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Hormonal Contraception for the Adolescent

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Drs Gupta, Corrado,
and Goldstein have
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contain a discussion
of an unapproved/
investigative use of a
commercial
product/device.

Objectives After completing this article, readers should be able to:

1. Discuss the oral contraceptive pill, its contraceptive and noncontraceptive benefits, and its absolute contraindications.
2. Identify the different routes of administration that have been developed, newer formulations of conventional methods, and novel contraceptive agents that are being developed.
3. Describe each of the contraceptive methods, including adverse effects, efficacy, and compliance.
4. Recognize external and internal barriers to use, commonly held misperceptions by adolescents, and the relation of such misperceptions to developmental stages.
5. Explain how to provide effective and acceptable contraceptive services for adolescents.

Introduction

The United States has the highest rate of teen pregnancy and births in the western industrialized world, with more than 750,000 women ages 15 to 19 years old becoming pregnant each year. About 80% of these pregnancies are unintended and occur in unmarried teens. Of these, about 30% end in abortions, 57% in live births, and 14% in miscarriage.

In the United States, oral contraceptive pills (OCPs) remain the most common form of hormonal contraception for adolescents and reproductive-age women. (Technically, these drugs are dispensed as tablets, but the term “pill” is so closely linked with oral contraception that it will be used in this article.) Although the failure rate of the OCP is 0.3 per 100 women-years with ideal use, typical use failure rates, particularly for adolescents, are much higher (3 to 8/100 women-years). Contraception efficacy for the most common methods used by adolescents (Table 1) indicates the continued need for more effective and nonuser-dependent contraception.

Over the past few years, both new OCPs and different delivery methods have been developed. These innovations have been driven by the effort to optimize efficacy and minimize adverse effects. There also has been a trend toward different modes of delivery in an attempt to improve tolerability, reduce the need for daily compliance, and make the efficacy of the method less dependent on administration by the user. This review summarizes formulations and methods that have been developed in the past 15 years and glances ahead at those that are nearing completion on the long road to contraceptive development and approval.

The Oral Contraceptive Pill

Over the past 4 decades, the formulation of OCPs has changed, making them a safe and effective choice of contraception for the adolescent. Many adolescents are not educated effectively about how to use the OCP or its adverse effects. They also may be ambivalent or forget to take the pill

Abbreviations

BMD:	bone mineral density
DMPA:	depot medroxyprogesterone acetate
EC:	emergency contraception
EE:	ethinyl estradiol
FDA:	Food and Drug Administration
IUD:	intrauterine device
IUS:	intrauterine system
LNG:	levonorgestrel
OCP:	oral contraceptive pill
PID:	pelvic inflammatory disease
POP:	progestin-only pill
SHBG:	sex hormone-binding globulin
WHO:	World Health Organization

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Table. Contraceptive Efficacy

Method	Percent of Women Experiencing an Unintended Pregnancy Within The First Year of Use		Percent of Women Continuing Use at 1 Year ³
	Typical Use ¹	Perfect Use ²	
(1)	(2)	(3)	(4)
No method ⁴	85	85	
Spermicides ⁵	29	18	42
Withdrawal	27	4	43
Condom ⁶			
Female	21	5	49
Male	15	2	53
Combined pill and minipill	8	0.3	68
Combined hormonal patch	8	0.3	68
Combined hormonal ring	8	0.3	68
Depot medroxyprogesterone acetate (DMPA)	3	0.3	56
Combined injectable ⁷	3	0.05	56
Intrauterine device			
Copper T	0.8	0.6	78
Levonorgestrel intrauterine system	0.2	0.2	80
Levonorgestrel implants	0.05	0.05	84
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

Emergency contraceptive pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%.

¹Among typical United States couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason. Estimates of the probability of pregnancy during the first year of typical use for spermicides, withdrawal, periodic abstinence, the diaphragm, the male condom, the pill, and DMPA are taken from the 1995 National Survey of Family Growth corrected for underreporting of abortion; see original source (Trussel J, 2004) for the derivation of the estimates for the other methods.

²Among United States couples who initiate use of a method (not necessarily for the first time) and who use it perfectly (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason; see original source (Trussel J, 2004) for the derivation of the estimates for each method.

³Among United States couples attempting to avoid pregnancy, the percentage who continue to use a method for 1 year.

⁴The percentages becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception to become pregnant. Among populations where contraception is not used, about 89% become pregnant within 1 year. This estimate was lowered slightly (to 85%) to represent the percentage who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception completely.

⁵Foams, creams, gels, vaginal suppositories, and vaginal film.

⁶Without spermicides.

⁷Not available in the United States.

Adapted by World Health Organization. *Medical Eligibility Criteria for Contraceptive Use*. 3rd and 4th eds. 2004 from Trussel J. Contraceptive efficacy. In: Hatcher RA, Trussell J, Stewart F, et al. *Contraceptive Technology*. 18th revised ed. New York, NY: Ardent Media; 2004. Adapted table available at: <http://www.who.int/reproductive-health/publications/mec/summary.html>. Accessed October 2007.

regularly. Given that poor compliance decreases the efficacy of OCPs, it is important for the clinician to be familiar with the various formulations of the pill, adverse effects, and contraindications to implement proper education. Compliance with a contraceptive method is associated with a perceived lack of adverse effects, older age of the user, and satisfaction with the selection of the contraceptive method.

Description and Method of Use

The OCP may be a combination of estrogen and progestin or a progestin-only pill (POP). The combined OCP is comprised of a synthetic estrogen and progestin. These drugs prevent ovulation primarily by inhibiting the

gonadotropin-releasing hormone axis. Contraception also is enhanced by thickening cervical mucus, creating endometrial atrophy, and changing the tubal transport mechanism, all changes associated with the progestin in the combined OCP.

Ethinyl estradiol (EE) is the synthetic estrogen in most OCPs. Mestranol is used in some, but this compound is converted rapidly in the body to EE. OCPs contain different amounts of EE, ranging from 20 to 50 mcg. The type of progestin also varies in the combined OCPs and must be taken into account when prescribing the pill. There are three generations of progestins. The first-generation progestins, or estranes, are ethynodiol diacetate, norethindrone acetate, and noreth-

indrone. These agents must be converted to norethindrone for them to become biologically active. Second-generation progestins, or gonanes, are norgestrel and levonorgestrel. Third-generation progestins, or high-potency gonanes, are desogestrel, norgestimate, and gestodene, the latter of which is not available in the United States. Desogestrel and gestodene are associated with a higher risk of vascular thromboembolism compared with other agents. Progressing from first to third generation, there is an increase in half-life, which may influence the choice of combined OCP. Combined OCPs are available in monophasic and multiphasic packs. Monophasic pills have a constant amount of estrogen and progestin; the amount of hormones varies through the cycle in multiphasic pills. Current recommendations are to begin with either type, but to start with a pill containing a low dose of estrogen (20 to 35 mcg) to minimize estrogen-related adverse effects. The OCP can be changed easily, according to individual responses, but a trial of 3 months is recommended because it may take that long for an individual to become used to the OCP and for the initial adverse effects to subside.

The OCP should be initiated on either day 1 of the menstrual cycle or on the Sunday after the menstrual cycle begins. The clinician who considers a patient to be at high risk for pregnancy may suggest that the medication be started when prescribed, with the caveat that there may be some irregular menstrual bleeding. Others have given emergency contraception and allowed patients to wait for withdrawal bleeding before initiating OCP therapy. Because this regimen can be confusing for the adolescent, initial teaching must be undertaken with care. It often is useful to tell the adolescent to start the regimen the first day she experiences bleeding because instructions sometimes are misconstrued that the regimen must be started only after bleeding stops. It is important to talk with the adolescent about ways to ensure daily compliance and taking of the pill at the same time every day. Finally, it is important to have the adolescent understand that if she misses taking the pill, she can catch up or continue for that month.

Drospirenone is a new progestin in a combined OCP (Yasmin[®]), developed by Schering AG and sold through Bayer Schering Pharma AG (Berlin, Germany), that was approved by the United States Food and Drug Administration (FDA) in 2001. The OCP contains 3 mg of drospirenone and 30 mcg of EE. Drospirenone is a 17- α -spironolactone derivative that possesses diuretic and antiandrogenic activity. This OCP causes few menstrual adverse effects and has a failure rate of 0.406 pregnancies in 100 women-years of exposure. The prep-

aration also had a favorable profile in its effects on parameters such as blood pressure, weight, and cholesterol. One potential advantage is that its antiandrogenic properties favor its use in adolescents who have polycystic ovary syndrome. However, because it contains a progestin that has antiminerlocorticoid activity, this OCP should not be used in adolescents who are at risk for hyperkalemia, such as those who have renal, hepatic, or adrenal insufficiency or are taking certain medications, including angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, and nonsteroidal anti-inflammatory drugs.

Compliance and Adverse Effects

Adverse effects may be related either to the estrogen or progestin components. The amount of estrogen in the pill can account for various adverse effects, including but not limited to, irregular menstrual bleeding, breast tenderness, fluid retention, nausea, increased appetite, headache, and hypertension. Such effects sometimes can be alleviated by a preparation that has a lower estrogen dose. However, lower estrogen doses are associated more commonly with breakthrough bleeding, although such bleeding also may be related to the type of progestin.

Adverse effects seen with the progestin component include, but are not limited to, menstrual changes, bloating, mood changes, and increased appetite with weight gain. Acne, hirsutism, and male-pattern hair loss also have been reported but are rare. These androgenic effects are related to the androgen-to-progesterone binding ratio, the affinity of the progestin for sex hormone-binding globulin (SHBG), and the ability of the progestin to inhibit 5- α reductase. Norgestimate has the highest androgen-to-progesterone binding ratio, has the least affinity for SHBG, and is the most powerful inhibitor of 5- α reductase compared with levonorgestrel, theoretically making it a better option for those experiencing acne, hirsutism, or hyperandrogenism. However, because all OCPs decrease free testosterone similarly, any of the low-dose OCPs is appropriate for the treatment of hyperandrogenic syndromes.

Along with the common adverse effects, physicians and patients must be aware of contraindications to OCP use. The World Health Organization (WHO) has developed guidelines to help the clinician determine the safety of OCPs and other contraceptive methods for each individual (http://www.who.int/reproductive-health/publications/mec/3_cocs.pdf). The four medical eligibility categories include Class 1, a condition for which there is no contraindication for OCP use. Class 2 is defined as a condition for which caution is advised but

benefits outweigh risks. Class 3 pertains to a condition in which OCPs should not be used unless there are no other options, such as having gallbladder disease, being fewer than 21 days postpartum, lactating in the first 6 months after giving birth, or receiving medications that may interfere with the efficacy of the OCP. Class 4 applies to a condition in which OCPs are contraindicated; such conditions should be screened for through a careful history. Class 4 conditions include, but are not limited to, a history of deep vein thrombosis, pulmonary embolism, cerebrovascular accident, known factor V Leiden mutation or other thrombophilic condition, and migraine headache with aura or neurologic changes. Adolescents should be educated about serious adverse effects. However, unless the adolescent or family has a past history of a class 4 contraindication, the adolescent should be reassured that although these adverse effects are of concern, they are rare, and the risk of pregnancy frequently is greater than the risks associated with the pill.

If the combined OCP is not tolerated or there is a contraindication to using an estrogen-containing pill, the POP may be an option. These agents provide contraception through the progestin effects described previously but do not prevent ovulation. It must be emphasized to the adolescent that contraceptive efficacy is limited and that pregnancy may occur if a dose is skipped or if the pill is not taken at the same time every day.

Noncontraceptive Benefits of the Combined OCP

Besides providing contraception, the combined OCPs have many other uses. They are helpful in treating dysfunctional uterine bleeding, dysmenorrhea, acne, hirsutism, polycystic ovary syndrome, and irregular menses. The combined OCPs decrease the risk of uterine and ovarian cancer.

Initiation of the Combined OCP

Adolescents do not need a pelvic examination to have birth control initiated. Routine preventive measures such as screening for sexually transmitted infections using urine or cervical nucleic acid amplification tests and performing Papanicolaou smears (3 years after sexual activity is initiated or at age 21 years) are important for all sexually active adolescents. A history, blood pressure measurement, and negative urine pregnancy test are sufficient to decide if OCPs can be initiated safely. Education about appropriate use, missed pills, and adverse effects must be given. The use of condoms should be

encouraged in conjunction with the pill to prevent transmission of sexually transmitted infections. Initial follow-up should be 6 weeks to 2 months after the initiation of therapy to monitor adverse effects and proper use of the OCP. Subsequent follow-up may be every 6 to 12 months, depending on age and compliance.

Misperceptions About OCPs

Adolescents require intense education and ongoing counseling for initiation and continuation of hormonal contraception. Misperceptions are common among adolescents and may result in reduced compliance. Many adolescents are concerned that OCPs cause weight gain or acne. Although they may increase appetite, they do not cause the documented weight gain associated with other forms of contraception, such as depot medroxyprogesterone acetate. Counseling about diet and exercise can aid in assuring that unnecessary weight gain does not occur. Mood changes are rare; if they do occur, they most often are associated with the progestin component. If this effect becomes a concern, the type of progestin can be varied. Finally, acne improves during OCP therapy. Most adolescents tolerate OCPs well, experiencing few adverse effects. Clinicians should feel comfortable reassuring the adolescent that OCPs are a safe, effective, and easy form of birth control.

Newer Oral Contraceptives Extended-cycle Regimes

New research has found that women can take continuous monophasic pills with good efficacy but without undergoing a withdrawal “bleed” every month. In 2003, the FDA approved the first extended-cycle regime containing 150 mcg of levonorgestrel (LNG) and 30 mcg of EE (Seasonale[®], Duramed Pharmaceuticals, subsidiary of Barr Pharmaceuticals Inc, Pomona, NY). This combination provides 84 days of active hormone tablets followed by 7 inactive ones, creating an extended cycle of 91 days and giving the user only four “menstrual” periods a year. Adverse effects that occur because of hormone withdrawal are reduced, such as premenstrual symptoms, headaches and migraines, mood changes, and heavy or painful monthly bleeding. An initial increase in the incidence of breakthrough bleeding is noted, but this effect improves after the first 6 months of use.

Lybrel[®] (Wyeth, Philadelphia, Pa.) is a new combination OCP that is the first extended-cycle oral contraceptive designed to supply hormones every day of the year. This formulation causes a complete cessation of menstruation for an entire year. Each pill contains 90 mcg of

LNG and 20 mcg of EE. The preparation is considered a low-dose, continuous, noncyclic combination OCP. However, any monophasic pill may be taken continuously for 2 or more months by omitting the inert pills in the pack.

Low-dose Formulations

Low-dose OCPs containing 20 to 35 mcg of EE have become popular over the past few years. These agents likely have reduced the incidence of major (eg, thromboembolic events) and minor adverse effects such as nausea and headaches without affecting contraceptive efficacy. However, some of the 20-mcg OCPs have been associated with poor cycle control because of the low dose of EE and the progestin chosen. New formulations containing a 24-day active and a 4-day placebo regimen also have been approved recently by the FDA and include Yaz[®] (Bayer Health Care Pharmaceuticals, Tarrytown, NY), which contains 3.0 mg drospirenone and 0.02 mg EE, and Loestrin 24[®] (Warner Chilcott, Rockaway, NJ), which contains 1 mg norethindrone acetate, 0.02 mg EE, and ferrous

In one clinical trial, women were more likely to use the patch correctly in 89% of cycles compared with proper usage in only 68% of cycles in OCP users.

fumarate. These combinations offer the advantage of reduced days of bleeding with a low dose of estrogen.

Desogestrel Progestin-only OCP

A new POP containing 75 mcg of desogestrel has been developed recently and is available in Europe and Latin America. This agent prevents pregnancy by thickening cervical mucus and inhibiting ovulation, can be taken up to 12 hours late without reducing contraceptive efficacy, and has a failure rate of 0.2 pregnancies per 100 women.

The Chewable Pill

Femcon Fe[®] (Warner Chilcott, Rockaway, NJ), containing 0.4 mg norethindrone and 35 mcg EE, is the first chewable pill on the market. It has a spearmint flavor, is as effective as other OCPs, and is believed to be more acceptable to young women who find it hard to swallow pills.

Transdermal Contraception

The contraceptive patch is the only transdermal contraception available. This formulation allows permeation of estrogen and progesterone directly through the skin, with elimination of first-pass hepatic circulation. The first contraceptive patch to be approved for use in the United States by the FDA was Ortho Evra[®] (Ortho-McNeil Pharmaceuticals, Raritan, NJ) in November 2001. This preparation's overall failure rate varies from 0.3% to 8% with perfect and typical use, respectively, in the first year of use. Evidence suggests that the patch is less efficacious in heavier women (>90 kg), possibly because heavier women metabolize hormones more rapidly or do not absorb the hormone as well.

Description and Method of Use

Ortho Evra[®] is a 20-cm² patch that contains 6 mg norelgestromin and 75 mg EE. The patch consists of a thin, matrix-type system that has three layers: the backing layer, composed of a translucent flexible polyester film; a middle drug adhesive layer that contains the active components; and a clear polyester film that protects the adhesive layer during storage and is removed just before application.

The patch is worn for 7 days at a time for 3 consecutive weeks, followed by 1 week without the patch. It is estimated that 150 mcg norelgestromin and 20 mcg EE is released every day.

A single patch is said to release enough hormone to last 7 days and prevent ovulation for up to 9 days. The patch can be applied to the buttocks, upper outer arm, lower abdomen, or upper torso (excluding the breasts). Efficacy is equivalent at all sites, but a new site is recommended when a new patch is applied. The site should be free of creams, oils, and cosmetics. Adolescents using this method may participate in regular activities, including exercise, bathing, swimming, and use of a whirlpool or sauna.

Fewer than 5% of patches had to be replaced because of partial or complete detachment in more than 70,000 patches worn. If the patch becomes detached, the same one may be reapplied or a new patch must be applied immediately to maintain hormone concentrations and efficacy. The patch subsequently is changed on the regular change day. If the adolescent is unaware of the amount of time that has lapsed since the patch became detached, she must use a new one and start the cycle again. Efficacy cannot be guaranteed in that circumstance.

Compliance and Adverse Effects

In one clinical trial, women were more likely to use the patch correctly in 89% of cycles compared with proper usage in only 68% of cycles in OCP users. The adverse effects of the patch reported most commonly were skin irritation and rash at the site of application, which could be mild or moderate but were a cause of discontinuation. Patch users also reported a higher incidence of breast symptoms (discomfort, engorgement, or pain) and dysmenorrhea than did OCP users. For most, the breast symptoms subsided after 3 months of use. Breakthrough bleeding was reported in the first month of use in about 18% of users, but this effect declined after the second month and was not significantly different from the experience in the OCP users. Contraindications to the patch are the same as those with other combined hormonal contraception, such as the OCP, although there are some differences in pharmacokinetics.

Recent Issues With the Contraceptive Patch

The FDA issued a warning in November 2005 stating that a woman using the Ortho Evra[®] patch was exposed to 60% more total estrogen in her blood compared with someone taking a 35-mcg OCP. In this warning, the FDA stated that increased exposure to estrogen might increase the risk of blood clots but that it was unknown whether contraceptive patch users actually were at increased risk of experiencing serious adverse effects. This concern resulted in a bolded warning in the package insert stating, “In general, increased estrogen exposure may increase the risk of adverse events. However, it is not known whether there are changes in the risk of serious adverse events based on differences in pharmacokinetic profiles of EE in women using Ortho Evra[®] compared with women using oral contraceptives containing 35 mg of EE.”

Newer Transdermal Methods

Several new transdermal methods are in various stages of development. The Population Council, an international, nonprofit, nongovernmental organization that focuses on reproductive health research, and an Australian pharmaceutical company are collaborating on the development of the first contraceptive spray for women that uses the fourth-generation progestin Nestorone[®] (Population Council, New York, NY). This versatile synthetic hormone is appropriate for use by breastfeeding women. The agent is not active when administered orally, but it can be used in rings, patches, gels, and implants. The spray-on approach allows for the transfer of a preset dose of the fast-drying hormone onto the skin that is absorbed

almost instantaneously, so there is no risk of it being washed off. The hormone is said to collect in the skin and be released slowly into the blood stream.

Injectable Contraceptives

Progestin-only Injectable Contraception Description and Method of Use

Depot medroxyprogesterone acetate (DMPA) was approved for use by the FDA in 1992 and is the primary injectable contraceptive available in the United States (Depo-Provera[®], Pharmacia & Upjohn Co, Division of Pfizer, Inc, New York, NY). It is a progestin-only contraceptive agent injected intramuscularly every 3 months in a dose of 150 mg that provides 3 months of contraception. The agent acts by inhibiting ovulation, thickening the cervical mucus, and thinning the endometrium to prevent implantation. It is extremely effective as a contraceptive agent, with only 0.3% to 3% of women experiencing pregnancy in the first year of use with perfect and typical use, respectively. The depot preparation does not depend on user compliance for efficacy and can be used privately. Because it does not contain estrogen, it can be used by women in whom estrogen is contraindicated.

Compliance and Adverse Effects

Discontinuation rates for DMPA are exceedingly high, with 33% of adolescents choosing not to receive a second injection at 3 months, and of those continuing, 75% discontinuing by 12 months. The primary adverse effects are menstrual irregularities, weight gain, and reduction in bone mineral density. Weight gain is one of the most important reasons for discontinuing DMPA, occurring in 54% of adolescents and cited as a reason for discontinuation by 41%. Some evidence shows that being overweight at the initiation of DMPA may result in greater weight gain and that African Americans tend to have significant increases in weight and body fat during the first 6 months of DMPA usage compared with white adolescents.

Concerns have been raised regarding DMPA usage and its effects on bone mineral density (BMD). Several prospective studies have shown that adolescents who use DMPA experience a relative loss of BMD compared with those not using hormonal contraception. Such bone density changes are of particular concern because bone mass accrual is highest during pubertal years. However, several other studies have shown a high degree of recovery in BMD upon discontinuation of DMPA, and others have documented a relative loss of BMD in teenagers who become pregnant.

In November 2004, the FDA introduced a “black box” warning stating that prolonged use of the drug may result in significant loss of bone density, that the loss is greater the longer the drug is administered, and that the loss may not be completely reversible. The position paper of the Society for Adolescent Medicine on this matter, however, stated that DMPA is an extremely effective contraceptive agent and that the clinical concern of loss in BMD must be placed within the context of likely bone recovery on discontinuation, low risk of fractures, and the benefits of preventing the consequences of unintended pregnancy in adolescents (Cromer et al, 2006). The Society believes, however, that adolescents and their parents should be made aware of these risks during contraceptive counseling.

New Subcutaneous DMPA Formulation

Subcutaneous DMPA was approved by the FDA in December 2004 under the name depo-subQ Provera 104™ (Pharmacia and Upjohn Company, Division of Pfizer, Inc, New York, NY). This preparation contains 104 mg of MPA compared with the 150 mg currently available in the intramuscular injection. The subcutaneous route, also administered every 3 months, provides slower and more sustained absorption of the DMPA and is as efficacious in preventing ovulation as the intramuscular injection. The subcutaneous injection is less painful and available only in a prefilled syringe, offering a potential for self-administration and, thus, increased compliance.

Combined Injectable Contraception

Combined injectable contraceptives contain both a progestin and an estrogen. These combinations are injected once a month in contrast to the progestin-only contraceptives that are administered once every 2 to 3 months, such as norethindrone enanthate and DMPA. Combined injectables became more popular than the progestin-only injectables among both patients and clinicians because of their reduced propensity to cause adverse effects such as irregular bleeding and weight gain and because they allowed a quicker return to fertility. In 2000, the FDA approved Lunelle® (Pharmacia, New York, NY), which contained 25 mg of MPA and 5 mg of estradiol cypionate, for use in the United States. Lunelle® was removed from the market by the manufacturer in 2002 because of concerns that there may not have been enough medication in the syringe to prevent pregnancy. However, other similar injectables, such as Cyclofem® (The Upjohn Company, New York, NY), Cyclo-Provera® (The Upjohn Company, New York, NY), and

Feminena® (The Upjohn Company, New York, NY), continue to be available in other parts of the world.

Vaginal Rings

Description and Method of Use

The combined formula vaginal ring, NuvaRing® (Organon USA, Inc, Roseland, NJ), was approved for use in the United States by the FDA in 2001. This formulation is unique in that, like the contraceptive patch, it does not depend on daily compliance. At the same time, unlike the patch, the ring is not visible to the eye and caters to the adolescent’s desire to have something that is not visible and often stigmatizing yet is effective as a contraceptive method.

NuvaRing® consists of a hormone-containing silicone ring that has an outer diameter of 5.4 cm and a cross-sectional diameter of 0.4 cm. It releases 120 mcg of the progestin etonogestrel, a biologically active metabolite of desogestrel, and 15 mcg of the estrogen EE per day. The hormones for contraception are implanted in the core of the ring and are released slowly and constantly into the vagina, subsequently passing into the general circulation.

The ring is flexible and easy to insert. Use of a tampon applicator can make it easier to place. The user inserts the ring into the vagina, placing it anywhere that feels comfortable, usually on the last day of her menstrual period. The ring remains in place all day and night and requires no additional attention. It is removed 3 weeks later and a withdrawal bleed ensues, resulting in a menstrual period. A new ring is inserted 1 week later. If it slips out, it may be reinserted after washing in lukewarm water. According to the manufacturer, the ring can be removed for up to 3 continuous hours without loss of efficacy.

Combined rings release enough estrogen and progestin to prevent ovulation. They also act by thickening cervical mucus and suppressing endometrial growth. Studies have found that the ring has failure rates that vary from 0.3% to 8% per woman during the first year of perfect and typical use, respectively.

Compliance and Adverse Effects

Compliance was found to be more than 90% over a 1-year period. Irregular bleeding was reported as an adverse effect but less so compared with OCPs. Adverse effects reported most commonly were vaginitis (14%), headache (12%), leukorrhea (6%), nausea (5%), and vaginal discomfort (4%). The most common causes for discontinuation were device-related events such as expulsion, foreign body sensation, and coital-related events.

New Vaginal Rings

Another ring consisting of a combination of 150 mcg of Nestorone[®] progestin and 15 mcg of EE per day is being developed by the Population Council and will be effective for more than 12 months. Users would keep the ring in place for 3 weeks, remove it for 1 week, and reinsert the same ring for another 3 weeks.

Two progestin-only rings are being developed. One contains the natural hormone progesterone and the other employs the synthetic progestin Nestorone[®]. These preparations are highly effective in lactating women and do not contain estrogen, which may impair milk production.

Subdermal Contraceptive Implants

Description and Method of Use

Subdermal implants are devised for women who are seeking a reliable and reversible method of contraception that does not require daily compliance and that provides protection from pregnancy for 1 to 5 years. These products are available as hormone-containing rods or capsules and are inserted surgically below the skin. All available implants are progestin-only and, thus, can be used by women in whom estrogen is contraindicated. After removal of the implant, return to fertility occurs promptly, compared with DMPA preparations, after whose use women may take up to 10 months to conceive.

Two types of implants are in use around the world. Norplant[®] (Wyeth-Ayers Pharmaceuticals, Philadelphia, Pa.) is no longer available in the United States but was the first subdermal system, consisting of six rodlike silicone capsules containing hormone. The newer version of Norplant[®] consists of only two rods and is called Norplant-2[®] or Jadelle[®] (Leiras Pharmaceuticals, Turku, Finland). This implant provides protection for 5 years.

The second type of implant consists of rods that have a matrix carrying the active hormone. The matrix is covered by a thin membrane that allows release of the hormone into the surrounding tissue and subsequently into the circulation. Implanon[™] (Organon USA Inc, Roseland, NJ) is such a single-rod system that contains the progestin etonogestrel and provides contraception for 3 years of use. Insertion of single-rod systems is much easier, with the devices being preloaded and disposable and removal often requiring only a 2-mm skin incision and some finger pressure. Implanon[™] has been ap-

proved by the FDA and is available for use in the United States. Clinicians must complete training for insertion.

At higher concentrations, as in the first few years of usage, LNG suppresses ovulation. Although ovulation is inhibited, the concentrations of hormone do not suppress follicular activity, so estrogen concentrations remain almost normal. Thus, there is less concern about effects on lipoproteins and BMD. At lower concentrations, LNG exerts its contraceptive action by thickening the cervical mucus, which prevents the penetration of sperm. Implanon[™] users, however, have few, if any, ovulatory cycles, and the chances of women experiencing an unintended pregnancy are 0.05% in the first year of both typical and perfect use.

Compliance and Adverse Effects

As with other progestin-only contraceptive agents, irregular bleeding is a common adverse effect and often leads to discontinuation. However, such bleeding usually diminishes with continued use; many women regain regu-

All available implants are progestin only and, thus, can be used by women in whom estrogen is contraindicated.

lar bleeding patterns after 6 to 9 months of use. Although insertion and removal were problems associated with older implants, newer implants such as Implanon[™] can be administered by using a preloaded disposable applicator and take less than 1 minute to insert.

New Implantable Devices

The Nestorone[®] implant is being developed by the Population Council and consists of a single rod made of a silicon rubber membrane that controls hormone release. It is suitable for lactating women and is said to be effective for 2 years. Studies have shown no detectable progestin in the blood of breastfeeding infants whose mothers are using this implant.

A biodegradable implant has a matrix made of a biodegradable material that is firm enough to be implanted. The matrix slowly degrades, simultaneously releasing the drug until it is completely used. Two such implants are being developed: one rod-shaped one containing LNG called Capronor[™] (Spherics, Inc, Lincoln,

RI), and another that has biodegradable pellets containing norethindrone or norgestimate that are injected subcutaneously. If successful, these devices would alleviate the discomfort of implant removal while providing the effective, long-term, nonuser-dependent contraception that adolescents desire.

LNG-releasing Intrauterine Contraceptive System

Description and Method of Use

The LNG-releasing intrauterine system (LNG IUS) has been approved for use in the United States for up to 5 years of use. The system consists of a 32-mm T-shaped polyethylene frame that has a cylinder wrapped around its stem. The cylinder contains 52 mg of LNG mixed with polydimethyl siloxane, which allows slow release of the hormone through the surface membrane. The amount of LNG released decreases from 20 mcg to 14 mcg every 24 hours from the first to the end of the fifth year. The device is impregnated with barium sulfate to make it readily visible on radiography and ultrasonography.

The mechanism of action of this device is primarily local. LNG is released locally and exerts its contraceptive effect by thickening cervical mucus to reduce sperm penetration, inhibiting sperm motility and function, and causing endometrial atrophy. The system suppresses ovulation in only 25% to 50% of users and, like other intrauterine devices (IUDs), also may induce a foreign body reaction that causes localized inflammation. Return to fertility is rapid after removal of the IUS.

The recommendations for this IUS are similar to those for other copper-bearing IUDs. It is recommended for parous women who have no history of pelvic inflammatory disease (PID) and are in stable, monogamous relationships. The size of the uterus should be assessed before insertion; the cavity should be 6 to 9 cm in length and unobstructed. Although being nulliparous is not a contraindication, it is recommended that women whose fertility is uncertain be counseled that although there is a rapid return to fertility following removal of the LNG IUS, there is no guarantee of the ability to conceive.

The WHO recommends that the LNG IUS be inserted within 7 days of commencement of menses, 4 or more weeks postpartum (if it can be determined a woman is not pregnant), and immediately after an abortion. They do not recommend prophylactic antibiotics. WHO also states that women who are at high risk for PID are not good candidates, but those who have had PID and have demonstrated their fertility may use the LNG IUS if they currently are at low risk for sexually transmitted

infections. This device may be used in adolescents who have heavy periods because it reduces the menstrual flow.

Contraindications are similar to those for other IUDs, including a specific contraindication for women who have a past history of or are at continuing risk for ectopic pregnancy.

Insertion of the IUS requires training but is fairly straightforward. It is inserted with the help of an applicator, involving a one-hand technique that allows continuous control of the uterine position of the device throughout the procedure.

The device is extremely efficacious as a contraceptive agent; pregnancy rates are comparable with those of female sterilization. It has a first-year failure rate of 0.2 pregnancies per 100 women with both typical and perfect use, and 80% of women choose to continue it at the end of their first year of use.

Compliance and Adverse Effects

Bleeding disturbances are common in the first 1 to 4 months after insertion, but the subsequent topical effect of the hormone results in endometrial atrophy and a reduction in intermenstrual bleeding. Over time, this contraceptive method causes less bleeding compared with a copper-bearing IUDs. Amenorrhea occurs by 1 year in 20% to 50% of users, which often is an advantage for adolescents who have menorrhagia. Other adverse effects include acne, dizziness, headaches, breast tenderness, nausea, vomiting, weight gain, and ovarian cysts. The chances of ectopic pregnancy are less than 1 per 1,000 women-years of use, slightly less than that of a copper-containing device.

Emergency Contraception

Description and Method of Use

Emergency contraception (EC), although not an ideal form of contraception, should be available to all adolescents. Use of contraceptives by adolescents is increasing and pregnancy rates are falling, but 8 of 10 adolescent pregnancies are unintended. EC should be available to any woman who is exposed to the risk of pregnancy, including failure or nonuse of contraceptive methods; broken condoms; delayed withdrawal; displaced diaphragms; and incorrect use of the contraceptive patch, ring, or OCP. All victims of sexual assault should be offered EC.

Hormonal methods of EC include POPs, combined oral contraceptives, and mifepristone (not available in the United States). The copper-releasing IUD also may be used for EC. Progestin-only EC (Plan B[®], Duramed Pharmaceuticals, Inc, Subsidiary of Barr Pharmaceuti-

als, Pomona, NY) consists of two tablets (0.75 mg each) of LNG administered 12 hours apart. The recommendation by the FDA is to use the first tablet as soon after unprotected intercourse as possible, but within 72 hours, and the second tablet 12 hours later. Recent studies have shown that EC via Plan B[®] is effective up to 120 hours after unprotected intercourse. Another study has demonstrated that administration of two tablets of LNG at the same time is as efficacious as taking the two 12 hours apart and may be better for adolescents, who may forget to take the second dose.

The “Yuzpe regime” involves the use of combined OCPs for the purpose of EC. The primary drawback of this method is that a large number of pills need to be taken, with resultant nausea and vomiting attributable to their estrogen content. Often, an antiemetic preparation also is prescribed and should be taken about 30 to 60 minutes before the first dose.

Mechanisms of action of both combination and progestin-only EC involve delaying or inhibiting ovulation, disrupting follicular development, or interfering with the maturation of the corpus luteum. There is no evidence of effects on implantation or postovulatory events.

Mifepristone is an antiprogesterin agent that blocks the binding of progestin to its receptor, thus preventing ovulation or disrupting the luteal phase of the menstrual cycle. When given in a dose of 10 mg within 120 hours of unprotected intercourse, it is as efficacious as Plan B[®], but this agent is not available in the United States.

Efficacy rates of EC depend on whether combined OCPs or POPs are used. The efficacy of EC that has LNG is 1.1% and that of the Yuzpe regime is 3.2%. The earlier the treatment is initiated, the more likely it is to prevent pregnancy. In general, treatment initiated within 72 hours of unprotected intercourse reduces the risk of pregnancy by at least 75%. The odds of pregnancy are increased by 50% if the first dose is delayed by 12 hours.

Compliance and Adverse Effects

Adverse effects are common after taking EC and are worse after the combined OCPs in the Yuzpe regime compared with the POPs. With the latter, rare adverse effects are headache, fatigue, nausea, and dizziness reported in the first week after taking the EC. With the combined OCPs, estrogen-related symptoms are more common and include nausea, vomiting, breast tenderness, and headache. Most of the symptoms are half as common in those taking POPs compared with those taking combined OCPs. Vaginal spotting also can occur with both.

Contraindications to use of POPs are allergy, pregnancy, and undiagnosed genital bleeding. However, there is no evidence that inadvertent use of EC during pregnancy interrupts a pregnancy after implantation or acts as a teratogen.

Role of Primary Care Practitioners

Primary care practitioners play an extremely important role in the care of the adolescent and preadolescent. They have the opportunity to counsel preteens and address concerns about adolescent sexuality at the annual office visit, before young people venture into the unknown and often dangerous realm of adolescence. The Guidelines for Adolescent Preventive Services, developed by the American Medical Association and supported by both the American Academy of Pediatrics and the Society for Adolescent Medicine, recommend, “All adolescents should receive health guidance annually regarding responsible sexual behaviors, including abstinence. Latex condoms to prevent sexually transmitted diseases (including HIV infection) and appropriate methods of birth control should be made available with instructions on ways to use them effectively” (Elster and Kuznets, 1994). Practitioners also need to counsel adolescents about the necessity of condom use during anal and vaginal intercourse as well as when practicing oral sex.

The primary care practitioner should be aware that teens often do not seek care until at least 6 months, and more often 1 year, after initiation of intercourse, and about 50% conceive within 6 months of first intercourse.

Adolescent developmental issues influence the initiation of contraception. The early adolescent is a concrete thinker, which limits his or her ability to make certain decisions and choices for the future. Most contraception requires some planning, which does not happen if one cannot predict the possibility of sexual activity. External barriers also may preclude adolescents from timely use of effective contraception and include, but are not limited to, access to a suitable clinic, lack of confidential care, fear of disapproval by parents and practitioners, absence of adolescent-friendly services, language and cultural barriers, fear of a pelvic examination, and issues of reimbursement and cost. Misconceptions about contraception concerning weight gain, future fertility, acne, and risk of cancer also may prevent adolescents from using effective hormonal contraception. These concepts often are perpetuated by peers, partners, and sometimes, by family members and Internet sources.

Hormonal contraception has progressed from the initial high-dose OCP to currently developing biodegradable implants. The types of hormones used, the

doses used, and the modes of administration have changed, with an aim to decrease adverse effects, improve acceptability, and ensure compliance. No matter how effective a method and how easy its administration, detailed contraceptive counseling is required for adolescent patients to bring pregnancy prevention results closer to the ideal.

Clinicians must educate themselves about all available options to help their adolescent patients make informed choices about what would suit them and their lifestyles best. They also must try to improve communication between teens and their parents, at the same time ensuring confidentiality. Being familiar with the developmental stages of their patients and with commonly held misconceptions and barriers to care can help clinicians develop rapport with their patients. Practitioners also should recommend the new quadrivalent human papillomavirus vaccine to both preteens and adolescent patients. Finally, none of the hormonal methods discussed is effective against sexually transmitted infections and human immunodeficiency virus. In the sexually active adolescent, condoms continue to be the most effective method of protection against both pregnancy and sexually transmitted infections and should be used during anal as well as vaginal intercourse.

Summary

- Evidence shows that 80% of adolescent pregnancies are unintended.
- Evidence shows that the OCP is an effective form of contraception in adolescents but may be less efficacious in adolescents compared with adults.
- The efficacy of a contraceptive method in adolescents is improved if the method does not require daily compliance.
- Evidence shows that contraceptive methods that have more adverse effects, especially irregular bleeding, are less acceptable to the adolescent user.
- Evidence shows that misperceptions about contracep-

tion as well as the presence of internal and external barriers may prevent effective use of contraception by adolescents.

- Evidence shows that the earlier emergency contraception is used, the more effective it is in preventing pregnancy.

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PIR Quiz

Quiz also available online at www.pedsinreview.aappublications.org.

6. Oral contraception pills (OCPs) contain estrogen and progestin or progestin only. Among the following, the progestin preparation that is *most* beneficial for patients who have polycystic ovary syndrome is:
 - A. Drospirenone.
 - B. Ethynodiol diacetate.
 - C. Levonorgestrel.
 - D. Norethindrone.
 - E. Norgestimate.

7. Although estrogen and progestin share many adverse effects, which of the following is *most* likely to be caused by progestin?
 - A. Breast tenderness.
 - B. Headache.
 - C. Increased appetite with weight gain.
 - D. Menstrual irregularities.
 - E. Nausea.

8. Which of the following is a class 4 contraindication to the use of OCPs?
 - A. Breastfeeding 4 months postpartum.
 - B. Chronic antifungal therapy.
 - C. Gallbladder disease.
 - D. History of stroke.
 - E. Tension headaches.

9. Discontinuation rates among users of depot medroxyprogesterone acetate are very high. Among the following, the *primary* reason for discontinuation is:
 - A. Comedonal acne.
 - B. Decreased bone mineral density.
 - C. Menstrual irregularity.
 - D. Pain at injection site.
 - E. Weight gain.

10. Progestin-only emergency contraception is recommended within 72 hours of intercourse, taken as two tablets of levonorgestrel 12 hours apart. Recent studies have shown that the two tablets can be taken together as a single dose as long after intercourse as:
 - A. 48 hours.
 - B. 72 hours.
 - C. 96 hours.
 - D. 120 hours.
 - E. 168 hours.

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