal use failure rate of 0.3% and a typical use failure rate of 3% in the first year.³ Depo-medroxyprogesterone acetate acts primarily by suppressing ovulation and thickening cervical mucus. Appropriate candidates include women who cannot use combination hormonal contraception due to estrogen content. Depo-medroxyprogesterone acetate is acceptable in breastfeeding women. Current breast cancer is the only contraindication.⁶

Depo-medroxyprogesterone acetate can provide relief from hemorrhagic ovarian cysts, dysmenorrhea, and endometriosis. Anticoagulated women benefit from prevention of hemorrhagic ovarian cysts. Women with sickle cell disease have fewer and less-intense pain crises. Depo-medroxyprogesterone acetate also appears to enhance control of grand mal seizures. Depo-medroxyprogesterone acetate has few known drug interactions. However, DMPA cannot be immediately withdrawn, as the depo-injection continues to provide blood levels of progesterone hormone. Resumption of spontaneous menses can take 10 months.

In terms of side effects, most women using DMPA note an increase in the length or time of menstrual bleeding and intermenstrual spotting. Others note decreased bleeding or skipped periods. Vaginal bleeding can be unpredictable for up to 6 to 9 months. After 1 year, 40% to 50% of users are amenorrheic. Weight gain is another reason frequently cited for discontinuation. Studies vary on weight gain reports, from noting weight loss, no weight gain, to a 9-pound increase in weight.¹² Some patients report depression; however, data to verify this association are lacking. Depression is not a contraindication to its use. Bone density loss data indicates a 1.5% to 2.5% loss in the first year, with the rate decreasing in subsequent years. After discontinuation, bone density recovers and is similar to that of women who have never used DMPA. The loss and recovery of bone density occurs similarly during lactation.^{12,13} Bone densitometry should not be used to dictate use of the injection for contraception because there is no correlation of fracture risk and bone densitometry results in premenopausal women. Women using the injection until menopause have not demonstrated an increased fracture risk after menopause.¹⁴

Injections can be administered anytime in the cycle if the clinician can be reasonably sure the patient is not pregnant. If it is given more than 7 days since the first day of her last period, a second method for 7 days should be recommended. The next injection should be 11 to 13 weeks later. Depo-medroxyprogesterone acetate is not teratogenic.

Progesterone-Only Pill ([POP] or Mini-Pill)

The POP contains 0.35 mg of norethindrone that is taken continuously (no hormone-free pills). The perfect use failure rate is 0.3% in the first year, and typical use failure is 8% to 9%.³ Possible mechanisms of action include ovulation suppression, thickening of the cervical mucus, reduced motility in the fallopian tube, and changes in the endometrium that reduce the chance of successful implantation. Current breast cancer is the only absolute contraindication to POP use.⁶ Women with liver disease or who are taking previously listed anticonvulsants or rifampin should consider a second or different method. Progesterone-only pills do not consistently suppress ovarian cyst formation and may increase their incidence.¹⁵ There is more breakthrough bleeding with POPs than with COCs. Appropriate candidates include any woman who cannot use estrogen and is willing to use a daily method. Lactating women are the most common users of POPs, as POPs will not interfere with milk supply when breastfeeding. Progesterone-only pills may decrease the frequency or intensity of painful sickle cell crises.

The patient may initiate the mini-pill the same way she would start COCs. These pills should be taken at the same time every day. If the patient is outside a 3-hour window, she should take the pill when she remembers, take the next one on schedule, and abstain or use condoms for 48 hours after she resumes her pill schedule. Emergency contraception should be offered if the patient has intercourse during this time.

Emergency Contraception

Levonorgestrel EC (EC or Plan B[®]) consists of 2 pills containing 750 µg of levonorgestrel taken either together or 12 to 24 hours apart. The risk of pregnancy can be decreased to 2%. EC should be taken within 72 hours after unprotected intercourse; however, EC has some efficacy of up to 120 hours (5 days). To maximize effectiveness, Emergency contraception should be used as soon as possible after unprotected intercourse. Mechanisms of action include a delay of ovulation and possible interference with corpus luteum function.¹⁶ It appears to inhibit sperm migration and function. There are no contraindications to EC. Side effects consist mostly of nausea and vomiting. These reactions are not as severe as those experienced with the Yuzpe regimen, which used COCs (estrogen and progesterone). Emergency contraception can also cause menstrual irregularity for the next cycle. Any patient using barrier methods, fertility awareness methods, and POPs should have a dose of EC available at home for emergencies. Rape victims should be informed of the availability of EC and offered the method.

Women who desire long-term contraception and recently had unprotected intercourse are good candidates for the use of the copper IUC as EC. Women who are considering this option should not have any of the IUC contraindications mentioned previously. The IUC should be placed within 5 days of unprotected intercourse and can reduce the risk of pregnancy due to recent unprotected intercourse to 0.2%.^{17,18}

Barrier and Spermicidal Contraception

Male and Female Condoms

Male condoms are usually made of latex, although polyurethane and lamb cecum are also available. The female condom is made of polyurethane. It has a rim that holds it against the vulva, a sheath that lines the vagina, and a ring that anchors it in the vagina. The failure rate for perfect male condom use is 2%; typical use is 15%. The failure rate for perfect use of a female condom is 5%; typical use is 21%.³ When used consistently and correctly, barrier methods are the only contraceptive methods effective at preventing sexually transmitted infection transmission. Other than an allergy to latex, barrier methods do not have any

contraindications. Oil-based lubricant weakens the latex, making condoms more prone to breakage. Thus, latex condoms should only be used with water-based lubricants. Adverse effects are mainly genital irritation or allergic reactions. These are sometimes due to spermicides or lubricants added to the condom.

Diaphragm, Cervical Cap, and Contraceptive Sponge

The diaphragm and cervical cap are dome-shaped rubber cups with a flexible rim. The diaphragm is considerably larger than the cap and fits into the vagina such that the cup covers the cervix. The cap is smaller and fits directly over the cervix. Spermicidal cream or jelly is typically placed in the diaphragm. The cervical cap can be used with spermicide, but it does not require it. The diaphragm is placed prior to intercourse and left in place for 6 hours after intercourse. It requires fitting by a provider and a prescription. It should be refitted after pregnancy or dramatic weight changes. Perfect use of the diaphragm has a failure rate of 6%; typical use failure rate is 16%.¹⁹ Efficacy of the cap is better for nulliparous women, with a 9% perfect use failure rate and a 16% typical use failure rate. Parous women experience a 26% perfect use failure rate and a 32% typical use failure rate.²⁰ Both the cap and the diaphragm are reusable and may offer some sexually transmitted infection (STI) protection.

A woman with an allergy to the rubber should not use a diaphragm or cap. Vaginal anomalies preventing appropriate placement are a contraindication. Women who cannot feel the cervix should not use a diaphragm or cap. The diaphragm increases the risk of urinary tract infections, and uncommonly can cause toxic shock syndrome if left in place for prolonged periods of time. The diaphragm should not be left in > 24 hours. The cap can be left in place for 24 to 48 hours.

The contraceptive vaginal sponge was recently reintroduced to the market. The sponge was developed as an alternative to the contraceptive diaphragm. The sponge is a soft, small, doughnut-shaped foam device made from polyurethane that contains spermicide. It does not require a fitting and can be used for more than one coital act within 24 hours. In nulliparous women, the sponge's efficacy is similar to that of the diaphragm. However, in parous women, the diaphragm is more effective.²¹ The sponge must be dampened with water before placement. It should remain in the vagina for 6 hours after last intercourse. Similar to the diaphragm, the sponge increases the risk of STIs and toxic shock syndrome. The sponge should not remain in for > 24 hours.

Spermicidal Contraception

Spermicides are marketed in the form of foam, gel, cream, suppository, or tablet. The product available in the United States, nonoxynol-9 (N-9), destroys the sperm membrane. Nonoxynol-9 can be used intermittently, can improve the effectiveness of barrier methods, is not teratogenic, and can augment lubrication. Perfect use (alone) has an 18% failure rate; typical use has a 29% failure rate.¹⁹ Spermicidal suppositories require 10 to 15 minutes after insertion for the spermicide to dissolve and disperse. The film needs to be placed on or near the cervix.

Women expecting to have intercourse more than 2 times a day should not use N-9 because it can increase vulnerability to HIV infection by disrupting vaginal epithelium if used very frequently.

Coitus Interruptus and Fertility Awareness

Coitus interruptus is most commonly known as withdrawal and involves removing the penis from the vagina prior to ejaculation. Coitus interruptus has a 4% failure rate with perfect use and a 27% failure rate with typical use.³

There are several fertility awareness-based (FAB) methods. Couples practicing FAB methods use barrier methods during the fertile times. Couples who routinely abstain during fertile days are practicing natural family planning. The standard days method and the calendar rhythm method involve counting days on the calendar and keeping track of menstrual cycles and a woman's most fertile period. The 2-day method, the Billings ovulation method, and the symptothermal method observe for signs of ovulation, such as changes in cervical secretions and basal body temperature. Fertility awareness-based methods have a 4% to 5% failure rate with perfect use and a 25% failure rate with typical use.³

Given the high typical failure rates of both withdrawal and FAB methods, most family planning providers do not advocate the use of these methods as primary methods for pregnancy prevention. Emergency contraception should be readily available if the couple has unprotected intercourse during the fertile period or if the male does not withdraw appropriately.

Conclusion

Fortunately for our patients, a variety of reversible contraceptive methods are available. The combination of each method's unique mechanism of action, side effects, method of administration, ability to prevent STIs, and failure rates should be reviewed with patients prior to initiation. The combination of these factors influences patient acceptability and proper use. Given the large discrepancy between perfect and typical use of most reversible methods, more family planning experts are emphasizing the low failure rate of LARC methods (IUCs and implants). Because these methods are not dependent on patient compliance, their typical effectiveness does not vary from perfect use. These methods rival sterilization in terms of efficacy and have very high satisfaction and continuation rates. These should be first-line contraceptive options for most women.

Acknowledgments

This research was supported in part by a Midcareer Investigator Award in Women's Health Research (K24 HD01298), by a Clinical and Translational Science Awards (UL1RR024992), and by Grant number K3054628 from the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and NIH Roadmap for Medical Research. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NCRR or NIH.

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Figure 1.
Subdermal implant (Implanon®).
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Figure 2.
Copper T380A intrauterine contraceptive (ParaGard®).
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Figure 3.
Contraceptive vaginal ring.
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Table 1
Percent of Women Experiencing Unintended Pregnancy in First Year of Use

Method		Unintended Pregnancy, % Typical Use	Unintended Pregnancy, % Perfect Use
Long-acting reversible contraception	Contraceptive implant ³	0.05	0.05
	Levonorgestrel IUS ³	0.2	0.2
	Copper T380 IUC ³	0.8	0.6
Combination hormonal methods	Oral contraceptives ³	8	0.3
	Vaginal ring ³	8	0.3
	Transdermal patch ³	8	0.3
Progesterone-only methods	DMPA ³	3	0.3
	Progesterone-only oral contraceptives ³	8	0.3
Barrier methods	Condoms: male ¹⁹	15	2
	Condoms: female ¹⁹	21	5
	Diaphragm ³	16	6
	Cap: nulliparous ²⁰	16	9
	Cap: parous ²⁰	32	26
	Sponge: nulliparous ³	16	9
	Sponge: parous ³	32	20
Spermicide ¹⁹		29	18
Fertility awareness ³		25	4–5
Sterilization	Female ²²	1.3	0.5
	Male ³	0.5	0.1

Abbreviations: DMPA, depo-medroxyprogesterone acetate; IUC, intrauterine contraceptive; IUS, intrauterine system.

Table 2
Medications Known to Reduce the Effectiveness of Combined Hormonal Contraceptive Methods

Barbiturates
Carbamazepine and oxcarbazepine
Felbamate
Phenytoin
Topiramate
Vigabatrin
Rifampin
Nelfinavir
Ritonavir, lopinavir, and nevirapine
St. John's Wort