

Update in Contraception

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Fifty percent of all pregnancies in the United States are unintended. Sixty percent of these unplanned pregnancies occur in woman using some contraceptive method.¹ These statistics demonstrate that although numerous methods of contraception are available, many women either are not finding a reliable method that suits their lifestyle or are not adhering to their current birth control method. Researchers continue to work on finding the “perfect” contraceptive—convenient, effective, affordable, and safe.

There is no single ideal method of contraception for all women. However, with the advent of several new products, clinicians now have an even wider range of reliable options to offer patients. New contraceptive options include newer low-dose oral contraceptive pills (OCPs), contraceptive vaginal rings, transdermal patches, and injectable contraceptives as well as new barrier and sterilization methods. An understanding of all of the available contraceptive methods will allow the health care provider to individualize treatment plans to encompass a wide variety of patient needs. This article reviews methods of contraception currently available in the United States, with a focus on options that have only recently been approved.

ORAL CONTRACEPTIVE PILLS

OCPs are currently the most widely used method of reversible contraception in the United States. Nearly 18 million women in the United States use OCPs, accounting for 30% of reproductive-age women.² When taken perfectly, OCPs have an annual failure rate of 0.1%, although with typical use, failure rates approach 8%³ due to patient noncompliance with the pill secondary to side effects or difficulty remembering to take the pill daily. Reasons for the popularity of OCPs include effectiveness, safety, and reversibility. OCPs also have several noncontraceptive benefits, including decreased dysmenorrhea, improved cycle control, decreased risk of ovarian and endometrial cancer, decreased risk of benign breast disease, decreased risk of ovarian cysts, and improvement of hirsutism and acne. Contraindications to OCPs are listed in **Table 1**;

for patients in whom OCPs are contraindicated, alternative methods of contraception should be prescribed.

Studies continue to evaluate the safety of OCPs. Evidence is conflicting regarding the relative risks of myocardial infarction among current users of OCPs in healthy nonsmokers. There is an increased risk of venous thromboembolism, although the absolute risk is small (4 events per 10,000 OCP users).⁴ There also appears to be a slightly increased risk of breast cancer among current users (relative risk, 1.24).⁵ The relative risk of developing breast cancer decreases steadily after discontinuation. There is no increased risk by 10 years after discontinuation.⁵

Current combination OCPs contain 20 to 35 µg of the estrogen ethinyl estradiol (EE); the dose of estrogen as well as the type and dose of progestin varies among different OCPs. The selection of OCPs continues to expand with the availability of new progestins and alternative estrogen dosing options. The type of combination OCP may be tailored to the patient based on the side effect profile. For example, a women suffering from perimenstrual bloating and fluid retention may benefit from a new OCP containing the unique progestin drospirenone, which is an analogue of spironolactone and therefore has antimineralocorticoid activity.⁶ This monophasic oral contraceptive (Yasmin, Berlex Laboratories, Montville, NJ) contains 3 mg drospirenone and 30 µg EE.⁷ The EE/drospirenone combination demonstrated similar efficacy and cycle control compared with other OCPs in an open-label multicenter study, with no significant effect on weight, blood pressure, or lipids. In addition, this OCP may reduce premenstrual symptoms.⁸ Contraindications to an oral contraceptive containing drospirenone include any condition that predisposes patients to hyperkalemia because drospirenone is an analogue of the potassium-sparing diuretic spironolactone.

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Table I. Contraindications to Oral Contraceptive Pills*

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*In women with these conditions, use of progestin-only oral contraceptives, depot medroxyprogesterone acetate, or an intrauterine device may be safer than combination oral contraceptive pills.

†Use of an IUD may not be an appropriate contraceptive choice in this setting.

New Low-Dose Oral Contraceptives

New OCPs have given patients the option of a lower estrogen component in a monophasic 20 or 25 µg EE dose (as compared with the standard 30 or 35 µg dose). Although no specific formulation of OCP has been shown to consistently reduce the incidence of minor side effects, these lower-dose OCPs may have the benefit of reducing some estrogen-related side effects in individual patients. The most common estrogen-related side effects are nausea, breast tenderness, and headaches, and are the most common reasons for discontinuation of OCPs. In fact, 37% of patients discontinue OCPs during the first year owing to side effects. Incidence of nausea is directly associated with higher EE levels in OCPs, particularly in the first cycle of use.⁹ In one study, nausea, bloating, and breast tenderness were approximately 50% more common in women using 35 µg EE preparations compared to 20 µg EE preparations.¹⁰ For such patients, 20 µg OCPs may lead to improved compliance.

For patients with hormonal withdrawal symptoms, OCPs with an additional prescription of “add-back” estrogen during the placebo week of pills may be helpful. One 20 µg EE OCP formulation (Mircette, Organon Inc., West Orange, NJ) includes 10 µg EE during 5 days of the last week of pills (20 µg EE + 150 µg desogestrel for 21 days, 2 inactive days, 10 µg of EE for

5 days). Another option is extended OCP use without monthly withdrawal bleeds. This regimen has been shown to decrease dysmenorrhea, premenstrual symptoms, and migraine headaches.¹¹ A recently approved OCP (Seasonale, Duramed Pharmaceuticals, Pomona, NY) is packaged with an 84-day dosing regimen that results in only 4 menses per year.

One disadvantage of 20-µg EE OCPs is that some patients may experience a higher rate of breakthrough bleeding compared to OCPs containing 30 to 35 µg EE.^{12,13} The rate of breakthrough bleeding in the 20-µg EE OCP Mircette, which includes “add-back” estrogen during the placebo week, is similar to that of 35-µg preparations.¹⁴ Two new triphasic OC formulations that include 25 µg of EE also report decreased breakthrough bleeding compared to 20-µg monophasic OCPs (Cyclessa, Organon Inc., West Orange, NJ; and Ortho Tri-cyclen Lo, Ortho-McNeil Pharmaceutical Inc., Raritan, NJ).¹⁵

EMERGENCY CONTRACEPTION

In 1974, Dr. Albert Yuzpe of Canada first described postcoital contraception utilizing a combination of estrogen and progesterone.¹⁶ In September 1998, the first dedicated emergency contraceptive product was approved for sale in the United States (Preven, Gynetics Inc., Somerville, NJ). The kit contains a pregnancy test and 4 oral contraceptive tablets, each containing 250 µg of levonorgestrel and 50 µg of EE. Patients are instructed to take the pregnancy test and, if it is negative, administer 2 of the tablets within 72 hours of unprotected intercourse and 2 tablets 12 hours later. The Yuzpe regimen reduces the risk of pregnancy by 75% by inhibiting or delaying ovulation, altering the endometrium, or altering sperm or ova transport.¹⁷ It will not interrupt an established pregnancy nor has it been proven to cause harm to a fetus during early gestation. Nausea occurs in 50% of women, with 20% experiencing vomiting.¹⁸ Antiemetics taken before the first contraceptive dose may decrease the occurrence of these side effects. The listed contraindications for the combination EE/levonorgestrel emergency contraceptive are similar to combination OCPs, although there is no evidence of increased risk among women with contraindications to OCPs. Some contraindications are based on long-term use and are not likely to pertain to the short duration used for emergency contraception.¹⁹

A progestin-only product (Plan B, Barr Laboratories Inc., Pomona, NY) is now available as well. The progestin-only pill is preferred for emergency contraception as it appears to be more effective and carry

fewer side effects than the Yuzpe combination regimen. In a randomized, double-blind trial, 1998 women at 21 centers worldwide received either the Yuzpe regimen or 0.75 mg levonorgestrel in 2 doses separated by 12 hours within 72 hours of unprotected intercourse. The pregnancy rate was 1.1% in the progestin-only group versus 3.2% in the Yuzpe group.²⁰ There was also significantly less nausea and vomiting. The progestin-only emergency contraceptive product is so safe that most major medical organizations have recommended that it be approved for over-the-counter availability. Only 3 contraindications exist for progestin-only emergency contraceptive: pregnancy, allergy to ingredients, and unexplained abnormal uterine bleeding.

Other available options for emergency contraception include use of combination oral contraceptives that contain progestins other than levonorgestrel and the insertion of a copper-containing intrauterine device (IUD) up to 5 days after unprotected intercourse.²¹ These strategies are less well studied for emergency contraception but likely have similar effectiveness.

INTRAUTERINE DEVICE

Intrauterine contraception is the world's most popular method of reversible birth control. However, only 0.8% of American women rely on IUDs for contraception.¹ The use of IUDs declined during the 1980s secondary to publicity involving the association between the Dalkon Shield IUD and pelvic inflammatory disease (PID), leading several manufacturers of IUDs to discontinue marketing their IUDs in the United States. However, currently available IUDs are extremely effective and safe with minimal risk. The pregnancy rate for women using the IUD is less than 1% with only a 1% risk of PID.²² Other advantages include ease of use and no systemic side effects. Contraindications to IUD placement are summarized in **Table 2**.

Patient selection is important when prescribing an IUD. The IUD is most appropriate for a parous patient in a monogamous relationship with a low risk of sexually transmitted infections. It also may be considered for patients interested in long-term contraception as well as patients with contraindications to estrogen-containing contraceptives. Disadvantages to IUDs include risk of PID, expulsion, and pregnancy complications if a patient becomes pregnant with an IUD in place.

The newest IUD is the levonorgestrel-releasing system (Mirena, Berlex Inc., Montville, NJ), which joins the 10-year copper T 380A IUD (ParaGard, FEI Women's Health LLC, New York, NY) and the 1-year progesterone-releasing IUD (Progestasert, Alza Pharmaceuticals, Palo Alto, CA). The levonorgestrel IUD

Table 2. Precautions to the Use of IUDs

Refrain from providing an IUD for women with the following diagnoses:

- Active, recent (within the past 3 months), or recurrent pelvic infection
 - Postpartum endometritis
 - Infection following an abortion
 - Active sexually transmitted infection
- Known or suspected pregnancy
- Severely distorted uterine cavity caused by anatomical abnormalities
 - Leiomyomata
 - Endometrial polyps
 - Cervical stenosis
 - Bicornuate uterus
 - Small uterus

Exercise caution for women with the following diagnoses:

- Risk factors for pelvic inflammatory disease
 - Purulent cervicitis, until treated
 - Any history of gonorrhea or chlamydia (especially recent)
 - Multiple sexual partners
- Impaired response to infection
 - Steroid treatment
 - HIV and/or AIDS
- Abnormal vaginal bleeding
- Previous problems with an IUD
 - Pregnancy
 - Expulsion
 - Uterine perforation
 - Pain
 - Heavy bleeding (unless switching IUD type)

Advantages generally outweigh the disadvantages for women with the following diagnoses:

- Valvular heart disease without complications
- Uterine anatomic abnormalities that do not distort the uterus
- Heavy or prolonged menstrual bleeding
- Woman who has never had a child

Adapted with permission from Hatcher RA, Trussell J, Stewart F, et al. *Contraceptive Technology*. WHO eligibility criteria for the use of IUDs. 17th ed. Rev ed. New York: Ardent Media; 1998:517–9.

IUD = intrauterine device.

offers clinicians and patients a new choice in long-acting, reversible contraception. The T-shaped frame of the levonorgestrel IUD is inserted in the uterus within 7 days of the onset of menses, and the stem releases 20 µg of levonorgestrel each day for 5 years.²³ The efficacy of this IUD is comparable to surgical sterilization, with a failure rates of 0.5%.²⁴ Patients need to be

counseled regarding the alterations in bleeding patterns that occur with this contraceptive method. Women may experience significant unexpected spotting and bleeding as the endometrial lining is thinning, particularly during the first several months of use. A significant percentage of women will stop menstruating entirely (20% at 12 months), and most others will experience lighter, shorter periods with continued use.²²

LONG-ACTING HORMONAL CONTRACEPTION **Transdermal Contraception**

A transdermal contraception system (Ortho Evra, Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ) is now available for clinical use. The transdermal patch delivers continuous daily doses of 150 µg norelgestromin (the active metabolite of norgestimate) and 20 µg EE to inhibit ovulation.²⁵ The patch is a thin adhesive applied to the lower abdomen, arm, buttock, or upper torso (except the breast) once a week for 3 consecutive weeks, followed by a patch-free week for a withdrawal bleed. The method failure rate is 0.6%.²⁶ There is a statistically significant increase in the number of women who were perfectly compliant with the patch compared to OCPs, suggesting that the transdermal system is easier to use than OCPs. With the patch, perfect use was achieved for a mean of 88.2% of total cycles compared with 77.7% with OCPs.²⁷ The failure rate with the patch was 1.24 per 100 woman-years of use compared to 2.18 in OCP users, although this difference was not statistically significant.²⁷

The incidence of side effects is similar to that of OCPs, except that patch users had a higher incidence of application site reactions (20.2%), breast symptoms (in the first 2 cycles only) (18%), and dysmenorrhea (13%). Fewer than 2% of patients discontinued use of the patch owing to any of these side effects.²⁸ Breakthrough bleeding rates are low, and fewer than 10% of women experience either breakthrough bleeding or spotting after 3 months.²⁶

Combined data from several studies show a failure rate of less than 1%. There is a suggestion based on clinical evidence that the patch may be less effective in a subgroup of women whose weight is greater than 90 kg (196 lb). In a report pooling data from 3 studies that included 3319 women using the patch in 22,000 treatment cycles, 15 pregnancies were reported, and nearly half of these occurred in women weighing 90 kg or more.²⁶ Although this subset represented less than 3% of the study group, it accounted for one third of the pregnancies. Clinicians should, therefore, use caution in prescribing the patch to obese women, although the overall chance of pregnancy is still quite low.

Intravaginal Contraceptive Ring

The hormonal vaginal contraceptive ring (Nuva-Ring, Organon Inc., West Orange, NJ), approved by the US Food and Drug Administration (FDA) in 2001, is made of flexible transparent ethylene vinyl acetate copolymer. The outer diameter is 5.4 cm with a cross-sectional diameter of 0.4 cm. The ring suppresses ovulation by releasing a steady dose of hormones—120 µg daily of etonogestrel (the biologically active metabolite of desogestrol) and 15 µg daily of EE. The ring is a reliable form of birth control with a failure rate of less than 1%.²⁹ The ring has minimal effects on lipid parameters with no adverse effect on blood pressure and no unfavorable effects on the cervix or vagina. The ring is placed high in the vaginal vault lying directly in contact with the epithelium for 3 continuous weeks. It is removed for week 4, during which time menses will occur, and then a new ring is inserted. Although labeling recommends continuous use, the ring may be removed for up to 3 hours—either inadvertently or purposefully, for intercourse—without requiring the use of a back-up method of birth control. Excellent cycle control is achieved with a low incidence of irregular bleeding. Only 2.6% of patients experience expulsion and most report easy removal and insertion of the ring.²⁹ Overall, patients and their partners reported satisfaction with the vaginal contraceptive ring, and in a study of more than 2000 women, 90% said that they would recommend it to others.³⁰ Side effects are similar to OCPs and include an increase in vaginal discharge (4.8%), vaginitis (5.8%), device-related events (4.4%), headache (5.8%), nausea (3.2%), breast tenderness (2.6%), and vaginal discomfort (2.4%).³⁰

Injectable Contraception

Depot medroxyprogesterone acetate (DMPA; Depo-Provera, Pfizer Inc., New York, NY) has been FDA-approved for contraception since 1992. The 150-mg solution is given by intramuscular injection every 3 months and works by blocking the luteinizing hormone (LH) surge to prevent ovulation. DMPA is highly effective, with a first-year failure rate of 0.3%.³¹ Menstrual changes are the most prominent side effect; patients often experience unpredictable, irregular bleeding, resulting in 50% of women discontinuing use in the first year.³² The irregular bleeding generally improves, and 75% of users experience amenorrhea with continued use. Uncommon side effects include headache, weight gain, depression, and hair loss. Resumption of fertility is delayed by 8 months or more, making this method undesirable in women wanting quick return of fertility.³² Some women are hesitant to

use DMPA because of concerns about potential weight gain. Results from observational studies have been conflicting, with some claiming weight gain and others reporting no change. A recent prospective trial was unable to document any weight effect from DMPA.³³ The paper concluded that in patients who experience weight gain concomitant with DMPA use, factors other than contraceptive method are likely important.

ADDITIONAL CONTRACEPTIVE OPTIONS

Permanent Sterilization

Sterilization is the most reliable form of contraception. However, it is an option only for patients not interested in future fertility. Options for permanent sterilization include tubal interruption or occlusion for women and vasectomy for men. Until recently, permanent sterilization for women required either a laparoscopy or mini-laparotomy with general anesthesia. A new device approved by the FDA in November 2002 gives women a new option for permanent contraception.³⁴ The procedure is performed by hysteroscopy in an outpatient surgical center or an office by inserting a special coil into the uterine opening of each fallopian tube. The entire insertion procedure takes approximately 15 minutes. Recovery time is reduced compared to traditional surgery. Most women go home within 45 minutes because general anesthesia is not required. Mild-to-moderate cramping may last from 1 to 3 days, and most women experience light vaginal bleeding for a few days. Many patients return to work the day after the procedure, and 99% are back to work within 3 days.

The procedure was highly effective in clinical trials. In fact, there were no pregnancies in more than 700 study volunteers studied for 1 to 2 years.³⁵ However, the procedure is difficult to perform in some women. In the initial studies, the coils could not be placed in 8% of the volunteers, and in an additional 4.5% the coils were incorrectly placed. Once the coils are properly placed into the fallopian tubes, it takes time for scar tissue to form a plug and block the tube. By 3 months, both tubes are closed in 96% of women, and by 6 months, both tubes are closed in 100%. A reliable contraceptive method is required until hysterosalpingogram confirms tubal occlusion.

Barrier Methods

Several forms of birth control provide a physical barrier to sperm entering the female reproductive tract. Barrier methods may be used intermittently and are noninvasive. They are easy for most patients to use, are reasonably effective if used properly, and may

reduce the risk of some sexually transmitted diseases, particularly if used with spermicide. Barrier methods include the male and female condoms, diaphragms, and cervical caps. Diaphragms and cervical caps require fitting by a health care provider prior to use. A new cervical cap, FemCap (FemCap Inc., Del Mar, CA) was approved in 2003. It is available by prescription and requires fitting by a healthcare professional. It can be left in place for 48 hours after intercourse without reapplying spermicide. In 2002, the FDA approved the Lea's Shield (Yama Inc., Union, NJ), a reusable female barrier contraceptive. It is available by prescription only but does not require clinician fitting as one size fits all women. It is similar to a cervical cap, with a 1-way valve that allows flow of fluid from the cervix to the vagina. It is easy to handle for easy removal. Pregnancy rates using the Lea's Shield are comparable to those of other barrier methods.³⁶

Implantable Contraceptives

No implantable methods of birth control have been available in the United States since the 6-rod subdermal implant (Norplant) was withdrawn from the market in 2000. Other long-acting implants are available in other countries and may eventually be marketed in the United States. These include a 2-rod implant (Jadelle, Wyeth-Ayerst, Madison, WI) that releases 25 to 30 µg daily of levonorgestrel and a 1-rod implant (Implanon, Organon Inc., West Orange, NJ) that releases the steroid hormone etonogestrel (the active metabolite of desogestrel) at a rate of 30 µg per day.

Jadelle received FDA approval in 1996 but is not yet available in the United States. It was first approved for a 3-year interval; however, a 5-year study of 594 women revealed a cumulative pregnancy rate of 0.8 per 100 women³⁷; therefore, it is currently approved for a 5-year interval. Side effects include irregular bleeding, headache, weight gain, mood change, and depression, with 17.7% of subjects discontinuing use because of menstrual disturbances. Implanon is used internationally but is not available in the United States at this time. It prevents pregnancy for up to 3 years, primarily by inhibiting ovulation. In a large study with 1716 women, there were no pregnancies after 3 years.³⁸ Side effects were similar to those seen with the 2-rod levonorgestrel implants, with rapid return to ovulation after removal.

CONCLUSION

Because no single method of contraception is ideal for all women, tailoring the contraceptive choice to a patient's lifestyle, concerns, and side-effect profile is

critical to ensure continued use and compliance. With the advent of several different contraceptive methods, clinicians now have a wider range of reliable options to offer patients. Familiarity with the various contraceptive options available will enable clinicians to better counsel patients, with the goals of increasing birth control usage among women not desiring pregnancy, improving compliance among women willing to utilize some method of birth control, and ultimately reducing the number of unintended pregnancies in this country. **HP**

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