Chapter 104: Contraception

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KEY CONCEPTS

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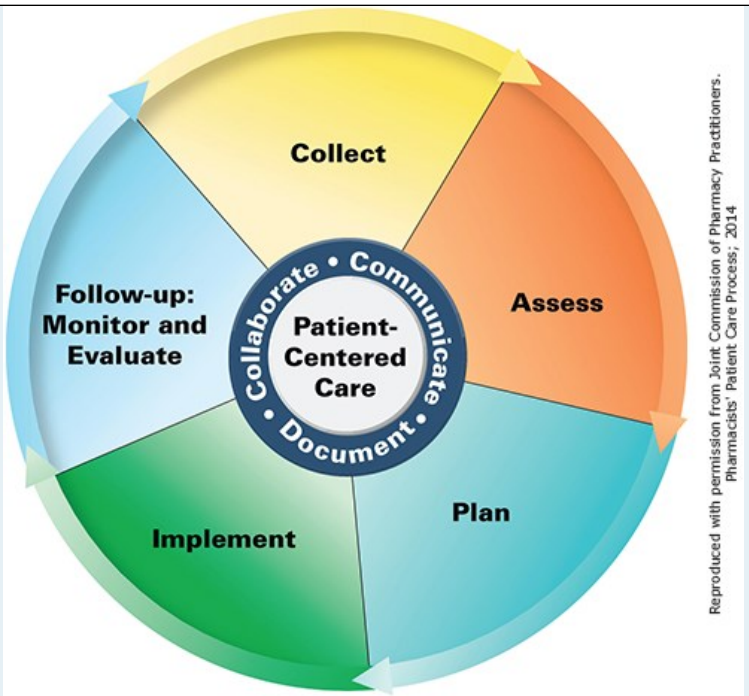
1. Unintended pregnancy is a public health issue. A majority of unintended pregnancies occur due to inconsistent use or nonuse of contraceptives.
2. Contraception implies the prevention of pregnancy; however, some hormonal contraceptives may also provide noncontraceptive benefits.
3. When selecting a contraceptive method consider the following: the effectiveness of the method, its noncontraceptive benefits and adverse medication effects, attitude of the patient and sexual partner toward a contraceptive method, the ability to use it correctly (which may alter its effectiveness), and the ability to pay for the method.
4. Patient-specific factors (eg, frequency of intercourse, age, smoking status, desire for return to fertility, concomitant diseases, medications, contraceptive method preference, and medication interactions) must be evaluated when selecting a contraceptive method.
5. A variety of contraceptive methods are available. Nonhormonal methods include fertility awareness, barriers, spermicides, and the copper intrauterine device. Hormonal methods include progestin-only or combination of estrogen/progestin products.
6. Adverse effects or difficulties in using the selected method should be monitored carefully and managed in regard to patient-specific factors.
7. Some medications may alter the effects of hormonal contraceptives or vice versa; therefore, concomitant medications should be assessed for medication interactions with hormonal contraceptives.
8. Accurate and timely counseling on the management of missed doses is critical for contraceptive effectiveness.
9. Counseling on the optimal use of the contraceptive method and strategies for minimizing sexually transmitted infections/diseases (STIs/STDs) must be provided to all patients being initiated on contraceptives and also for those using contraception on an ongoing basis.
10. Emergency contraception (EC) may prevent pregnancy after unprotected intercourse or when regular contraceptive methods have failed.
11. Mifepristone and misoprostol may be used in regimens for medical abortion.

PATIENT CARE PROCESS

Patient Care Process for Contraception



Collect

- Patient characteristics (eg, age, sex, date of last menstrual period, pregnant, recently postpartum, breastfeeding, desire for pregnancy/return to fertility)
- Patient medical history (personal and family)
- Medication allergies
- Social history (eg, tobacco/ethanol use, relationships, sexual history)
- Current medications including over-the-counter (OTC), herbal products, dietary supplements
- Previous or current use of contraceptives
- Objective data: BP, height, weight

Assess

- Pregnancy status
- Effectiveness of previous contraceptive methods used (Tables 104-1 and 104-2)
- BP
- Weight and optimal method for use
- Precautions and contraindications to various types of contraceptives utilizing the CDC Medical Eligibility for Contraceptive Use, 2024 (see Table 104-6)
- Venous thromboembolism (VTE) risk factors (eg, recent surgery, plaster casting of lower extremity, cancer, prolonged immobility, recent hospitalization, recently postpartum)
- Medication interactions with various forms of contraception (see Table 104-6 for a select listing of medication interactions)

- Patient ability/willingness to use, adhere, or pay for various forms of contraception (Tables 104-1 and 104-2)

Plan*

- Medication therapy regimen including specific contraceptive dosage forms, dose, route, frequency, and duration (see Table 104-3 for select examples)
- Monitoring parameters including effectiveness and safety (eg, ACHES [abdominal pain, chest pain, headaches, eye problems, and severe leg pain]) (Tables 104-4 and 104-5)

Implement*

- Provide patient education regarding all elements of contraceptive plan (eg, adherence, missed doses, adverse medication effects)
- Schedule appropriate follow-up to assess adverse medication effects, adherence issues, access to contraceptive

Follow-up: Monitor and Evaluate

- Presence of adverse effects (Tables 104-3, 104-4, and 104-5)
- For intrauterine devices (IUDs), appropriate placement (eg, checking for strings)
- Changes in medical history (eg, increase in BP, migraines, VTE risk, body mass index [BMI], new medications)
- Patient adherence to treatment plan using multiple sources of information

****Collaborate with patient, caregivers, and other healthcare professionals.***

BEYOND THE BOOK

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Watch the video entitled "The Menstrual Cycle" (https://www.youtube.com/watch?v=7HlHGLr1hTA) on YouTube from Osmosis. This is a 11-minute video that gives an overview of the menstrual cycle and discusses the cycle phases, ovulation, and the hormones involved. This video is helpful in serving as a quick refresher of the menstrual cycle physiology. A clear understanding of the menstrual cycle is important to understand the mechanisms of action for contraceptive products.

INTRODUCTION

[1]Unintended pregnancy is a significant public health issue. In the United States, approximately 5.5 million individuals become pregnant each year. About 42% of pregnancies are unintended, with the highest rates occurring in individuals aged 20 to 24 years, and in individuals aged 15 to 19 when taking into account only sexually active persons. About 34% of all unintended pregnancies end in abortion, and 41% occur in sexually active couples who claim they used some method of contraception. Education on the use and effectiveness of contraceptive methods must be improved and provided, if the goal of contraception, for all pregnancies to be planned and desired, is to be realized. While cis-women are the primary users of hormonal contraception, these preparations may also be used by transgender individuals, and thus, this chapter is written with this in mind.

EPIDEMIOLOGY

[2,3]Contraception implies the prevention of pregnancy by two methods: first by inhibiting viable sperm from coming into contact with a mature ovum (ie, methods that act as barriers or prevent ovulation) and second, by preventing a fertilized ovum from successfully implanting in the

endometrium (ie, mechanisms that create an unfavorable uterine environment). These methods differ in their relative effectiveness, safety, and patient acceptability (Tables 104-1 and 104-2).

TABLE 104-1

Pregnancy and Continuation Rates for Various Pharmacologic Contraceptive Methods

Method	Pregnancy Typical Use	Pregnancy Ideal Use	Continuation After 1 Year
Combined and progestin-oral contraceptive	7%	<1%	67%
• Drospirenone-only contraceptive	4%	–	–
Combined hormonal transdermal contraceptive patch			
• Norelgestromin/ethinyl estradiol	7%	<1%	–
• Levonorgestrel/ethinyl estradiol	3%	–	–
Combined hormonal vaginal contraceptive ring			
• Etonogestrel/ethinyl estradiol	7%	<1%	–
• Segesterone/ethinyl estradiol	3%	–	–
Depo-medroxyprogesterone acetate	4%	<1%	56%
Copper IUD	<1%	<1%	78%
Levonorgestrel IUD	<1%	<1%	80%
Progestin-only implant	<1%	<1%	89%

TABLE 104-2

Comparison of Methods of Nonhormonal Contraception

				Percent of with Pregnancy[a]	
Method	Absolute Contraindications	Advantages	Disadvantages	Perfect Use	Typical Use
Condoms, external (traditionally known as male)	Allergy to latex or rubber	Inexpensive STI/STD protection, including HIV (latex only)	High user failure rate Poor acceptance Possibility of breakage Efficacy decreased by oil-based lubricants	2	13

			Possible allergic reactions to latex in either partner		
Condoms, internal (traditionally known as female)	Allergy to polyurethane History of TSS	Can be inserted just before intercourse or ahead of time STI/STD protection, including HIV	High user failure rate Dislike ring hanging outside vagina Cumbersome	5	21
Diaphragm with spermicide	Allergy to latex, rubber, or spermicide Recurrent UTIs History of TSS Abnormal gynecologic anatomy	Low cost Decreased incidence of cervical neoplasia Some protection against STIs/STDs	High user failure rate Decreased efficacy with increased frequency of intercourse Increased incidence of vaginal yeast UTIs, TSS Efficacy decreased by oil-based lubricants Cervical irritation	16	17
Cervical cap (FemCap)	Allergy to spermicide History of TSS Abnormal gynecologic anatomy Abnormal papanicolaou smear	Low cost Latex-free Some protection against STIs/STDs FemCap reusable for up to 2 years	High user failure rate Decreased efficacy with parity Cannot be used during menses	22	22[b]
Spermicides/Vaginal pH modulator alone (various nonoxynol-9/Phexxi)	Allergy to spermicide/vaginal pH modulator	Inexpensive	High user failure rate Must be reapplied before each act of intercourse May enhance HIV transmission No protection against STIs/STDs	12	21[c]
Sponge (Today)	Allergy to spermicide Recurrent UTIs History of TSS Abnormal gynecologic anatomy	Inexpensive	High user failure rate Decreased efficacy with parity Cannot be used during menses No protection against STIs/STDs	12[d]	17[e]

HIV, human immunodeficiency virus; STI/STD, sexually transmitted infection/disease; TSS, toxic shock syndrome; UTI, urinary tract infection.

[a]Failure rates in the United States during first year of use.

[b]Failure rate with FemCap reported to be 24% per package insert.

[c]Failure rate with Phexxi reported to be 27.5% per package insert.

[d]Failure rate with Today sponge reported to be 20% in parous individuals.

[e]Failure rate with Today sponge reported to be 27% in parous females.

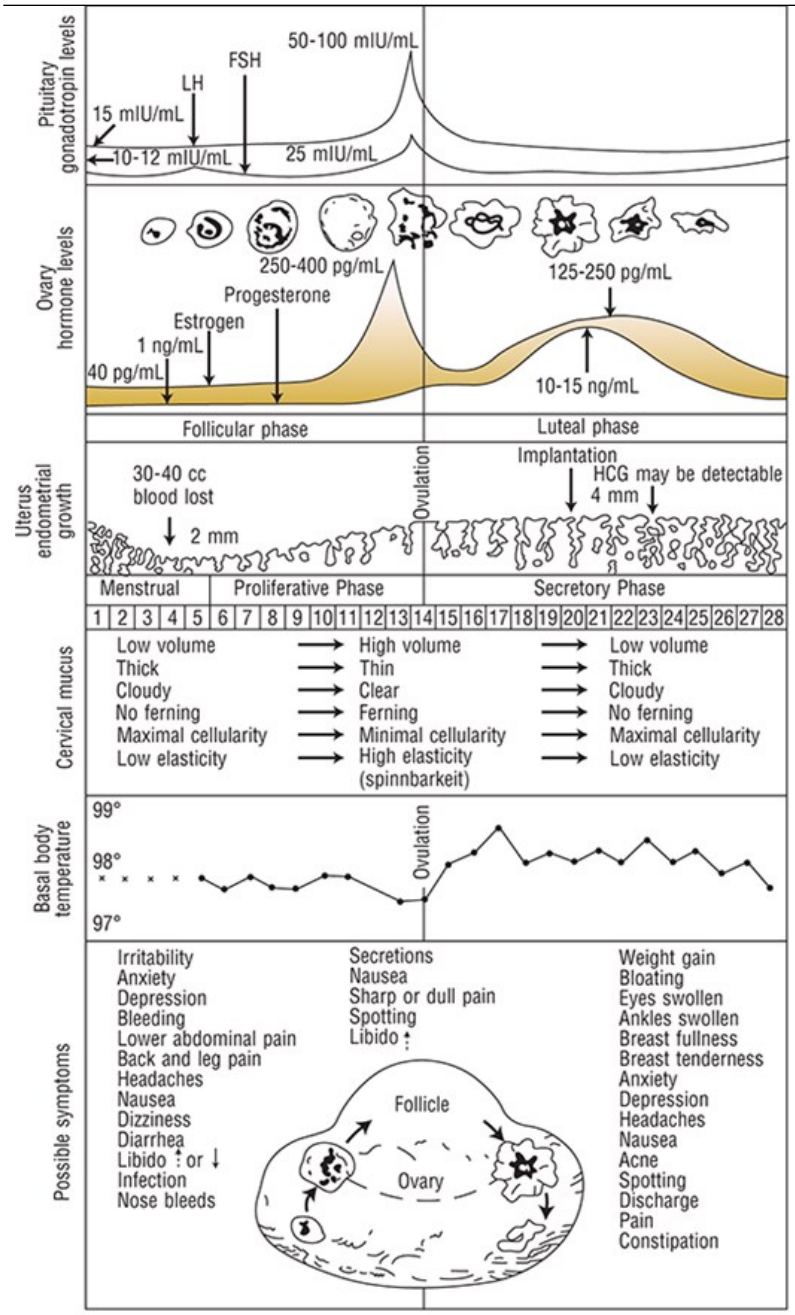
The actual effectiveness of any contraceptive method is difficult to determine because many factors affect failure (eg, patient had an unintended pregnancy). Failure rates are described as perfect-use failure or typical-use failure. A failure in a patient who used the contraceptive agent properly is considered a method failure or perfect-use failure. User failure or typical-use failure rates take into account the perfect-use failure rate plus the user's ability to follow directions correctly and consistently and is usually higher. Because the typical-use rate includes both the method and user failure rates, it is used most often.

ETIOLOGY AND PATHOPHYSIOLOGY

Comprehension of the normal menstrual cycle hormonal regulation is essential to understanding contraception (Fig. 104-1). The menstruation cycle begins with menarche, usually around age 12 years, and continues to occur in nonpregnant individuals until menopause, usually around age 50 years. Factors such as race, body weight, medical conditions, and family history can affect the menstrual cycle. The cycle concludes in the vaginal discharge of sloughed endometrium called *menses* and is comprised of three phases: (1) follicular (or preovulatory), (2) ovulatory, and (3) luteal (or postovulatory).

FIGURE 104-1

Menstrual cycle events, idealized 28-day cycle. (FSH, follicle-stimulating hormone; HCG, human chorionic gonadotropin; LH, luteinizing hormone.)



Source: Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, Lisa M. Holle, Jennifer Cocohoba, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 13th Edition*

The Menstrual Cycle

The first day of menses is referred to as *day 1 of the menstrual cycle* and marks the beginning of the follicular phase which continues until ovulation, which typically occurs on day 14. The time after ovulation is referred to as the *luteal phase*, which lasts until the beginning of the next menstrual cycle. The median menstrual cycle length is 28 days, but can range from 21 to 40 days. Generally, cycle length variation is greatest in the follicular phase, particularly in the years immediately after menarche and before menopause.

The menstrual cycle is influenced by the hormonal relationships among the hypothalamus, anterior pituitary, and ovaries. The hypothalamus secretes gonadotropin-releasing hormone (GnRH) in a pulsatile fashion which stimulates the anterior pituitary to secrete bursts of gonadotropins, follicle-stimulating hormone (FSH), and luteinizing hormone (LH). Secretion of FSH and LH directs events in the ovarian follicles that result in the production

of a fertile ovum.

Follicular Phase

In the first 4 days of the menstrual cycle, FSH levels rise and allow the recruitment of a small group of follicles for continued growth and development (see Fig. 104-1). Between days 5 and 7, one follicle becomes dominant and later ruptures, releasing the oocyte. The dominant follicle develops increasing amounts of estradiol and inhibin, which cause a negative feedback on the hypothalamic secretion of GnRH and pituitary secretion of FSH, causing atresia of the remaining follicles recruited during the cycle.

Once the follicle has received FSH stimulation, it must receive continued FSH stimulation or it will die. FSH allows the follicle to enlarge and synthesize estradiol, progesterone, and androgen. Estradiol stops the menstrual flow from the previous cycle, thickening the endometrial lining of the uterus to prepare it for embryonic implantation. It is responsible for increased production of thin, watery cervical mucus, which will enhance sperm transport during fertilization. FSH regulates the aromatase enzymes that convert androgens to estrogens in the follicle. If a follicle has insufficient aromatase, it will not survive.

Ovulation

When estradiol levels remain elevated for a sustained period of time, the pituitary releases a mid-cycle LH surge (see Fig. 104-1). This LH surge stimulates the final stages of follicular maturation and ovulation (follicular rupture and release of the oocyte). On average, ovulation occurs 24 to 36 hours after the estradiol peak and 10 to 12 hours after the LH peak. The beginning of the LH surge, which occurs about 36 hours before a follicle ruptures, is the most clinically useful predictor of approaching ovulation. After ovulation, the oocyte is released and travels to the fallopian tube, where it can be fertilized and transported to the uterus for embryonic implantation. Conception is most successful when intercourse takes place from 2 days before ovulation to the day of ovulation.

Luteal Phase

After rupture of the follicle and release of the ovum, the remaining luteinized follicles become the corpus luteum, which synthesizes androgen, estrogen, and progesterone (see Fig. 104-1). Progesterone helps maintain the endometrial lining, which sustains the implanted embryo, maintaining pregnancy. It also inhibits GnRH and gonadotropin release, preventing the new follicle development. If pregnancy occurs, human chorionic gonadotropin prevents regression of the corpus luteum and stimulates continued estrogen and progesterone secretion to maintain the pregnancy until the placenta is able to fulfill this role.

If fertilization or implantation does not occur, the corpus luteum degenerates, and progesterone production declines. The life span of the corpus luteum depends on the continuous presence of small amounts of LH, and its average duration of function is 9 to 11 days. As progesterone levels decline, endometrial shedding (menstruation) occurs, and a new menstrual cycle begins. At the end of the luteal phase, when estrogen and progesterone levels are low, FSH levels start to rise, and follicular recruitment for the next cycle begins.

CLINICAL PRESENTATION

CLINICAL PRESENTATION: Contraception

Traditionally, hormonal contraception required breast and pelvic examinations. However, the need for the physical examination may delay contraception access and reinforces the incorrect perception that these methods of contraceptives are harmful. Therefore, in practice, provision of hormonal contraception is followed after a simple medical history, including weight and BP measurement.

[3] [4] Most annual preventative medicine visits should include an assessment of and counseling about reproductive health, including contraception and STIs/STDs prevention education. Additionally, other preventive measures, such as pelvic and breast examinations, provision of the human papillomavirus vaccine, and screening for cervical neoplasia, can be accomplished during these visits.

TREATMENT

Desired Outcomes

[2]The desired goal of all conceptive methods is to prevent pregnancy. However, other health benefits are associated with various contraceptive methods, including prevention of STIs/STDs (with condoms), improvements in menstrual cycle regularity (with hormonal contraceptives), improvements in certain health conditions (with hormonal contraceptives), and management of perimenopause (with hormonal contraceptives).

General Approach to Treatment

Nonpharmacologic Therapy

Fertility Awareness-Based Methods

[3][4][5]Motivated couples may use fertility awareness-based methods that entail avoiding sexual intercourse during the days of the menstrual cycle when conception is likely to occur. These typically include calendar-based methods such as the standard days or rhythm methods. In addition, there are symptoms-based methods that are based on observed physiologic changes, such as basal body temperature and cervical mucus to determine the fertile period. There are many technology apps available for these methods and the Food and Drug Administration (FDA) approved the first app in this category (Natural Cycles) in 2018. The major drawbacks of these methods are relatively high pregnancy rates and avoidance of intercourse for several days during each menstrual cycle.

Barrier Techniques

[3][4][5][9]The effectiveness of barrier methods (eg, condoms, diaphragms, cervical caps, and sponges) depends almost exclusively on the motivation to use them consistently and correctly (see Table 104-2). Their major disadvantage is higher failure rates compared to most hormonal contraceptives; thus, provision of counseling and an advanced prescription for emergency contraception (EC) are recommended for all patients using barrier methods as their primary contraception means.

External condoms (traditionally known as male condoms) create a mechanical barrier, preventing direct contact of the vagina with semen, genital lesions, and infectious secretions. Most condoms in the United States are made of latex, which is impermeable to viruses. However, a small proportion are made from lamb intestine, which is permeable to viruses and should not be used to prevent STIs/STDs. Synthetic condoms manufactured from polyurethane are another latex-free option that protect against viruses. Condoms are used worldwide for STIs/STDs protection, including human immunodeficiency virus (HIV). When used in conjunction with any other barrier method, their effectiveness theoretically approaches 98%. Spillage of semen or perforation and tearing of the condom can occur, but proper use minimizes these problems. Mineral oil-based vaginal medication formulations (eg, Cleocin, Premarin, and Monistat), lotions, or lubricants can decrease the latex barrier strength and are not recommended, thus water-soluble lubricants (eg, Astroglide and K-Y Jelly) are the preferred choice. Condoms sold with prelubricated spermicides are no longer recommended as they do not provide additional protection against pregnancy or STIs/STDs and may increase vulnerability to HIV.

The internal condom (traditionally referred to as the female condom) is a prelubricated, loose-fitting polyurethane sheath which is closed at one end and has flexible rings at both ends. This method protects against viruses, including HIV. Properly positioned, the ring at the closed end covers the cervix, and the sheath lines the vaginal walls. The outer ring remains outside the vagina, covering the labia. The pregnancy rate of the internal condom is higher compared to external condoms. External and internal condoms should not be used together, as slippage and device displacement may occur.

The diaphragm, a reusable dome-shaped rubber cap with a flexible rim that is inserted vaginally, fits over the cervix to decrease access of sperm to the ovum. The diaphragm must be fitted to the patient for the correct size and requires a prescription. Its efficacy is increased when used in conjunction with a spermicidal cream or jelly. The diaphragm may be inserted up to 6 hours before intercourse and must be left in place for at least 6 hours afterward. However, leaving it in place for more than 24 hours is not recommended due to the potential for toxic shock syndrome (TSS). With subsequent acts of intercourse, the diaphragm should be left in place, and a condom should be used for additional protection.

The cervical cap (FemCap) is a soft, deep cup with a firm round rim that is smaller than a diaphragm and fits over the cervix like a thimble. The cervical cap is available in three sizes, is fitted into the patient for the correct size, and requires a prescription. It should be filled with spermicide prior to use. It should be inserted 6 hours prior to intercourse and not be removed for at least 6 hours after intercourse. It can remain in place for multiple episodes

of intercourse without adding more spermicide but should not be worn for more than 48 hours at a time to reduce the risk of TSS. Failure rates with the cervical cap are higher than with other methods. Diaphragms and cervical caps do not protect against some STIs/STDs, including HIV; thus, condoms should also be used.

Pharmacologic Therapy

Spermicides and Spermicide-Implanted Barrier Techniques

[3,4,5,9] Spermicides, most of which contain nonoxynol-9, are chemical surfactants that destroy sperm cell walls and act as barriers to prevent sperm from entering the cervical os. They are available as creams, films, foams, gels, suppositories, sponges, and tablets. Spermicides offer no protection against STIs/STDs. In fact, when used frequently (more than two times per day), nonoxynol-9 may increase the risk of transmission of HIV by causing small disruptions in the vaginal epithelium. The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) do not promote products containing nonoxynol-9 for protection against STIs/STDs.

A new prescription spermicide, more recently described as a vaginal pH modulator, marketed as Phexxi, is a combination of lactic acid 1.8%, citric acid 1%, and potassium bitartrate 0.4%, and does not contain nonoxynol-9. The product works to lower pH and reduce sperm motility, and can be used immediately or within 1 hour of application before sexual intercourse and with each act of intercourse. Some precautions include avoiding use in individuals with frequent cystitis as this product has been reported to increase risk.

[3,4,5] The vaginal contraceptive sponge (Today) contains 1 g of the spermicide nonoxynol-9. It has a concave dimple on one side to fit over the cervix and a loop on the other side to facilitate removal. After being moistened with water, the sponge is inserted into the vagina up to 6 hours before intercourse and provides protection for 24 hours, regardless of the frequency of intercourse during this time. After intercourse, the sponge must be left in place for at least 6 hours but should not be left in place for more than 24 to 30 hours to reduce the risk of TSS. Sponges should not be reused and should be discarded after removal. They come in one size and are available OTC.

The copper IUD (Paragard T380A) contains copper and affects sperm motility to prevent fertilization and implantation (see “Intrauterine Devices” section).

Hormonal Contraception

[3,4,5] Hormonal contraceptives contain a combination of estrogen and progestin or a progestin alone. Oral contraceptive (OC) preparations first became available in the 1960s, but options have expanded to include transdermal patches, vaginal rings, a long-acting injection, a subdermal implant, and IUDs.

Combined Hormonal Contraceptives

Combined hormonal contraceptives (CHCs) contain both estrogen and progestin and work primarily before fertilization to prevent conception. Progestins provide most of the contraceptive effect by thickening cervical mucus to prevent sperm penetration, slowing tubal motility, delaying sperm transport, and inducing endometrial atrophy. Progestins block the LH surge, to inhibit ovulation, and estrogens suppress FSH release from the pituitary, which may contribute to blocking the LH surge to prevent ovulation. However, the estrogen’s primary role in hormonal contraception is to stabilize the endometrial lining and provide cycle control.

Estrogens

The synthetic estrogens found in hormonal contraceptives available in the United States are ethinyl estradiol (EE), estradiol valerate, and more recently estetrol (E4), with EE being the most commonly used. Most combined oral contraceptives (COCs), including transdermal patches, and vaginal rings contain EE at doses of 20 to 50 mcg, with a few lower than 20 mcg.

Progestins

Progestin is a term used for a synthetic progesterone and a variety available in the United States. They vary in their progestational activity and differ with respect to inherent estrogenic, antiestrogenic, and androgenic effects. Their estrogenic and antiestrogenic properties are secondary to the extent of their metabolism to estrogenic substances and their androgenic activity depends on the presence of sex hormone (testosterone)-binding globulin (SHBG-TBG) and the androgen-to-progesterone activity ratio. If the amount of SHBG-TBG is decreased, free testosterone levels increase, and their

androgenic adverse medication effects are more prominent.

Combined Oral Contraceptives

[3][4][5] With perfect use, COCs have a 99% efficacy rate, but with typical use up to 7% of users may become pregnant (see Table 104-1). The COCs currently available are modifications of the original products introduced in the 1960s and contain significantly less estrogen and progestin. The older high-dose formulations were associated with vascular and embolic events, cancers, and significant adverse medication effects, but reductions in hormone doses are associated with fewer complications.

Monophasic COCs contain the same amounts of estrogen and progestin for 21 days, followed by a 7-day placebo phase. Multiphasic pills (biphasic, triphasic, or quadriphasic) contain variable amounts of estrogen and progestin for 21 days, also followed by a 7-day placebo phase. Multiphasic and monophasic products are equally effective. Extended-cycle tablets and continuous combination regimens may offer some benefits for patients in terms of adverse effects and convenience. With COCs, the types and doses of estrogen and progestin remain constant during the 21 to 24 days that active tablets are taken, though the doses and ratios of estrogens and progestins vary from one preparation to another. The inclusion of three additional days of active pills to shorten the pill-free interval is thought to reduce hormone fluctuation between menstrual cycles. With extended use of COCs, active combination tablets are taken continuously for 84 days or longer followed by 7 days of inactive pills or estrogen-only pills. Table 104-3 lists the available OC products by brand name and specifies hormonal composition.

TABLE 104-3

Composition of Commonly Prescribed Oral Contraceptives[a]

Common Brand Names	Estrogen	Micrograms[a] (Number of Days)	Progestin	Milligrams[a] (Number of Days)	Spotting and Breakthrough Bleeding by Third Cycle (Up to Tenth Decimal)	Comments
Monophasic Preparations						
Kelnor 1/50	Ethinyl estradiol	50	Ethynodiol diacetate	1	13.9	
Zovia 1/35E, Kelnor 1/35	Ethinyl estradiol	35	Ethynodiol diacetate	1	37.4	
Apri, Cyred, Cyred EQ, Emoquette, Enskyce, Isibloom, Juleber, Kalliga, Reclipsen	Ethinyl estradiol	30	Desogestrel	0.15	13.1	
Azurette, Bekyree, Kariva, Mircette, Pimtrea, Simliya, Viorele, Volnea	Ethinyl estradiol	20 (21) 10 (5)	Desogestrel	0.15	19.7	Contains 2 days of placebo, 5 days of EE 10 mcg only
Nextstellis	Estetrol	14.2 (mg)	Drospirenone	3	N/A	Contains 24 active tablets, 4 days of placebo Contains estetrol (E4), known to have native estrogen

						selective actions in tissues, acts as nuclear agonist on vascular system, liver, bone, uterus, and vagina; acts as a membrane antagonist on breast, liver, bone, and vascular system.
Ocella, Safyral, Syeda, Tydemy, Yasmin, Zarah, Zumandimine	Ethinyl estradiol	30	Drospirenone	3	14.5	Safyral and Tydemy are FDA-approved for acne, premenstrual dysphoric disorder (PMDD), and provide folate supplementation, 21 active pills with 0.451 mg of levomefolate calcium and 7 days of 0.451 mg of levomefolate calcium instead of placebos.
Beyaz,[f] Gianvi, Jasmiel, Loryna, Lo-Zumandimine, Nikki, Rajani,[f] Vestura, Yaz[b]	Ethinyl estradiol	20	Drospirenone	3	13.8[c]	Extended cycle—24 active hormone tablets, 4 placebo FDA-approved use for treatment of acne and PMDD Beyaz and Rajani provide folate supplementation, 21 active pills with 0.451 mg of levomefolate calcium and 7 days of 0.451 mg of levomefolate

						calcium instead of placebos
Altavera, Ayuna, Chateal, Chateal EQ, Kurvelo, Levora 0.15/30, Marlissa, Portia-28	Ethinyl estradiol	30	Levonorgestrel	0.15	14	
Iclevia, Introvale, Jolessa, Setlakin[d]	Ethinyl estradiol	30	Levonorgestrel	0.15	15.1[c]	Extended cycle—91 tablets (84 active hormone tablets and 7 placebo pills)
Amethia, Ashlyna, Camrese, Daysee, Jaimiess, Seasonique, Simpesse	Ethinyl estradiol	30 (84) 10 (7)	Levonorgestrel	0.15	14.3[e]	Extended cycle—91 tablets (84 active hormone tablets and 7 tablets of EE 10 mcg instead of placebos) Considered monophasic since only last 7 days are lower estrogen and act similarly to a placebo
Afirmelle, Aubra EQ, Aviane, Balcoltra, Delyla, Falmina, FaLessa, Joyeaux, Larissia, Lessina, Lutera, Orsythia, Sronyx, Tyblume, Vienva	Ethinyl estradiol	20	Levonorgestrel	0.1	26.5	Balcoltra contains 7 tables of ferrous bisglycinate instead of placebo Tyblume is a chewable formulation
Camrese Lo, LoJaimiess, LoSeasonique	Ethinyl estradiol	20/10	Levonorgestrel	0.1	21.5[e]	Extended cycle—91 tablets (84 active hormone tablets and 7 tablets of EE 10 mcg instead of placebos)
Amethyst, Dolishale	Ethinyl estradiol	20	Levonorgestrel	0.09	N/A[c]	Extended cycle—intended for 1-year continuous use available in

						packs of 28 active pills
Estarylla, Mili, Mono-Linyah, Nymyo, Previfem, Sprintec, VyLibra	Ethinyl estradiol	35	Norgestimate	0.25	14.3	
–	Ethinyl estradiol	50	Norgestrel	0.5	N/A	
Cryselle, Elinest, Low-Ogestrel, Turqoz	Ethinyl estradiol	30	Norgestrel	0.3	9.6	
Balziva, Briellyn, Gildagia, Nexesta Fe chewable, Philith, Vyfemla, Wymzya Fe chewable, Zenchent	Ethinyl estradiol	35	Norethindrone	0.4	11	"Fe" contains 7 days of 75 mg ferrous fumarate instead of placebos "Chewable"—chewable formulation, must drink with 8 oz (~240 mL) of water and rinse mouth
Necon 0.5/35, Nortrel 0.5/35, Norminest Fe, Wera	Ethinyl estradiol	35	Norethindrone	0.5	24.6	
Alyacen 1/35, Cyclafem 1/35, Dasetta 1/35, Nortrel 1/35, Nylia 1/35, Ortho-Novum 1/35, Pirmella 1/35	Ethinyl estradiol	35	Norethindrone	1	14.7	
Generess Fe chewable, Kaitlib Fe chewable, Layolis Fe chewable	Ethinyl estradiol	25	Norethindrone	0.8	19.0	Extended cycle—24 active hormone tablets, 4 days of ferrous fumarate 75 mg instead of placebos "Chewable"—chewable formulation, must drink with 8 oz (~240 mL) of water and rinse mouth
Aurovela 1.5/30-21, Aurovela 1.5/30-28, Aurovela Fe 1.5/30, Blisovi Fe 1.5/30, Hailey Fe 1/20, Gildess Fe 1.5/30, Junel 1.5/30, Junel Fe	Ethinyl estradiol	30	Norethindrone acetate	1.5	25.2	"Fe" contains 7 days of 75 mg ferrous fumarate

1.5/30, Larin 1.5/30, Larin Fe 1.5/30, Loestrin Fe 1.5/30, Microgestin 1.5/30, Microgestin Fe 1.5/30						instead of placebos
Aurovela 1/20, Aurovela Fe 1/20, Blisovi 1/20, Hailey Fe 1/20, Junel Fe 1/20, Junel 1/20, Larin (Fe) 1/20, Loestrin 1/20; Fe 1/20, Microgestin 1/20; Microgestin Fe 1/20, Tarina Fe 1/20, Tarina Fe 1/20 EQ	Ethinyl estradiol	20	Norethindrone acetate	1	29.7	"Fe" contains 7 days of 75 mg ferrous fumarate for 7 days "Chewable"—chewable formulation, must drink with 8 oz (~240 mL) of water and rinse mouth
Aurovela 24 Fe, Blisovi 24 Fe, Charlotte 24 Fe chewable, Finzala chewable, Gemmily capsules, Junel Fe 24, Hailey 24 Fe, Larin 24 Fe, Minastrin 24 Fe chewable, Merzee capsules, Melodetta 24 Fe chewable, Mibelas 24 Fe chewable, Microgestin 24 Fe, Tarina 24 Fe, Taytulla capsules	Ethinyl estradiol	20	Norethindrone acetate	1	23.2[c]	Extended cycle—24 active hormone tablets, 4 placebo "Fe" contains 4 days of 75 mg ferrous fumarate instead of placebos "Chewable"—chewable formulation, must drink with 8 oz (~240 mL) of water and rinse mouth Gemmily, Merzee, Taytulla—capsule formulations and also contain 75 mg ferrous fumarate for 7 days, instead of placebos
Lo Loestrin-24 Fe[b]	Ethinyl estradiol	10	Norethindrone acetate	1	52.0[c]	Extended cycle—24 active tablets, 2 days of EE 10 mcg only and 2 days of 75 mg ferrous fumarate tablets
Multiphasic Preparations (Biphasic, Triphasic, and Quadriphasic)						

–	Ethinyl estradiol	35 (10) 35 (11)	Norethindrone	0.5 (10) 1 (11)	N/A	Biphasic
Caziant, Cyclessa, Velivet	Ethinyl estradiol	25 (7) 25 (7) 25 (7)	Desogestrel	0.1 (7) 0.125 (7) 0.15 (7)	11.1	Triphasic
Enpresse, Trivora, Levonest Myzilra	Ethinyl estradiol	30 (6) 40 (5) 30 (10)	Levonorgestrel	0.05 (6) 0.075 (5) 0.125 (10)	15.1	Triphasic
Tri-Estarylla, Tri-Linyah, Tri-Mili, Tri-Nymyo, TriNessa, Tri-Previfem, Tri-Sprintec, Tri-VyLibra	Ethinyl estradiol	35 (7) 35 (7) 35 (7)	Norgestimate	0.18 (7) 0.215 (7) 0.25 (7)	17.7	Triphasic FDA-approved use for treatment of acne
Ortho-Tri Cyclen Lo, Tri-Lo Estarylla, Tri-Lo-Marzia, Tri-Lo-Mili, Tri-Lo-Sprintec, Tri-VyLibra Lo	Ethinyl estradiol	25 (7) 25 (7) 25 (7)	Norgestimate	0.18 (7) 0.215 (7) 0.25 (7)	11.5	Triphasic
Alyacen 7/7/7, Cyclafem 7/7/7, Dasetta 7/7/7, Nortrel 7/7/7, Nylia 7/7/7, Ortho Novum 7/7/7/, Pirmella 7/7/7	Ethinyl estradiol	35 (7) 35 (7) 35 (7)	Norethindrone	0.5 (7) 0.75 (7) 1 (7)	14.5	Triphasic
Aranelle, Leena	Ethinyl estradiol	35 (7) 35 (9) 35 (5)	Norethindrone	0.5 (7) 1 (9) 0.5 (5)	25.5	Triphasic
Estrostep Fe, Tilia Fe, Tri-Legest Fe	Ethinyl estradiol	20 (5) 30 (7) 35 (9)	Norethindrone acetate	1 (5) 1 (7) 1 (9)	21.7	Triphasic Estrophasic (estrogen content changes), FDA-approved use for treatment of acne, “Fe” contains 75 mg ferrous fumarate instead of placebos

Fayosim, Quartette, Rivelsa	Ethinyl estradiol	20 (42) 25 (21) 30 (21) 10 (7)	Levonorgestrel	0.15	N/A[e]	Quadriphasic, Estrophasic (estrogen content changes), extended cycle—91 tablets (84 active tablets and 7 tablets of EE 10 mcg instead of placebo)
Natazia	Estradiol valerate	3 (2) 2 (5) 2 (17) 1 (2)	Dienogest	0 (2) 2 (5) 3 (17) 0 (4)	14	Quadriphasic, Estrophasic FDA-approved use for heavy menstrual bleeding
Progestin-Only Oral Contraceptives						
Camila, Deblitane, Errin, Heather, Incassia, Jencycla, Lyleq, Lyza, Ortho Micronor, Nora-BE, Norlyda, Norlyroc, Sharobel, Tulana	Ethinyl estradiol	–	Norethindrone	0.35 (28)	42.3	Contains 28 days of active tablets, no placebos
Opill	Ethinyl estradiol	_	Norgestrel	0.075 (28)	N/A	Contains 28 days of active tablets, no placebos, available over-the-counter
Slynd	Ethinyl estradiol	–	Drospirenone	4 (24)	N/A	Contains 24 days of active tablets, 4 days placebo

[a]28-day regimens (21-day active pills, then 7-day pill-free interval) unless otherwise noted.

[b]Number in parentheses refers to the number of days the dose is received in multiphasic oral contraceptives.

[c]28-day regimen (24-day active pills, then 4-day pill-free interval).

[d]91-day regimen (84-day active pills, then 7-day pill-free interval).

[e]Percent reporting after 6 to 12 months of use.

[f]Also contains levomefolate calcium 0.451 mg in all 28 tablets.

N/A—data not available per references.

Initiating a Combined Oral Contraceptive

[8]COCs may be initiated by different methods, including on the first day of bleeding during the menstrual cycle, or on the first Sunday after the menstrual cycle begins, or using the quick start method. The first day method is when the woman starts the COC on the first day of her menstrual cycle. The patient should be instructed to use a second method of contraception (typically recommend condoms) for at least 7 days after initiation for maximum effectiveness, though some sources state that no backup contraceptive method is required for the first day of menses start method. The "Sunday start" method requires taking tablets on the first Sunday after the menstrual cycle begins and may provide weekends free of menstrual periods. Individuals should also be instructed to use a second method of contraception (typically recommend condoms) for at least 7 days after initiation for maximum effectiveness. It may be preferable to have individuals use additional contraception for the entire first cycle, due to user failure in the first month. In the "quick start" method, the patient takes the first tablet on the day of her office visit. Patients should be instructed to use a second method of contraception for at least 7 days and potentially until she begins her next menstrual cycle to ensure optimal effectiveness. Patients should be informed that the menstrual period will be delayed until completion of the active tablets in the current OC pack. This method is more successful in getting individuals to start OCs and to continue using OCs through the third cycle of use. The CDC recommends that individuals start or resume hormonal contraception no sooner than 5 days after use of the emergency contraceptive ulipristal acetate to maximize the effectiveness of both products (use of the two products together may decrease effectiveness). Long-acting reversible contraception (LARC) methods such as the IUD and implant, however, can be started at the time of ulipristal acetate use.

Selecting a Combined Oral Contraceptive

[4][5][3]Because all COCs are similarly effective in preventing pregnancy (see Table 104-1), the initial choice is based on the hormonal content and dose, preferred formulation, and coexisting medical conditions (see Table 104-6). In individuals without coexisting medical conditions, an OC containing 35 mcg or less of EE is recommended (see Table 104-3). This strategy is based on evidence that complications and adverse effects of CHC (ie, VTE, stroke, or myocardial infarction [MI]) result from excessive hormonal content. With nonadherence to OCs, the risk of pregnancy may be greater in individuals taking COCs containing less than 35 mcg of EE. Individuals with oily skin, acne, or hirsutism should be given low androgenic COCs. Choice of an agent based upon coexisting medical conditions can be found in Table 104-6.

It may be easier to identify/manage adverse medication effects and easier to manipulate to alter the timing of the menstrual cycle in patients taking monophasic COCs. Continuous COCs either eliminate or reduce the number of menstrual cycles per year, leading to less premenstrual symptoms and dysmenorrhea. Commercially available continuous COCs or monophasic 28-day OCs can be cycled by skipping the 7-day placebo phase. With continued use of extended-cycle or continuous COCs for 1 year, no significant changes in adverse effects have been noted. However, long-term studies have not been performed to assess the risk of cancer, VTE, or changes in fertility. Extended-cycle regimens provide a shortened pill-free interval, from the traditional 7 days to 2 to 4 days. These various extended-cycle and continuous regimens may be beneficial for patients with symptoms such as dysmenorrhea, severe premenstrual syndrome, or menstrual migraines.

Managing Combined Oral Contraceptive Adverse Medication Effects

[6]Adverse medication effects occurring with early COC use (eg, nausea, bloating, breakthrough bleeding) may improve spontaneously by the third cycle after adjusting to the altered hormone levels. Patients should be counseled to continue their COC for 2 to 3 months before changing products unless a serious adverse effect is present. Despite the 2- to 3-month adjustment period, a large majority of individuals who discontinue COCs do so because of the adverse medication effects. Therefore, patient education and early reevaluation within 3 to 6 months are necessary to identify and manage adverse effects, and to improve adherence. The most common adverse effect is irregular bleeding. Individuals on extended-cycle regimens should be counseled to expect this during the first 6 months. For those experiencing bleeding irregularities beyond the recommended time frame, the estrogen or progestin content may need to be adjusted. Early breakthrough bleeding is typically due to insufficient estrogen and late breakthrough bleeding is due to insufficient progestin. Nausea may occur due to the estrogenic effects of these hormonal contraceptives. Skin breakouts occur more often in products with higher androgenic effects. Serious adverse effects that may occur with the use of CHCs are listed in Table 104-4, and common adverse medication effects along with recommended monitoring are reviewed in Table 104-5. Patients should be instructed to consult with their provider immediately and likely should discontinue CHCs if they experience serious warning signs, described as ACHES.

TABLE 104-4

Symptoms of a Serious or Potentially Serious Nature Associated with Combined Hormonal Contraception

Symptom	Possible Cause
SERIOUS: Stop Immediately	
Loss of vision, proptosis, diplopia, papilledema	Retinal artery thrombosis
Unilateral numbness, weakness, or tingling	Hemorrhagic or thrombotic stroke
Severe pains in chest, left arm, or neck	Myocardial infarction
Hemoptysis	Pulmonary embolism
Severe pains, tenderness or swelling, warmth or palpable cord in legs	Thrombophlebitis or thrombosis
Slurring of speech	Hemorrhagic or thrombotic stroke
Hepatic mass or tenderness	Liver neoplasm
POTENTIALLY SERIOUS: May Continue with Caution While Being Evaluated	
• Absence of menses • Spotting or breakthrough bleeding • Breast mass, pain, or swelling • Right upper-quadrant pain • Mid-epigastric pain • Migraine headache • Severe nonvascular headache • Galactorrhea • Jaundice, pruritus	• Cervical endometrial or vaginal cancer • Cholecystitis, cholelithiasis, or liver neoplasm • Pituitary adenoma • Cholestatic jaundice • B6 deficiency • Leiomyomata, adenomyosis • Depression, sleepiness • Uterine size increase

TABLE 104-5

Medication Monitoring Table for Hormonal Contraception

Medication (or Medication Class)	Adverse Medication Effect	Monitoring Parameter	Comments
Combined hormonal contraception	• Nausea/vomiting • Breast tenderness • Weight gain • Acne, oily skin • Depression, fatigue • Breakthrough bleeding/spotting • Application site reaction (transdermal) • Vaginal irritation (vaginal ring)	• Patient symptoms • Weight • Visual inspection • Depression screening • Menstrual symptoms • Visual inspection • Patient symptoms	• Typically improves after two to three cycles; consider changing to lower estrogenic • Consider changing to lower androgenic • Data are limited and conflicting • Consider changing to higher estrogenic
Depo-medroxyprogesterone acetate	• Menstrual irregularities[a] • Weight gain • Acne • Hirsutism • Depression • Decreased bone density	• Menstrual symptoms • Weight • Visual inspection • Depression screening • Bone mineral density (BMD)	• Typically improves after 6 months • Data are limited and conflicting • Do not routinely screen with dual-energy X-ray absorptiometry (DXA)
Levonorgestrel IUD	• Menstrual irregularities[a] • Insertion-related complications • Expulsion • Pelvic inflammatory disease (PID)	• Menstrual symptoms • Cramping, pain, spotting, dyspareunia, missing strings • Lower abdominal pain, unusual vaginal discharge, fever	• Typically spotting, amenorrhea • Prophylactic nonsteroidal anti-inflammatory drugs (NSAIDs) or local anesthetic may reduce occurrence • IUD strings should be checked regularly to ensure IUD properly placed • Risk of developing is rare, but counseling on STI/STD prevention is important
Copper IUD	• See levonorgestrel IUD above	• See levonorgestrel IUD above	• Menstrual irregularities are typically heavier menses with copper IUD
Progestin-only implant	• Menstrual irregularities[a] • Insertion-site reactions	• Menstrual symptoms • Pain, bruising, skin irritation, erythema, pus, fever	• Typically well tolerated and resolved without treatment; infection is rare

[a]Suggested management of irregular bleeding may include use of NSAIDs for 5 to 7 days; hormonal treatment (if medically eligible) with COC or estrogen therapy for 10 to 20 days of treatment.

Managing Combined Oral Contraceptive Medication Interactions

[4] [6] [7] The effectiveness of a COC is sometimes limited by medication interactions that interfere with GI absorption, increase intestinal motility due to altered gut bacteriologic flora, and alteration of the metabolism, excretion, or binding of the COC. The lower the dose of hormone in the COC, the greater the risk that a medication interaction will compromise effectiveness. Individuals should be instructed to use an additional method of contraception if there is a possible medication interaction altering COC effectiveness. Although less well documented, these recommendations generally apply to patients receiving transdermal and vaginal CHC products.

Rifampin is the one with a true documented COC pharmacokinetic interactions. Pharmacokinetic studies of other antibiotics have not shown any consistent interaction, but individual case reports have shown a reduction in EE levels when OCs are taken with tetracyclines and penicillin derivatives, possibly due to the inhibition of enterohepatic recirculation. Individuals receiving concomitant rifampin (or derivatives) and OCs should be counseled on the possibility for decreased efficacy and to use an additional nonhormonal contraception while on the combination and for at least 7 days after the rifampin therapy has been discontinued. Some OC manufacturers recommend to use a backup method for 28 days after the use of any enzyme inducer such as rifampin. It may be prudent to inform patients of the slight risk of decreased effectiveness with other antimicrobials as well; however, this is not necessarily supported with strong evidence. If a patient is going to be receiving an interacting medication for more than 2 months, switch to depot medroxyprogesterone acetate (DMPA) or an IUD to avoid the interaction and eliminate the need for long-term additional nonhormonal contraception.

[7] Individuals receiving certain anticonvulsants for a seizure disorder should be offered another form of contraception such as DMPA or LARC methods rather than OCs (see Table 104-6). Some anticonvulsants (mainly phenobarbital, carbamazepine, phenytoin) induce the metabolism of estrogen and progestin, inducing breakthrough bleeding and potentially reducing contraceptive efficacy. In addition, some antiseizure medications are known as teratogens. Use of COCs with lamotrigine may decrease the effectiveness of lamotrigine and increase the possibility of worsening the seizure disorder.

TABLE 104-6

US Medical Eligibility Criteria for Contraceptive Use: Classifications for Combined Hormonal Contraceptives

Category 4: Unacceptable Health Risk (method not to be used)

- Breastfeeding or non-breastfeeding <21 days postpartum
- Current breast cancer
- Severe (decompensated) cirrhosis
- Current DVT/PE
- History/higher risk of DVT/PE (not on anticoagulant therapy)
- History/higher risk of DVT/PE (established on anticoagulant therapy for 3 months or greater)
- Thrombogenic mutations
- Major surgery with prolonged immobilization
- Migraines with aura, any age
- Systolic BP ≥160 mm Hg or diastolic ≥100 mm Hg
- Hypertension with vascular disease
- Current and history of ischemic heart disease
- Benign hepatocellular adenoma or malignant liver tumor
- Peripartum cardiomyopathy, moderately or severely impaired cardiac function; normal or mildly impaired cardiac function <6 months
- Smoking ≥15 cigarettes per day and age ≥35
- Complicated solid organ transplantation, graft failure
- History of cerebrovascular accident
- SLE; positive or unknown antiphospholipid antibodies
- Current nephrotic syndrome
- Hemodialysis
- Peritoneal dialysis
- Diabetes mellitus (type 1 or type 2), nonvascular disease
- Gallbladder disease; symptomatic and treated by cholecystectomy or asymptomatic
- Migraines without aura
- History of pregnancy-related cholestasis
- History of high BP during pregnancy
- Benign liver tumors; focal nodular hyperplasia
- BMI ≥30 kg/m^2 (Obesity)
- Breastfeeding 30-42 days postpartum without other VTE risk factors
- Breastfeeding 42 days or more postpartum
- Non-breastfeeding 21-42 days postpartum without other risk factors for VTE
- Rheumatoid arthritis on or off immunosuppressive therapy
- Smoking and <35 years old
- Uncomplicated solid organ transplantation, graft failure
- SLE with severe thrombocytopenia or on immunosuppressive therapy or without antiphospholipid antibodies
- Unexplained vaginal bleeding before evaluation
- Uncomplicated valvular heart disease

- Sickle cell disease
- Complicated valvular heart disease

Category 3: Theoretical or Proven Risks Usually Outweigh the Advantages

- Breastfeeding 21-30 days postpartum with or without risk factors for VTE
- Breastfeeding 30-42 days postpartum with other risk factors for VTE
- Non-breastfeeding 21-42 days postpartum with other risk factors for VTE
- Past breast cancer and no evidence of disease for 5 years
- History of DVT/PE (not on anticoagulant therapy or established on anticoagulant therapy for at least 3 months), but lower risk for recurrent DVT/PE
- Current gallbladder disease, symptomatic and medically treated
- History of bariatric surgery; malabsorptive procedures (*COCs only, vaginal ring/transdermal patch category 1*)
- History of cholestasis, past COC-related
- Hypertension; systolic BP 140-159 mm Hg or diastolic 90-99 mm Hg
- Adequately controlled hypertension
- Peripartum cardiomyopathy, normal or mildly impaired cardiac function ≥6 months
- Smoking <15 cigarettes per day and age ≥35
- Use of fosamprenavir
- Use of certain antiseizure medications (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine, and lamotrigine)
- Use of rifampicin or rifabutin therapy
- Diabetes with vascular disease or >20 years duration (*possibly category 4 depending upon severity*)
- Multiple risk factors for arterial cardiovascular disease (older age, smoking, diabetes, low HDL, high LDL, or high triglycerides and hypertension) (*possibly category 4 depending on category and severity*)
- Acute flare of viral hepatitis (*possibly category 4 depending on severity [initiation]*)
- Multiple sclerosis with prolonged immobility
- Current or history of superficial venous thrombosis

Category 2: Advantages Generally Outweigh Theoretical or Proven Risks

- Age ≥40 (in the absence of other comorbid conditions that increase CVD risk)
- Undiagnosed breast mass
- Cervical cancer and awaiting treatment; cervical intraepithelial neoplasia
- Family history (first-degree relatives) of DVT/PE
- Major surgery without prolonged immobilization
- Use of antiretrovirals other than fosamprenavir (*category 1 or 2 depending on agent*)
- Use of St. John's wort
- Inflammatory bowel disease (*possibly category 3 for those with increased risk of VTE*)
- Acute flare of viral hepatitis occurring during use of product (*continuation, category 3 or 4 for initiation of product*)

Category 1: No Restriction (method can be used)

- Thalassemia, iron deficiency anemia
- Mild compensated cirrhosis
- Benign ovarian tumors
- Benign breast disease or family history of cancer
- Family history of cancer
- Schistosomiasis
- Cystic fibrosis
- Cervical ectropion
- Viral hepatitis (carrier/chronic)
- Minor surgery without immobilization
- Depression
- Gestational diabetes mellitus
- Endometrial cancer/hyperplasia, endometriosis
- Epilepsy
- Gestational trophoblastic disease
- Nonmigrainous headaches
- History of bariatric surgery; restrictive procedures
- History of pelvic surgery
- HIV infected or high risk
- Malaria
- Multiple sclerosis without prolonged immobility
- Ovarian cancer
- Past ectopic pregnancy
- Parity, parous, or nulliparous
- PID
- Postabortion
- Non-breastfeeding more than 42 days postpartum
- Severe dysmenorrhea
- STIs
- Varicose veins
- Vaginal bleeding—irregular pattern without heavy bleeding or heavy, prolonged bleeding
- Thyroid disorders
- Tuberculosis
- Uterine fibroids
- Use of SSRIs
- Use of broad-spectrum antibiotics, antifungals,

	and antiparasitics

CVD, cardiovascular disease; DVT, deep vein thrombosis; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PE, pulmonary embolism; PID, pelvic inflammatory disease; SSRI, selective serotonin reuptake inhibitors.

Other medications that may affect COCs include HIV antiretrovirals such as protease inhibitors which, depending on the HIV medication, may decrease COC effectiveness or the COC may possibly alter the levels of protease inhibitor. In addition, monitoring of potassium levels may be needed in individuals who take medications that increase potassium with drospirenone-containing COCs. Drospirenone is a derivative of spironolactone, a potassium-sparing diuretic, that also has anti-mineralocorticoid activity. Caution may be warranted in patients with a history of hyperkalemia or in patients taking concomitant medications that increase potassium levels or in high-risk patients taking strong inhibitors of CYP3A4. Patients should also be counseled that an OTC herbal product, St. John's wort, may also possibly decrease OC effectiveness. Because there are several possible medication interactions that could affect the levels of COCs, assess all patient medications for possible interactions with COCs.

Patient Instructions with Combined Oral Contraceptives

[9] Many individuals who take OCs are not educated properly on the appropriate use of these medications. They should be given the package insert that accompanies all products and instructed to read it, as well as supplementing this information with verbal education describing the mechanism of the medication, common and serious adverse medication effects (ie, ACHES symptoms), and their management. Although several transient self-limiting adverse medication effects often occur, the patient should be aware of the danger signals that require immediate medical attention (see Table 104-4). The benefits and risks should be discussed, including the fact that OCs provide no physical barrier to the transmission of STIs/STDs, including HIV. Detailed instructions on when to start taking the OC should be provided. Patients should be told the importance of routine daily administration to ensure consistent plasma concentrations and improve adherence.

Missed Doses of Combined Oral Contraceptives

[8] Specific instructions should be given regarding what to do if a tablet is missed. For individuals who routinely have difficulty with adhering to daily dosing, counseling regarding other options such as the vaginal ring, transdermal patch, DMPA, implants, or IUDs should be provided. If warranted, suggesting EC may also be necessary.

For COCs, if one tablet is missed or late then it should be taken as soon as remembered, and the rest of the tablets should be continued as prescribed (for most this that means two tablets are taken on the same day). Typically, no additional nonhormonal contraception methods are warranted. If two or more consecutive tablets are missed, then take one missed tablet as soon as remembered and discard the other missed tablets. Continue taking the OC tablets as scheduled which means two tablets may need to be taken on the same day (ie, one of the missed tablets and one of the regularly scheduled tablets). If tablets were missed in the last week of hormonal tablets, finish the remaining active tablets (tablets with hormone) and then omit the hormone-free interval (skip taking the placebo tablets) and start a new pack of tablets. For both of these scenarios, counsel patients to use additional nonhormonal contraception until active hormone tablets have been taken for 7 consecutive days. For all scenarios when two or more consecutive tablets are missed, consider counseling on EC use if warranted.

Vomiting and Severe Diarrhea While on Combined Oral Contraceptives

[6] [9] Efficacy of COCs may be decreased when vomiting or severe diarrhea occurs, and recommendations for dosing in this situation have been developed. These recommendations are based on theoretical concerns and are identical to missed tablet instructions. If vomiting or diarrhea occurs for less than 48 hours, then no redosing of COCs is warranted. If vomiting or diarrhea persists greater than 48 hours then continue taking tablets. If this scenario occurs during the last week of the hormonal tablets, then finish the tablets, skip the hormone-free tablets, and begin a new pack. Patients should be instructed to use additional nonhormonal contraception until hormonal tablets have been taken for 7 consecutive days after the vomiting or diarrhea subsides and counsel patients on use of EC if warranted.

Transdermal Contraceptives

[3] [4] [5] There are two CHCs available as transdermal patches (Xulane, originally marketed as Ortho Evra, and Twirla). Xulane is a 14-cm^2 square transdermal patch that delivers 35 mcg of EE and 150 mcg of norelgestromin, the active metabolite of norgestimate. Twirla is a 28-cm^2 circular patch that provides 30 mcg of EE and 120 mcg of levonorgestrel daily. The EE/norelgestromin patch is as effective as COCs in patients weighing less than 90

kg. Of the 15 pregnancies reported in the clinical trials, 5 were among individuals weighing more than 90 kg; therefore, this product is not recommended as a first-line option for these patients. Similar to the EE/norelgestromin patch, the EE/levonorgestrel patch is recommended for individuals with a BMI of less than 30 kg/m^2, but may also have reduced effectiveness with BMIs ranging from 25 to 30 kg/m^2. Typical-use failure rates for EE/norelgestromin and EE/levonorgestrel patches are 7% and 3%, respectively (Table 104-1).

Managing Transdermal Patch Contraceptive Adverse Medication Effects and Medication Interactions

[6] [7] Some patients experience application-site reactions, but other adverse medication effects are similar to those experienced with COCs (eg, breast discomfort, headache, breakthrough bleeding, and nausea). A warning from the EE/norelgestromin manufacturer states that individuals using the patch are exposed to approximately 60% more estrogen than from a typical COC containing 35 mcg of EE, which may lead to an increased thromboembolic risk. The labeling for these patches now contains a warning of this risk. Medication interactions with the patches are similar to those of COCs. Please see section "Managing Combined Oral Contraceptive Medication Interactions."

Patient Instructions with Transdermal Patch Contraceptives

[9] The patch is designed to provide estrogen (EE) and progestin (norelgestromin or levonorgestrel) for 7 days. One patch should be worn at a time and applied to the abdomen, buttocks, upper torso, or upper arm. Start applying the patches at the beginning of the menstrual cycle. They should be changed weekly on the same day which is labeled the "Patch Change Day." Apply a new patch weekly for 3 weeks with the fourth week being patch-free for a 4-week cycle.

Missed Doses of Transdermal Patch Contraceptives

[8] [9] If the patch detaches and is off less than 24 hours, the detached patch or a new patch can be reapplied, and no additional hormone contraception is necessary. If application is delayed for more than 24 hours, start a new 4-week cycle by applying a new patch as soon as possible. An additional nonhormonal contraception should be utilized until the new patch has been worn for 7 consecutive days. This will be the new "Patch Change Day." If the delayed application or detachment occurs in the third patch week, the hormone-free week should be omitted and a new patch should be applied immediately.

If an individual forgets to change the patch at the end of the week, instructions on what to do vary based on where they are in the cycle. If they forget to apply a new patch after the hormone-free week, they will need to use a backup method of nonhormonal contraception until they have worn a patch for 7 days. If they forget to apply a new patch in week 2 or 3 (left an active hormone patch on and forgot to replace it with a new one) and the delayed application is for only 1 or 2 days (up to 48 hours), a new patch should be applied immediately. The next patch should be changed on the same "Patch Change Day," and no backup contraception is needed. If the delayed application of a new patch (old one is still on) is longer than 2 days (more than 48 hours), then they will need to start a new 4-week cycle of patches and use a backup nonhormonal method of contraception until a new patch has been placed for 7 days. If the patient forgets to remove the patch for the hormone-free week, they should remove it as soon as they remember and start the next cycle of patches on the regular "Patch Change Day" (day after day 28 of the cycle). No backup contraceptive method is required in this situation. There should not be more than 7 days where a patch is not worn. If this occurs, the individual must use a backup nonhormonal contraceptive method until a new patch has been applied for 7 days. Users have greater adherence with the patch than with a COC, but whether this results in reduced pregnancy rates remains to be seen. The benefits of adherence must be weighed against the risk of increased estrogen exposure and possibility of VTE.

Vaginal Rings

[3] [4] [5] There are two marketed vaginal contraceptive rings (NuvaRing and Annovera). NuvaRing is a 54-mm flexible ring, 4 mm in thickness which when vaginally inserted releases approximately 15 mcg/day of EE and 120 mcg/day of etonogestrel. It is formulated to be used for 3 weeks and then discarded.

Annovera is 56 mm in diameter and 8.4 mm in cross-sectional diameter vaginally inserted ring which releases 13 mcg of EE and 150 mcg of segesterone acetate. It is formulated to be used for 3 weeks at a time, but is not discarded. It is used again for a total of 13 cycles.

The vaginal ring is as effective as COCs.

Patient Instructions with Vaginal Ring Contraceptives

[9] On the first cycle of use, the ring should be inserted on or before the fifth day of the menstrual cycle, remain in place for 3 weeks, then removed for 1 week to allow for withdrawal bleeding. The ring should be inserted on the same day of the week as it was during the last cycle, similar to starting a

new COC pack or transdermal patch on the same day of the week.

In contrast to diaphragms and cervical caps, precise placement is not an issue because the hormones are absorbed anywhere in the vagina. Individuals should be in a comfortable position, and compress the ring between the thumb and index finger to push it into the vagina. There is no danger of inserting the ring too far because the cervix will prevent it from traveling up the genital tract. Removal of the ring is performed in a similar manner, pulling it out. The NuvaRing should be discarded into the foil patch (the ring should not be flushed down the toilet). The Annovera ring should be removed, washed with warm water, and placed in its original container for later use. After one ring-free week, the Annovera ring can be vaginally inserted again and can be used for a total of 13 cycles. Annovera does not require refrigeration; however, NuvaRing may require it if not being used promptly. Individuals should be discouraged from douching, but other vaginal products, including antifungal creams and spermicides, can be used.

Missed Doses of Vaginal Ring Contraceptives

[8][9] If the NuvaRing has been displaced for less than 3 hours, or less than 2 hours for Annovera, a new ring should be inserted as soon as possible and kept in until the scheduled removal day, with no additional nonhormonal contraception necessary. If there is a delay of 3 or more hours, for NuvaRing or 2 or more hours for Annovera, a new ring (for NuvaRing) or current ring (Annovera) should be inserted immediately and either additional nonhormonal contraception should be utilized, or intercourse should be avoided until the ring has been in place for 7 consecutive days. If the delayed reinsertion occurs during the third week of ring use, a new ring (for NuvaRing) or current ring (for Annovera) can be reinserted right away to start the next 21-day cycle. There may be some spotting or vaginal bleeding.

If a person forgets to remove the ring after the third week, and there has been prolonged use of the ring for up to one extra week (not more than 4 weeks in place for NuvaRing), they will still be protected and no backup protection will be necessary. Though, the individual should take into account the number of extra weeks the Annovera ring was inserted vaginally and subtract those weeks from the total 13 cycles for use. The ring should be removed for the ring-free week, and a new ring can be inserted after the ring-free week. If NuvaRing has been left in place longer than 4 weeks, the ring should be removed. The individual should then check for possible pregnancy. Once pregnancy has been ruled out, a new cycle of the vaginal ring with 7 days of a nonhormonal contraceptive method may be started. With Annovera, a ring-free week should occur and then the regular 3-week ring cycle should be restarted.

Managing Vaginal Ring Contraceptive Adverse Medication Effects and Medication Interactions

[6][7] Adverse medication effects, precautions, and contraindications for use of the vaginal ring are similar to those for all CHCs. Specific medication interactions with Annovera have been reported that include 1-day or the 3-day oil-based miconazole suppository use increasing exposure up to 67% for EE and 32% for segesterone acetate. These medications and oil-based vaginal suppositories should be avoided with Annovera. Water-based products may be used. Unlike NuvaRing, tampon use with Annovera should be avoided until further studies are completed. The most common reasons for discontinuation of use were device-related issues, such as foreign-body sensation, device expulsion, and vaginal symptoms. Cycle control with the vaginal ring appears to be equal or better than with COCs, with a low incidence of breakthrough bleeding and spotting after the second cycle of use. Patient acceptability of the delivery system has been studied, and the majority of patients do not complain of discomfort in general or during intercourse. A potential concern is the possibility of increased VTE.

Considerations with Combined Hormonal Contraceptive Use

[2][3][4][5] When selecting a CHC, clinicians are challenged by weighing the benefits and risks associated with the many formulations available. The clinician must determine if the form of contraception is appropriate based upon the patient's lifestyle and potential adherence. A complete medical examination and papanicolaou (Pap) smear are not necessary before a CHC is prescribed. A medical history and BP measurement should be obtained before prescribing a CHC, along with a discussion of the benefits, risks, and adverse effects with each patient. For example, OCs are associated with noncontraceptive benefits, including relief from menstruation-related problems (eg, decreased menstrual cramps, decreased ovulatory pain [mittelschmerz], and decreased menstrual blood loss), improvement in menstrual regularity, alleviating acne and premenstrual dysphoric disorder, and decreased iron deficiency anemia. Individuals who take COCs have a reduced risk of ovarian and endometrial cancer, which is a 50% reduction after 5 years or more. This protection may persist for more than 10 years post-use. COCs may also reduce the risk of ovarian cysts, ectopic pregnancy, pelvic inflammatory disease (PID), endometriosis, uterine fibroids, and benign breast disease. The CHC transdermal patches and vaginal rings are combined hormonal options that may be more convenient than taking a tablet each day.

[3][4][6][9] Adverse effects may hinder adherence and therefore efficacy, so they should be discussed prior to initiating a hormonal contraceptive agent. Excessive or deficient amounts of estrogen and progestin are related to the most common adverse effects. An important concern regarding the

use of CHCs is the lack of protection against STIs/STDs. Because of their high efficacy in preventing pregnancy, patients may choose not to use condoms. In addition to public health awareness, clinicians must encourage patients to use condoms for the prevention of STIs/STDs. The health risks associated with pregnancy, the specific health risks associated with CHCs, and the noncontraceptive benefits of CHCs should be factored into risk-to-benefit considerations. To help provide guidance on absolute and relative contraindications to CHC use, the CDC developed a graded list of precautions for clinicians to consider when initiating CHCs (Table 104-6).

Individuals Older Than 35 Years

Use of a CHC in individuals older than 35 is controversial. Older individuals, especially those in their 40s, retain a level of fertility even in the perimenopausal state and can use hormonal contraception to prevent pregnancy. Formulations with lower doses of estrogen (less than 30 mcg) have increased the use of CHCs in these individuals. In addition to the benefit of pregnancy prevention, they may improve or decrease the chance of developing perimenopausal and menopausal symptoms and increase bone mineral density (BMD). However, the benefits of using CHCs must be weighed against the risks in individuals older than 35. The increased risk of VTE should be considered especially in perimenopausal individuals older than 40. Older data suggest an increased risk of MI is present in older individuals using CHCs, although many of them in these studies were current smokers and used older formulations containing higher doses (greater than 50 mcg) of estrogen. There is no increased risk of cardiovascular disease when low-dose formulations of CHCs are used in healthy, nonobese individuals. Other concerns include the increased risk of ischemic stroke in those with migraines and the increased risk of breast cancer in older individuals.

The risks and benefits of using CHCs in individuals greater than 35 must be considered on an individual basis. The use of CHCs (with less than 50 mcg of estrogen) may be considered in healthy nonsmoking individuals. CHCs should not be recommended in individuals older than 35 years with migraine (with aura), uncontrolled hypertension, smoking, or diabetes with vascular disease.

Smoking

COCs with 50 mcg EE or more have been associated with MI in individuals who smoked cigarettes. Older individuals are at higher risk. Therefore, practitioners should prescribe CHC with caution, if at all, to those older than 35 years who smoke. Smoking 15 or more cigarettes per day by those in this age group is a contraindication to CHCs, and the risks generally outweigh the benefits of CHCs in those who smoke fewer than 15 cigarettes per day. Progestin-only or nonhormonal contraceptive methods should be considered for individuals in this group.

Hypertension

CHCs can cause small increases (ie, 6-8 mm Hg) in BP, regardless of estrogen dosage. This is presented in both normotensive and mildly hypertensive individuals when given an OC with 30 mcg EE. OCs have been associated with an increased risk of MI and stroke. Use of low-dose CHC is acceptable in those younger than 35 years with well-controlled and frequently monitored hypertension. If a CHC-related increase in BP occurs, CHC discontinuation usually restores BP to pretreatment values within 3 to 6 months. Systolic BP ≥160 mm Hg or diastolic BP ≥100 mm Hg is considered a contraindication to the use of CHCs. Hypertensive individuals who have a systolic BP of 140 to 159 or diastolic BP of 90 to 99 mm Hg should also avoid CHCs as the risks generally outweigh the benefits. Risks versus benefits should be considered for those who have additional cardiovascular risk factors along with hypertension. Individuals with hypertension who are taking potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or aldosterone antagonists may have increased serum potassium concentrations if they are also using an OC-containing drospirenone, which has anti-aldosterone properties.

Dyslipidemia

Generally, synthetic progestins may adversely affect lipid metabolism by decreasing high-density lipoprotein (HDL) and increasing low-density lipoprotein (LDL). Estrogens tend to have more beneficial effects by enhancing removal of LDL and increasing HDL levels. They may also moderately increase triglycerides. Today, most low-dose CHCs have no significant impact on HDL, LDL, triglycerides, or total cholesterol, although historically this was not felt to be true. Although the lipid effects of CHCs theoretically can influence cardiovascular risk, the mechanism of increased cardiovascular disease in CHC users is believed to be due to thromboembolic and thrombotic changes, not atherosclerosis. CHCs use is generally acceptable in individuals with dyslipidemia as the single cardiovascular risk factor. However, careful consideration should be taken in persons with dyslipidemia along with other cardiovascular risk factors and in many cases alternative methods of contraception may be recommended.

Diabetes

Any effect of CHCs on carbohydrate metabolism is thought to be due to the progestin component. However, most products used today contain low doses of progestins and do not significantly alter insulin, glucose, or glucagon release or daily insulin requirements. CHCs do not appear to alter the hemoglobin A1c values or accelerate the development of microvascular complications in individuals with diabetes. Therefore, nonsmoking patients younger than 35 years with diabetes but no associated vascular disease can safely use CHCs. Diabetic individuals with vascular disease (eg,

nephropathy, retinopathy, neuropathy, or other vascular disease) or diabetes of more than 20 years duration should not use CHCs.

Migraine Headaches

Individuals with migraine headaches may experience a decreased or an increased frequency of migraine headaches when using CHCs. A higher risk of stroke is seen in patients experiencing migraine with aura compared to those with simple migraine. The risk of stroke in individuals with migraines has been elevated twofold to threefold. However, given the low absolute risk of stroke in those less than 35 years of age, CHCs in healthy, nonsmoking individuals with migraine headaches without aura may still be considered. Likewise, individuals with nonmigrainous headaches may also use CHCs without restriction. However, individuals of any age who have migraine with aura should not use CHC, and those who develop migraines with aura while receiving CHC should discontinue use and consider a progestin-only option. Individuals developing migraines without aura while receiving CHC should have their headaches evaluated to determine severity, evaluate for signs of an aura, and to discuss the risk versus benefit of CHC use.

Breast Cancer

Breast cancer may be hormone sensitive and risk may be slightly elevated with the use of hormonal contraception. If hormones are discontinued, the breast cancer risk returns to the same levels seen for persons who never used them, although it may take longer for those who had taken for more than 5 to 10 years. For healthy young individuals, the benefits of hormonal contraception in preventing unwanted pregnancies and associated other benefits outweigh any risks. For those over the age of 40 or those who have an elevated risk of breast cancer because of family history or other factors, alternatives may be considered. The choice to use CHCs should not be affected by the presence of benign breast disease or a family history of breast cancer with either mutation. In individuals identified with BRCA1 or BRCA2 mutations, increased risk of breast cancer with COCs has been controversial. Until additional data are available, it is important to understand these risks and ensure they are discussed with patients as even a small increase in risk may be clinically important. Patients with current or past history of breast cancer should not use CHCs.

Thromboembolism

Estrogens increase hepatic production of factor VII, factor X, and fibrinogen in the coagulation cascade, therefore increasing thromboembolic event risk (eg, deep vein thrombosis and pulmonary embolism). These risks are increased in individuals who have underlying hypercoagulable states (eg, deficiencies in antithrombin III, protein C, and protein S; factor V Leiden mutations, prothrombin G2010 A mutations) or who have acquired conditions (eg, obesity, pregnancy, immobility, trauma, surgery, and certain malignancies) that predispose them to coagulation abnormalities. The incidence of thromboembolism and mortality is increased threefold in current OC users compared to nonusers. However, this risk is still less than the risk of VTE incurred during pregnancy. COCs containing new progestins such as third-generation progestins (eg, desogestrel and norgestimate) and a fourth-generation progestin (eg, drospirenone) have been associated with a slightly higher risk of thromboembolism. Although the mechanisms for this increased risk are unclear, this increased risk may be due to: (a) a greater effect on the procoagulant, anticoagulant, and fibrinolytic pathways than earlier generation progestins; (b) an increased resistance to the anticoagulant effect of activated protein C; (c) increased levels of sex hormone–binding globulin; and (d) antiandrogenic effects of drospirenone make the CHC more estrogenic. A continuous, higher exposure to estrogen seen with the transdermal patch or vaginal ring is the reason for an increased thromboembolic risk with these agents as well. An advisory committee to the FDA decided to change the product labeling of the transdermal patch as well as products containing drospirenone to include additional information about the increased risk of thromboembolism. In addition, the vaginal ring also has an additional precaution in the product labeling. Therefore, for individuals at an increased risk of thromboembolism (eg, older than 35 years, obesity, smoking, personal or family history of venous thrombosis, prolonged immobilization), it would be prudent to first consider low-dose oral estrogen contraceptives containing older progestins, progestin-only contraceptive methods, or barrier methods. A recent systematic review of progestin-only contraceptives did not suggest an overall significant increase in venous or arterial events. Limited evidence suggests slight increases in thromboembolism in those using these for therapeutic indications or in those with other thromboembolic risk factors. Any slight increase in risk likely translates into a small increase in absolute numbers of thrombotic events at the population level.

Weighing the risks versus benefits of using CHCs containing third- and fourth-generation progestins, transdermal patch, and vaginal ring to determine their place in therapy is controversial. The risk of VTE with CHC use is 3 to 12 per 10,000 person-years, compared with 1 to 5 per 10,000 person-years in non-CHC users and nonpregnant biologically female individuals. The risk increases to about 10 per 10,000 person-years with drospirenone-containing COCs. Risk of VTE is also higher with the transdermal patch and possibly with the vaginal ring. A continuous, higher exposure to estrogen seen with these formulations may be the cause of this increased risk. Regardless of contraceptive product, the risk is still lower than the risk of thromboembolism during pregnancy (5-20 per 10,000 person-years).

Obesity

The prevalence of obesity continues to rise each year among all age groups, including patients of childbearing age. Individuals with increased body

weight have increased basal metabolic rates and induction of hepatic enzymes, leading to increased hormonal clearance and decreased serum concentrations of hormonal contraceptives. In addition, patients who are obese have more adipose tissue, increasing hormonal sequestration, and decreased free hormone serum concentrations, resulting in lower efficacy. Regardless of body weight, IUDs, implants, and DMPA have low failure rates, and progestin-only contraceptives are considered safe in obese individuals. In addition, the advantages of using an estrogen-containing contraceptive method (pill, patch, ring) generally outweigh the risks. DMPA is associated with more weight gain than other methods. With regard to EC, the copper IUD is the most reliable method in obese individuals. Oral EC products may be less effective and the effectiveness of levonorgestrel, in particular, is diminished.

Obese individuals are also at risk of VTE, although studies evaluating the incidence of thromboembolism in obese persons taking hormonal contraceptives have produced conflicting results. At baseline, obesity doubles the risk of thromboembolism compared to someone with a normal BMI. Progestin-only hormonal contraception may be more appropriate for obese individuals over the age of 35 years, although the CDC considers the benefits of estrogen-containing contraceptives to outweigh the risks as well. Patients should be counseled on any risks and consider alternative contraceptive methods on an individual basis. The risk of thromboembolism during pregnancy and in the peripartum period is significantly greater than the risk with any hormonal contraceptive agent.

Postpartum Use of CHCs

In the postpartum phase, there is concern about use of CHCs due to hypercoagulability risks and the effects on lactation. In the first 21 days postpartum (when the risk of thrombosis is higher), estrogen-containing hormonal contraceptives should be avoided (see Table 104-6). If contraception is required during this period, progestin-only contraceptive methods may be acceptable alternatives. Breastfeeding individuals must avoid CHCs for the first 42 days postpartum if they have risk factors for VTE and for 30 days without risk factors. In those individuals who are not breastfeeding, CHCs should be avoided for up to 42 days postpartum in those with risk factors for VTE and for 21 days for those without VTE risk factors (CDC MEC Category 2). After 42 days postpartum, there is no restriction to the use of CHCs (CDC MEC Category 1 for non-breastfeeding and CDC MEC Category 2 for breastfeeding).

Systemic Lupus Erythematosus

Contraception is important in biologically female individuals with systemic lupus erythematosus (SLE) because the risks associated with pregnancy are high in this population. CHCs exacerbated the symptoms of SLE, postulating that estrogen may cause cutaneous lupus to progress to systemic lupus by promoting B-cell hyper-responsiveness and inducing or increasing autoimmunity. OCs with less than 50 mcg ethinyl estradiol do not increase the risk of flare in individuals with stable SLE without antiphospholipid/anticardiolipin antibodies. Therefore, CHCs should be avoided in patients with SLE and antiphospholipid antibodies or vascular complications as the risks outweigh the benefits of progestin-only contraceptive use in patient population. The copper IUD may be the best option in this situation. For patients with SLE without antiphospholipid antibodies or vascular complications, progestin-only contraceptives or the copper IUD may be an alternative to CHCs; however, those with SLE and severe thrombocytopenia should avoid the copper IUD and DMPA injection.

Discontinuing Combined Hormonal Contraceptives and Return of Fertility

There is no evidence that CHC, transdermal patches, or vaginal ring use decreases subsequent fertility. Return to fertility with CHC use is usually within a few months. However, delayed ovulation is more common in individuals with a history of irregular menses. If amenorrhea does continue beyond 6 months, patients should be counseled to see a physician for further fertility workup. Individuals were counseled to allow two to three normal menstrual periods before becoming pregnant to permit the reestablishment of menses and ovulation. However, infants conceived in the first month after discontinuation of an OC had no greater chance of miscarriage or being born with a birth defect than those born in the general population.

Progestin-Only Contraceptives

[3] [4] [5] There are a few hormonal contraceptives that contain only progestin. Formulations include oral tablets, injections, a subdermal implant, and IUDs that are available with a prescription or from a clinician. More recently, a progestin-only oral tablet was approved for over-the-counter (OTC) use and is available without a prescription. Sustained progestin exposure blocks the LH surge, thus inhibiting ovulation. Should ovulation occur, progestins reduce ovum motility in the fallopian tubes. Even if fertilization occurs, progestins thin the endometrium, reducing the chance of implantation. Progestins also thicken the cervical mucus, producing a barrier to sperm penetration. Individuals who may benefit from progestin-only contraceptives are those who are breastfeeding, those who are intolerant to estrogens (ie, have a history of estrogen-related headache, breast tenderness, or nausea), or those with concomitant medical conditions or contraindications in which estrogen is not recommended (see Table 104-6). This method of contraception does not provide any protection from STIs/STDs.

Oral Progestin-Only Contraceptives and Administration

[8] [9] There are three progestin-only oral products available: norgestrel, norethindrone, and drospirenone. Norethindrone and norgestrel tablets are also known as “minipills” and have similar effectiveness to COCs with a perfect-use failure rate of 0.3% and typical-use failure of 7% (Table 104-1). The norethindrone 35-mg product and the OTC norgestrel 0.075 mg product consist of 28 days of active hormone per cycle, which must be taken every day of the menstrual cycle at approximately the same time to maintain contraceptive efficacy. As with other OCs, initiating norgestrel or norethindrone tablets may be done any time during the cycle. If taken within the first 5 days of menstrual bleeding, a backup contraceptive method is not required. Starting any other time in the cycle requires an additional contraceptive method for 2 days. If a norgestrel or norethindrone-only OC is taken more than 3 hours late, patients should use a backup method of contraception for 48 hours.

Drospirenone 4-mg tablets known as the product Slynd contain 24 days of active hormone and 4 days placebo. Drospirenone-only tablets have a typical-use failure rate of 4%. Slynd can be started on day 1 of menses with no additional backup method. If started later in the cycle, a backup contraceptive method is required. There is more flexibility in dose administration with drospirenone compared with norethindrone, a missed dose is considered more than 24 hours after the scheduled administration time. The individual can take the missed tablet as soon as possible and continue with the pill pack as no backup contraception is needed. If two or more active tablets are missed, the individual should take the last missed tablet as soon as possible and continue taking one tablet daily as instructed while using an additional contraceptive method for 7 days.

Oral Progestin-Only Contraceptives Adverse Effects, and Considerations

[3] [6] [7] Progestin-only pills may not block ovulation, as nearly 40% of patients continue to ovulate normally, so the risk of ectopic pregnancy is higher with their use than with other hormonal contraceptives. Common progestin adverse medication effects may include irregular menses, acne, headache, nausea, or libido changes. Drospirenone products may have less acne adverse medication effects, but may need monitoring for thromboembolism, hyperkalemia, and bone loss.

Medication interactions are also a consideration for oral progestin-only tablets. In particular, norethindrone and norgestrel formulations are metabolized via the liver through the cytochrome P450 system. Medications that induce the P450 system like phenytoin, carbamazepine, oxcarbazepine, primidone, topiramate, protease inhibitors, and St. John’s wort, as examples may affect oral progestin metabolism. With the exception of rifampin, broad-spectrum antibiotics do not affect levels of oral progestins. Considerations for drospirenone-only tablets also include medications that may increase potassium levels, such as ACE inhibitors, potassium-sparing diuretics, and high-dose ibuprofen. The concurrent use of these medications with drospirenone should be avoided due to the potential risk of hyperkalemia.

Similar to estrogen-containing contraceptives, oral progestin-only contraceptives should be avoided in individuals with a history of breast cancer, unexplained bleeding, and SLE with antiphospholipids. Caution may be needed in patients with a history of current VTE, complicated diabetes, heart or hepatic disease. Starting oral progestin contraceptives postpartum or while breastfeeding may be used, though follow-up may be required per the CDC recommendations. The OTC progestin-only product is contraindicated in individuals sensitive to FD&C Yellow No. 5. In addition, with the OTC product, individuals may need some clarification regarding the difference and use of norgestrel 0.075 mg tablet versus the emergency contraceptive levonorgestrel 1.5 mg tablet (discussed later in the chapter) as they are both progestin-only products and OTC but used differently to prevent pregnancy.

Progestin Injections

Steroid hormones provide longer-term contraception when injected into the skin. In addition, injectable progestins are beneficial for individuals with adherence issues, as they have lower failure rates than CHC methods (see Table 104-1).

Depo-Provera (DMPA) is similar in structure to naturally occurring progesterone and is administered every 3 months either by deep intramuscular injection in the gluteal or deltoid muscle or subcutaneously in the abdomen or thigh within 5 days of onset of menstrual bleeding. With perfect use, the efficacy of DMPA is more than 99%; however, with typical use, 3% of individuals experience unintended pregnancy. The primary mechanism of action is suppression of ovulation. Depo-Provera is available as a 150 mg/mL injection vial or prefilled syringe for IM injection, and Depo-SubQ Provera 104 mg is available as a prefilled syringe. The subcutaneous formulation is also FDA-approved for use in treating endometriosis. Administration of both formulations of DMPA requires a medical office visit; however, studies of patient self-administration of subcutaneous DMPA have demonstrated

positive results.

Progestin Injection Administration

[5,8,9] Depo-Provera may be administered at any time as long as it is reasonably certain that the patient is not pregnant. If it is administered between days 1 and 7 of the menstrual cycle in individuals who have not previously used hormonal contraception, then no backup method is needed. If it is administered at any other time of the menstrual cycle, then an additional nonhormonal contraceptive is needed as backup method for 7 days. Additional recommendations on initiating the implant when switching from other methods of contraception are included in the package insert. Although these injections may inhibit ovulation for up to 14 weeks, the dose should be repeated every 3 months (12 weeks) to ensure continuous contraception. The patient must be confirmed to not be pregnant if there is a lapse of more than 13 weeks between injections for the intramuscular formulation or 14 or more weeks between injections for the subcutaneous formulation. However, CDC recommendations differ and state for either formulation, and pregnancy should be excluded in individuals with a lapse of 15 or more weeks.

Progestin Injection Considerations

[3,4,5,6] As with other contraceptive agents, concomitant conditions should be evaluated prior to use of DMPA. Although no adverse effects have been documented in infants exposed to DMPA through breast milk, DMPA must not be initiated until 6 weeks postpartum in breastfeeding patients. However, the CDC cites a lack of evidence supporting this claim and classifies DMPA use during this time frame as a category 1 or 2 suggesting that the benefit may outweigh the theoretical risk. Patients who are not breastfeeding but require contraception can receive DMPA immediately postpartum. It is contraindicated in individuals with a current diagnosis of breast cancer due to potential hormonally sensitive tumors, and should be used with precaution in those with a past history of breast cancer, vascular, cardiovascular, or cerebrovascular disease, multiple risk factors for cardiovascular disease, and lupus. There is some concern that the impact of DMPA on lipids (potentially decreased HDL) and the hypoestrogenic pharmacologic effects may increase the risk of a vascular event. However, the risks with DMPA are much lower than with CHCs so risks and benefits should be weighed on an individual basis. Patients with sickle cell disease are good candidates for DMPA, due to a reduction in sickle cell pain crises in those using DMPA. In addition, patients with seizure disorders may experience fewer seizures when taking DMPA for contraception, and there is not a concern with antiseizure medications reducing the contraceptive efficacy of DMPA. Because return of fertility may be delayed after discontinuation of DMPA, it should not be recommended to individuals desiring pregnancy in the near future. The median time to conception from the first omitted dose is 10 months and 68% of those are able to conceive within 12 months, 83% within 15 months, and 93% within 18 months of the last injection.

Progestin Injection Adverse Effects

[6] Menstrual irregularities are the most frequent adverse effects of both formulations of DMPA and are most common in the first year of use. These irregularities include spotting, prolonged bleeding, and amenorrhea; counseling patients on these possibilities is important before initiation of the method. Individuals who cannot tolerate prolonged bleeding may benefit from a short course of NSAIDs (for 5-7 days) during the bleeding, and in addition, a short course of estrogen (if no contraindications are present) for approximately 10 to 20 days. The incidence of irregular bleeding decreases from 30% to 50% in the first 2 years to 10% thereafter, and after 12 months of therapy, 55% of patients report amenorrhea, with the incidence increasing to 68% after 2 years.

Other adverse effects, including breast tenderness and depression, occur less commonly. Weight gain is a concern for many patients using DMPA, and the incidence and amount gained vary widely. It has been reported that weight gain in some patients averages 1 kg annually and may not resolve until 6 to 8 months after the last injections. However, use of DMPA in obese patients should not be excluded. Appropriate consideration of multiple factors should be evaluated for obese patients and individualized decisions made. For all patients, weight and BMI should be monitored for patients receiving DMPA.

DMPA has been associated with short-term bone loss in younger individuals of reproductive age. This potential adverse effect may be due to lower ovarian estrogen production that occurs when gonadotropin secretion is suppressed. Because longitudinal studies demonstrated effects on BMD, the FDA issued a black box warning for DMPA in 2004. It states that DMPA should be continued for more than 2 years, only if other contraceptive methods are inadequate. It also states that the loss of BMD seems to be greater with increasing duration of use and may not be completely reversible. However, the majority of clinicians view the effects of DMPA on BMD (which in the majority of cases is reversible) as a surrogate marker and there are no clear data that demonstrate the effects of DMPA on fracture risk. The ACOG and CDC continue to recommend that for most patients the benefits of DMPA outweigh the risks even when used beyond 2 years of use. It is not routinely recommended to use DMPA in individuals on long-term corticosteroids (eg, patients with rheumatoid arthritis) with a history or high risk of fractures. While the ACOG does not recommend the routine screening of BMD in most patients, a discussion regarding the risks and benefits of this contraceptive option is recommended prior to initiation and with prolonged use.

Subdermal Progestin Implants

[3][4][5]Nexplanon (similar to the original product Implanon marketed in the United States) is a single 4-cm-long implant, containing 68 mg of etonogestrel, which releases etonogestrel at a rate of 60 mcg daily for the first month, then decreases to an average of 30 mcg daily at the end of the 3 years of recommended use. The etonogestrel implant is placed under the skin of the upper arm using a preloaded inserter, and clinicians must receive training from the manufacturer to properly insert or remove the device. The primary mechanism of action is suppression of ovulation. When ovulation is not suppressed, etonogestrel still is effective as the progestin thickens the cervical mucus and produces an atrophic endometrium. With both perfect and typical use, the efficacy rate is over 99%. However, in overweight and obese individuals weighing more than 130% of their ideal body weight, the efficacy is possibly decreased. However, it is noted that overweight individuals were excluded from studies, and recent small studies have not demonstrated any decreased effects.

Progestin Implant Insertion

[9]The etonogestrel implant can be inserted at any time as long as it is reasonably certain the individual is not pregnant. If the implant is inserted between days 1 and 5 of the menstrual cycle in those who have not previously used hormonal contraception, then no backup method is needed. If it is inserted at any other time of the menstrual cycle, then an additional nonhormonal contraceptive is needed as backup method for 7 days. Additional recommendations on initiating the implant when switching from other methods of contraception are included in the package insert. After removal, fertility returns within 30 days.

Progestin Implant Adverse Effects

[6]The major adverse effect associated with Nexplanon is irregular menstrual bleeding. Patients should be counseled about the risk of irregular bleeding patterns so that patients will not request early removal of Nexplanon. Some patients may become amenorrheic with continued use, but many continue to have prolonged bleeding and spotting. Those who cannot tolerate prolonged bleeding may benefit from a short course of NSAIDs (for 5-7 days) during the bleeding and from a short course of estrogen (if no contraindications are present) for approximately 10 to 20 days. Insertion and removal complications are rare (less than 2%). Nexplanon is radio-opaque, making it easy to locate for removal by conducting an x-ray if needed. Information from the manufacturer suggests using precaution when there is potential for medication interactions in the presence of potent CYP450 inducers (eg, rifampin, phenytoin, and carbamazepine). This information conflicts with CDC recommendations which classify combining those medications with Nexplanon as a category 2, and suggest that the benefits may outweigh the theoretical risks. However, the CDC does still recommend use of additional nonhormonal contraception or switching to DMPA or an IUD as the preferred methods of managing these potential medication interactions.

Intrauterine Devices

[3][4][5]Currently, five IUDs are available, four of them contain levonorgestrel (Mirena, Skyla, Liletta, and Kyleena), one contains copper (ParaGard T 380A, many times referred to as ParaGard). All of the mentioned IUDs are T-shaped and clinicians must receive training from the manufacturer to learn effective insertion or removal of the IUDs. These IUDs have several possible mechanisms of action, including inhibition of sperm migration, damaging ovum or disrupting transport, and possibly damaging the fertilized ovum. Due to the presence of local progestin, the Mirena, Skyla, Liletta, and Kyleena IUDs have additional mechanisms of endometrial suppression and thickening cervical mucus. The most recent evidence regarding the mechanisms of action demonstrates that the contraceptive activity of IUDs occurs before implantation. Efficacy rates with IUDs are greater than 99% with both perfect- and typical-use, and should not be inserted in the presence of current pregnancy, current PID, current STI/STD, puerperal or postabortion sepsis, purulent cervicitis, undiagnosed abnormal vaginal bleeding, malignancy of genital tract, uterine anomalies or fibroids distorting uterine cavity, allergy to an IUD component, or Wilson's disease (for copper IUD). If an IUD is already in place and the patient contracts an STI/STD, the IUD in most cases can remain in place while the STI/STD is being treated. The risk of PID among IUD users is low, and there are no long-term effects on fertility, and average time to return of fertility is similar to oral contraceptives. The influence of medication interactions on the efficacy of IUDs is not a primary concern based on manufacturer and CDC recommendations.

[6][9]ParaGard is a highly effective IUD that contains copper and can be left in place for 10 years. A disadvantage of ParaGard is increased menstrual blood flow and dysmenorrhea, as the average monthly blood loss among users increased by 35%. Mirena, Skyla, Liletta, and Kyleena contain the progestin levonorgestrel and are approved for the prevention of pregnancy in the United States. Liletta and Mirena are also approved for pregnancy prevention up to 8 years of use and also approved for up to 5 years of use for the treatment of heavy menstrual bleeding. They release 20 mcg of levonorgestrel daily, decreasing over time. Kyleena can be used for up to 5 years and releases 17.5 mcg of levonorgestrel daily, decreasing over time.

Skyla can be used for up to 3 years and releases 14 mcg of levonorgestrel daily, decreasing over time. For all of the levonorgestrel IUDs, the systemic absorption of the progestin is minimal and considerably less than with OCs. There are no direct comparisons of safety or efficacy; when used appropriately all are highly effective and well tolerated.

Intrauterine Device Insertion

[9] IUDs can be inserted at any time as long as it is reasonably certain that the user is not pregnant. If the IUD is inserted between days 1 and 7 of the menstrual cycle in those who have not previously used hormonal contraception, then no backup method is needed. If it is inserted at any other time of the menstrual cycle, then it is recommended to use an additional nonhormonal contraceptive backup method for 7 days. Additional recommendations on initiating an IUD when switching from other methods of contraception are included in the package inserts.

Concerns about pain and infection upon insertion of the IUD are common; however, for most patients, insertion-pain is minimal and is not prolonged. If needed, common OTC pain relievers such as NSAIDs or acetaminophen may be helpful. Premedicating with misoprostol or paracervical lidocaine blocks have been studied, but based on the evidence, misoprostol is not recommended for most patients due to lack of efficacy. Paracervical lidocaine blocks may be recommended for pain reduction, but it is not a commonly accepted standard of care. Risk of infection upon IUD insertion is minimal, and it is not recommended to prophylactically treat with antibiotics. Individuals with current PID or STI/STD should delay having their IUD inserted. In contrast, users with an IUD in place that develop PID or an STI/STD should treat the infection, but it is not typically recommended to remove the IUD. Users who have not been screened for STIs/STDs according to CDC guidelines should be screened at the same time as insertion. If results come back positive, then the STI/STD can be treated at that time.

Intrauterine Device Adverse Effects

[6] The major adverse effect associated with IUDs is irregular menstrual bleeding. The levonorgestrel IUD produces its effects locally via suppression of the endometrium, causing a reduction in menstrual blood loss over time. In contrast to the copper IUD, menstrual flow in users of the levonorgestrel IUD is decreased, and development of amenorrhea has been observed in 20% of users in the first year and 60% in the fifth year. Mirena and Liletta specifically have an additional indication for treatment of heavy menstrual bleeding (menorrhagia). A disadvantage of the levonorgestrel IUD is increased spotting in the first 6 months of use; users should be counseled that the spotting will decline gradually over time. Those who cannot tolerate prolonged bleeding may benefit from a short course of NSAIDs (for 5-7 days) during the bleeding. In addition, a short course of estrogen (if no contraindications are present) could be used for approximately 10 to 20 days.

IUD use in nulliparous and adolescent individuals was considered a precaution. However, recent evidence, clinical experience, and expert opinion do not preclude use in these populations. Risks versus benefits should be considered, and the users must be counseled on the efficacy and potential adverse effects. Strong consideration of an IUD is appropriate in this population due to high efficacy rates and low complication rates. In addition, Skyla and Liletta included adolescent patients less than 18 years of age in clinical trials.

Long-Acting Reversible Contraception

[3] [5] LARC refers to a category of hormonal and nonhormonal contraceptives that include IUDs and implants. This type of contraception is highly efficacious in preventing pregnancy, but the effects are quickly reversible upon removal. As LARC does not require effort or adherence by the patient once they are inserted, perfect-use and typical-use efficacy rates do not differ, and the efficacy rate is similar to that of surgical options such as tubal ligation (see Table 104-1). When compared to other methods of hormonal contraception, especially OCs, LARC methods are not used as frequently in the United States; however, increased education campaigns are demonstrating effectiveness. The use of LARC has increased to 14% of all individuals biologically female between the ages of 15 and 44, and all patients should be considered potential candidates for this method. Due to the high efficacy rates and emerging evidence of LARC methods, increased use may decrease unintended pregnancy rates.

Emergency Contraception

[10] EC is used to prevent unintended pregnancy after unprotected or inadequately protected sexual intercourse (eg, no contraception, condom breakage, contraceptive mishap, or nonadherence, sexual assault). Pregnancy occurs when the fertilized egg is implanted into the endometrial lining. After intercourse, implantation of the fertilized egg typically takes approximately 5 days. Progestin-only and progesterone receptor modulator products are approved by the FDA and recommended as first-line EC options. Insertion of ParaGard (copper IUD) or prescribing higher doses of COCs

(Yuzpe method) are other options.

Currently, the progestin-only formulation containing levonorgestrel 1.5 mg tablet × 1 dose is approved specifically for EC in the United States. The primary mechanism of action of progestin-only EC is inhibiting or delaying ovulation. The levonorgestrel-containing EC formulation is the regimen of choice due to availability, improved tolerability, and potentially increased efficacy rates. All formulations are now offered as one-dose options, to be given within 72 hours (3 days) of unprotected intercourse. However, the earlier the medication is given, the greater the efficacy and less chance of a pregnancy. Notably, this regimen may be effective for up to 5 days after unprotected intercourse; but consideration of ulipristal or the copper IUD may be a better option if a patient can get access in time. Levonorgestrel-containing EC products are available without a prescription to patients of all ages in the United States.

[10] Ulipristal acetate (ella) was approved for use as an EC and is a selective progesterone receptor modulator with mixed progesterone agonist and antagonist properties. Its mechanism of action depends on the timing of administration relative to the patient's menstrual cycle. However, the primary mechanism of action appears to be delay of ovulation. Ulipristal acetate is available by prescription only as a single dose of 30 mg taken within 120 hours (5 days) after unprotected intercourse so that it maintains efficacy for the full 120-hour window. Data also exist to support noninferiority of ulipristal acetate compared to levonorgestrel-containing EC.

Ulipristal acetate is not recommended for use in breastfeeding patients. Ulipristal acetate affects progesterone receptors and may interfere with ongoing hormonal contraception. A reliable barrier method is recommended for intercourse that occurs in the same menstrual cycle with ulipristal acetate use, even if the patient is on a regular hormonal contraceptive. In addition, the individual should avoid using a hormonal contraceptive method or initiating a new hormonal contraceptive for at least 5 days after ulipristal acetate administration. Taking hormonal contraception sooner may alter the effect of ulipristal acetate as well as may compromise the effect of the hormonal contraceptive.

[10] Determining the exact effectiveness rate of EC is difficult; however, the range has been reported to be between 59% and 94%. EC may prevent an average of 75% of expected pregnancies when taken appropriately. Individuals must have an advanced prescription on hand or access to an OTC formulation to maximize the effectiveness of EC.

Controversy exists regarding the potential for decreased efficacy of oral EC (both levonorgestrel and ulipristal) in overweight or obese individuals. No large-scale studies have been designed to fully resolve the controversy, and data from randomized trials have suggested an association with increased body weight and decreased efficacy of oral EC. However, data demonstrate that there may be a decline in efficacy of levonorgestrel in females weighing greater than 75 kg. As oral EC is the most widely used EC method due to its accessibility, this issue is controversial. In 2016, the FDA announced that there was not enough evidence to change levonorgestrel labeling and encouraged further studies. There is no effect of increased body weight on efficacy of a copper IUD.

[6] Common adverse effects of EC include nausea, vomiting, and irregular bleeding. Nausea and vomiting occur significantly less when progestin-only and progesterone receptor modulator EC is administered. Many patients will experience irregular bleeding regardless of which EC method is used, with the menstrual period usually occurring 1 week before or after the expected time. Routine screening prior to or after receiving progestin-only and progesterone receptor modulator EC is not recommended. If a pregnancy already exists, the oral EC will not disrupt or harm the embryo. In addition, there are no contraindications to the use of these methods of EC (for the Yuzpe and copper IUD methods clinicians must adhere to their contraindications and precautions). No current data regarding the safety of repeated-use EC are available, but current consensus suggests that the risks are low, and patients can receive multiple regimens if warranted, though use of a regular ongoing contraceptive should be encouraged. Appropriate counseling should be provided regarding timing of the dose, common adverse effects, and use of a regular contraceptive method (additional nonhormonal contraceptive methods should be used after EC for at least 7 days).

Pregnancy Termination

[11] For various reasons, medications may be needed for pregnancy termination. There are a variety of protocols and considerations that will not be covered in depth within this chapter. Medications used in early pregnancy (≤70 days) termination supported by most national and international medical organizations include mifepristone and misoprostol typically used in combination or with misoprostol alone.

Mifepristone is a steroid that binds progesterone receptors and causes abortion by blocking progesterone, softening the cervix, increasing uterine contractility, and increasing prostaglandin sensitivity. Progesterone is needed to maintain the corpus luteum during pregnancy. Softening of the cervix

and increasing prostaglandins also affects the pregnancy by stimulating contractions. Mifepristone is usually administered orally. Prescribing of mifepristone is restricted to a prescriber that has met the training and qualifications of the manufacturer and certified under the FDA Mifepristone REMS program, and it is only dispensed out of the certified prescriber's facility or a certified pharmacy with prescription issued by a certified prescriber. Although it is only used short term for pregnancy termination, it requires monitoring for medication interactions as it is metabolized by the CYP450 3A4 system. Therefore, caution should be taken when administered with strong inhibitors or inducers of that system.

Boxed warnings for mifepristone include infection and bleeding. Bacterial infections and sepsis may occur without findings upon pelvic examination after the abortion or without signs of infections such as bacteremia and fever. Excessive bleeding may occur and could be a sign of incomplete abortion or other complications and needs prompt medical attention. Prescribers need to inform patients of these risks prior to use and also educate patients on what to do if they feel they experience these events by discussing a patient agreement created by the manufacturer. When used as an abortifacient, mifepristone is contraindicated in patients with bleeding disorders or on anticoagulants.

Misoprostol is a prostaglandin E1 analog, currently marketed as a protective agent in patients at risk for gastric ulcers that also causes softening of the cervix and stimulates uterine contractions. Off-label uses include abortion, labor induction, preventing and treating postpartum hemorrhage, cervical ripening for medical procedures, and treatment of early pregnancy loss. Adverse medication effects of misoprostol may include stomach upset, diarrhea, headache, dizziness, chills, and fever. There are a variety of dosage forms available, including oral, vaginal, buccal, and sublingual. The oral form is not recommended because of decreased efficacy, as the other formulations have better adsorption. In addition, the vaginal route may cause less gastrointestinal adverse medication effects.

Abortion regimens include mifepristone–misoprostol (most common), or misoprostol used alone. The mifepristone–misoprostol regimen approved for use by the FDA includes mifepristone 200 mg orally on day 1 and then misoprostol 800 mcg administered buccally 24 to 48 hours after the mifepristone dose. The efficacy of this regimen has been reported as 98% in pregnancies up to 49 days. Efficacy is higher if the regimen is used earlier in the pregnancy. The mifepristone–misoprostol regimen, compared to misoprostol alone, works faster and is more effective in later gestational ages.

In all cases, further assessment by the treating provider is required in the days that follow medication administration to ensure complete abortion and to assess for any complications. Abdominal cramps and bleeding are common after medical abortion. An individual should be counseled that they will likely have heavy menstrual bleeding, but it is important for them to recognize if there is too much bleeding. Those experiencing bleeding that soaks two maxi pads per hour for 2 consecutive hours should contact their healthcare provider promptly. Acetaminophen or NSAIDs such as ibuprofen may be used to help relieve pain and cramping. Use of NSAIDs inhibits new prostaglandins but will not affect the use of misoprostol in pregnancy termination.

EVALUATION OF THERAPEUTIC OUTCOMES

9 Selecting a contraceptive method should involve the patient and clinician using a shared decision-making model. Contraceptive pharmacotherapy should be personalized for each patient, taking into account desired outcomes from a contraceptive and noncontraceptive perspective. Factors to consider include effectiveness, presence of coexisting medical conditions or medications, safety, adverse effects, cost, return to fertility time, and patient preference of the contraceptive method (eg, long-acting, short-acting, hormonal, oral, nonoral, barrier). Patients should receive both verbal and written instructions on the chosen method of contraception. In addition, access to timely contraception is important. With the introduction of the first OTC progestin-only oral contraceptive, accessibility to hormonal contraceptives is increasing. Furthermore, some states have (or are in the process of obtaining) expanded scope of practice to include provision of hormonal contraception by a pharmacist increasing access to self-administered contraceptives for the public. Follow-up appointments can increase adherence and provide opportunities to address other health maintenance issues. The contraceptive outcome of pregnancy prevention can be assessed when needed by obtaining a serum or urine pregnancy test.

Monitoring of the Pharmaceutical Care Plan

3 4 5 8 Contraceptive users should receive an annual preventative medicine exam that may include a cytologic screening (if appropriate) and pelvic and breast examination. Consultation should provide routine health maintenance screening and to assess for clinical problems or adverse effects related to contraception (see Tables 104-4, 104-5, and 104-6). These annual screenings do not have to occur prior to prescribing hormonal contraception.

Annual BP monitoring is recommended for all users of CHC. When a patient with a history of glucose intolerance or diabetes mellitus begins or

discontinues the use of hormonal contraception, glucose levels must be monitored. Monitoring for the presence of adverse effects related to hormonal content or the presence of coexisting medical conditions is recommended for individuals using CHCs. Those using the etonogestrel implant should be monitored annually for menstrual cycle disturbances, local inflammation, or infection at the implant site, acne, breast tenderness, headaches, and hair loss. Patients using DMPA should be asked at 3-month follow-up visits about weight gain, menstrual cycle disturbances, and fractures. Those using IUDs should be asked at 1- to 3-month follow-up visits about IUD placement (checking for IUD strings to ensure the IUD is still in the proper position), changes in menstrual bleeding patterns, and symptoms and protection against STIs/STDs. Clinicians should check for proper IUD positioning and symptoms of upper genital tract infection.

Finally, clinicians should monitor, and when indicated, screen for HIV and STIs/STDs. All individuals should receive counseling about healthy sexual practices including the use of condoms to prevent the transmission of STIs/STDs when necessary.

CONCLUSION

A variety of contraceptive methods are available. Selection of a contraceptive method depends on many factors. Patient preference, method effectiveness, medical history, contraceptive adverse medication effects, desire for a return to fertility, and available access to products all play a role in choosing the best contraception method for a patient. Clinicians play a critical role in helping patients carefully select an appropriate contraceptive method, monitoring adverse medication effects, and providing education on optimal use, effectiveness, and STI/STD prevention that can help reduce STIs/STDs and unintended pregnancies.

KEY RESOURCES

KEY RESOURCES

ACOG Practice Bulletin No. 206. Use of hormonal contraception in women with coexisting medical conditions. Obstet Gynecol 2019;133(2):e128–50. DOI:10.1097/AOG.0000000000003072. Erratum in: Obstet Gynecol 2019;133(6):1288.

An article providing clinical guidance, recommendations, and interpretation of U.S. Medical Eligibility Criteria for Contraceptive Use by the American College of Obstetricians and Gynecologists regarding management and contraceptive use in individuals with chronic medical conditions.

American College of Obstetricians and Gynecologists. Emergency contraception. Practice Bulletin No. 152. Obstet Gynecol 2015;126:e1–11. DOI:10.1097/AOG.0000000000001047.

An article providing information, recommendations and clinical guidance of use of emergency contraception in individuals. It discusses data for efficacy, safety, and use of available emergency contraceptive methods.

Committee on Practice Bulletins—Gynecology; Society of Family Planning. Medication abortion up to 70 days of gestation: ACOG practice bulletin, number 225. Obstet Gynecol 2020;136(4):e31–47. DOI:10.1097/AOG.0000000000004082.

An article providing information and recommendations regarding safety, efficacy, and use of medications for abortion. It discusses dosing, adverse effects, and compares and contrasts efficacy between various regimens.

Nguyen AT, Curtis KM, Tepper NK, et al. U.S. medical eligibility criteria for contraceptive use, 2024. MMWR Recomm Rep 2024;73(No. RR-4):1–126. DOI:10.15585/mmwr.rr7304a1. Available at: https://www.cdc.gov/mmwr/volumes/65/rr/rr6503a1.htm?s_cid=rr6503a1_w

Recommendations that serve as clinical guidance for using different forms of contraceptives in individuals that have various characteristics or medical conditions. Includes information about contraindications that categorizes risks for contraceptive use along with a summary chart that is helpful in selecting the appropriate contraceptive product for an individual.

Curtis KM, Nguyen AT, Tepper NK, et al. U.S. selected practice recommendations for contraceptive use, 2024. MMWR Recomm Rep 2024;73(No. RR-3):1–77. DOI:10.15585/mmwr.rr6504a1. Available at: https://www.cdc.gov/mmwr/volumes/65/rr/rr6504a1.htm?s_cid=rr6504a1_w

Recommendations that serve as clinical guidance for using various forms of contraception in patients. Includes descriptions, effectiveness rates, initiation recommendations, missed dose instructions, and special considerations for different forms of contraceptives.

ABBREVIATIONS

ACHES	abdominal pain, chest pain, headaches, eye problems, and severe leg pain
ACOG	American College of Obstetricians and Gynecologists
BMD	bone mineral density
BMI	body mass index
CDC	Centers for Disease Control and Prevention
CHC	combined hormonal contraceptive
COC	combined oral contraceptive

DMPA	depot medroxyprogesterone acetate
DXA	dual-energy x-ray absorptiometry
EC	emergency contraception
EE	ethinyl estradiol
FDA	Food and Drug Administration
FSH	follicle-stimulating hormone
GnRH	gonadotropin-releasing hormone
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
IUD	intrauterine device
LARC	long-acting reversible contraception
LDL	low-density lipoprotein
LH	luteinizing hormone
MI	myocardial infarction
NSAID	nonsteroidal anti-inflammatory drug
OC	oral contraceptive
OTC	over-the-counter
Pap	papanicolaou (smear)
PMDD	premenstrual dysphoric disorder
SHBG-TBG	sex hormone (testosterone)-binding globulin
SLE	systemic lupus erythematosus
STI/STD	sexually transmitted infection/disease
TSS	toxic shock syndrome
VTE	venous thromboembolism
WHO	World Health Organization

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SELF-ASSESSMENT QUESTIONS

1. A 36-year-old individual who had difficulty adhering to medication schedules is seeking contraception. PMH: mitral valve prolapse. Current medications: metoprolol succinate extended-release 25 mg every day, multivitamin every day. Social history: smoker, occasional drinking. Family history: noncontributory. What would be the most appropriate product for this patient?

   A. Combined oral contraceptive

   B. Progestin-only oral contraceptive

   C. Injectable depot medroxyprogesterone acetate

   D. Vaginal ring contraceptive

2. A 32-year-old patient comes to the pharmacy to pick up their prescription for an OC containing norgestimate 0.25 mg/ethinyl estradiol 35 mcg. This patient complains of significant nausea and headaches since starting her oral contraceptive 5 months ago. What is the most appropriate recommendation?

A. Call the physician to change the prescription to another OC with less estrogen.

B. Call the physician to change the prescription to another OC with less progestin.

C. Buy a home pregnancy test to rule out pregnancy.

D. Wait for another 1 to 2 months to see if symptoms improve.

3. A 36-year-old individual is considering starting drospirenone-only contraceptive tablets. Their medical history includes hypertension which is controlled by hydrochlorothiazide and ramipril and GERD for which famotidine is used as needed. Which of the following should be considered for the patient?

A. There are no issues to consider and discuss.

B. Drospirenone is contraindicated for use in patients with hypertension.

C. There may be a risk of hyperkalemia while using drospirenone and ramipril.

D. Famotidine may decrease the effectiveness of drospirenone.

4. An 18-year-old patient with a seizure disorder seeks contraception today. They are taking phenytoin and have a BMI of 32 kg/m^2. Which of the following contraceptive methods would be most appropriate?

A. Combined oral contraceptive

B. Intrauterine device

C. Transdermal contraceptive

D. Progestin-only pill

5. A 23-year-old patient comes to the pharmacy frantically asking for advice. It is the first week of their pill pack and their partner's condom broke last night during sexual intercourse. The patient states that they are currently taking a low-dose COC but missed the last 2 days of pills. The patient's BMI is 23 kg/m^2. What is best to recommend?

A. Take all missed pills today and resume normal dosing for remainder of the month. Backup protection is not needed.

B. Make an appointment with their physician to discuss the use of ulipristal.

C. Take the most recent missed pill as soon as possible and then resume normal dosing for the remainder of the month. No backup protection is needed.

D. Buy and use an OTC levonorgestrel-containing emergency contraception at the pharmacy.

6. A 28-year-old individual has been given a prescription for rifampin x 7 days. You notice that they also take the oral contraceptive, EE 35 mg/norgestimate 0.25 mg, for contraception. What is the most appropriate counseling point today?

A. They should change their contraceptive to a vaginal ring or transdermal patch.

B. They should add a barrier method to their current regimen while taking the antibiotic and for at least 7 days after and possibly up to 28 days after rifampin therapy.

C. They should ask their physician for a different antibiotic.

D. They should be switched to a high-dose estrogen OC to overcome the loss of estrogen effectiveness caused by the antibiotic.

7. Once discontinued, which of the following contraceptives is considered to have the longest return to fertility time?

A. Combined oral contraceptives

B. Progestin-only injection

C. Transdermal contraceptive patch

D. Progestin-only oral contraceptives

8. The World Health Organization and CDC Medical Eligibility Criteria for Contraceptive Use list which of the following as category 4 (a condition which represents an unacceptable health risk if the contraceptive method is used)?

A. Uterine fibroids

B. Cluster headaches

C. Hypertension with vascular disease

D. Obesity age over 30 years

9. LR is a 27-year-old patient who started on a low-dose COC containing 20 mcg of ethinyl estradiol 2 months ago and is currently nursing. They went out of town for the weekend and missed one dose of her medication yesterday. It is the second week of their pill pack and is now asking for your opinion on how they should handle the situation. What would be the most appropriate response?

A. Take the missed active tablet as soon as possible plus your regularly scheduled tablet for today (two tablets total today) and then continue taking tablets daily, one each day as prescribed. No additional contraceptive protection is recommended.

B. Recommend an OTC levonorgestrel-containing emergency contraceptive.

C. Discard the current pack, allow bleeding to occur, and then restart a new pack, taking one tablet each day. Use condoms or abstain from sex until the new pill pack has been taken for 7 days in a row.

D. An OTC levonorgestrel-containing emergency contraceptive should be recommended, but because they are nursing, they cannot use it.

10. Your patient is a 39-year-old patient with a history of migraines with aura. They are a nonsmoker and have two children with no immediate plans to get pregnant. This patient is obese (weighs 115 kg) and does not want to gain any more weight. What contraceptive method would be the best option?

A. Levonorgestrel IUD

B. Injectable depot medroxyprogesterone acetate

C. Combined oral contraceptive

D. Vaginal ring contraceptive

11. Which of the following nonhormonal contraceptive methods do not require a prescription or an office visit to a clinician?

A. Cervical cap

B. Copper IUD

C. Diaphragm

D. Internal condom

12. Which of the following medications may be commonly used in pregnancy termination regimens?

A. Depot medroxyprogesterone acetate

B. Ethinyl estradiol

C. Mifepristone

D. Drospirenone

13. Use of the vaginal contraceptive ring would be most appropriate in which situation?

A. 30-year-old patient with hypothyroidism

B. 38-year-old patient who smokes one pack per day

C. 36-year-old patient having migraines with aura

D. 28-year-old breastfeeding patient 18 days postpartum

14. AT is a 26-year-old patient with a history significant for depression and dysmenorrhea. They are currently using a transdermal contraceptive patch that fell off 5 days ago. Due to traveling, they were not able to place a new patch. They had unprotected sexual intercourse 4 days ago. What is the most appropriate recommendation?

A. Buy OTC levonorgestrel-containing emergency contraception at the pharmacy and counsel this patient to not restart their contraceptive transdermal patch for at least 5 days after taking the EC and use an alternate nonhormonal contraceptive in the meantime.

B. Buy a home pregnancy test.

C. Inform this patient that there is no EC option for this particular situation.

D. Call their clinician with a recommendation for a verbal order for ulipristal emergency contraception and counsel the patient to not restart their contraceptive transdermal patch for at least 5 days after taking the EC. They will need an alternate nonhormonal contraceptive in the meantime.

15. A 25-year-old single, nulliparous patient who is a nonsmoker with no significant medical history wants an easy method of contraceptive that they do not have to remember, is highly effective, and quickly reversible. What would you recommend?

A. Combined oral contraceptive

B. Progestin implant

C. Injectable depot medroxyprogesterone acetate

D. Progestin-only oral contraceptive

ANSWERS

1. **C.** Depot medroxyprogesterone acetate is the most appropriate recommendation. Combined hormonal contraceptives are contraindicated due to age and smoking history, so nonhormonal or progestin-only contraceptives are the remaining options. Progestin-only pills would not be appropriate for this patient due to a history of nonadherence. Refer to sections "Oral Progestin-Only Contraceptives and Administration" and "Progestin Injections."

2. **A.** Changing the OC to a product with less estrogen is the most appropriate recommendation. Nausea and vomiting is generally due to estrogen adverse effects. The patient is currently on a product with 35 mcg of ethinyl estradiol. Products with lower estrogen content are available and generally adverse effects become less over the first 3 months of use. As the patient has been using the product for 5 months, it would be appropriate to switch to another at this time. Refer to section "Managing Combined Oral Contraceptive Adverse Medication Effects."

3. **C.** Drospirenone is a derivative of the potassium sparing diuretic, spironolactone, and has some aldosterone blocking activity. It may increase

potassium levels and may interact with ACE inhibitors such as ramipril increasing the risk of hyperkalemia. Famotidine does not affect drospirenone effectiveness and drospirenone may be used in patients with hypertension. Refer to "Progestin-Only Contraceptives" section.

4. **B.** The IUD would be the most appropriate recommendation, as it will not interact with the phenytoin, which is an enzyme inducer (see Table 104-6). Agents will be affected and although less likely, vaginal and transdermal products may be affected as well.

5. **D.** In this particular situation, it would be important to counsel on starting EC sooner rather than later (ie, do not wait to make physician appointment). The patient is in her first week of taking hormones along with missing two tablets that puts her at risk for unintended pregnancy. For missed doses, if two or more consecutive tablets are missed then one missed tablet must be taken as soon as remembered and discard the remaining missed tablets. Continue taking the OC tablets as scheduled. Counsel to use additional nonhormonal contraception (such as condoms) until tablets have been taken for 7 consecutive days. Consider use of EC based upon situation if unprotected intercourse occurred and in this case, the patient did have unprotected intercourse making EC the best option. Refer to "Emergency Contraception" section.

6. **B.** There has been clinical significance of an interaction with the antibiotic rifampin. It is therefore prudent to use a backup method throughout any antibiotic use and for at least 7 days after and possibly up to 28 days after rifampin therapy. The CDC does rate this a category 3 for use (Table 104-6). Do not increase the dose of estrogen in the OC, change contraceptive products, or change antibiotics when there is a short course of treatment and the patient is doing well otherwise.

7. **B.** The progestin-only injection, depot medroxyprogesterone, is considered to have the longest return to fertility reported to be as high as 12 months. OCs (combined and progestin-only) and transdermal contraceptives have a quicker return to fertility time. Refer to "Progestin-Only Contraceptives" and "Combined Oral Contraceptives" sections.

8. **C.** Hypertension with vascular involvement is the only category 4 diagnosis listed (see Table 104-6).

9. **A.** If one tablet is missed or late then the tablet must be taken as soon as remembered and the rest of the tablets must be taken as prescribed (for most patients that means two tablets taken on the same day). Typically, no additional nonhormonal contraception methods are warranted. Currently, nursing does not affect any of the recommendations. Refer to "Missed Doses of Combined Oral Contraceptives" and "Emergency Contraception" sections.

10. **A.** Since the patient has a history of migraines with aura, it would be recommended to avoid products with estrogen (Table 104-6) and best to use progestin-only or nonhormonal products. The progestin injectable form tends to cause more weight gain. Therefore, the IUD would be the most appropriate recommendation.

11. **D.** The internal condom is the correct choice since it is available OTC. All the other nonhormonal contraceptives listed (cervical cap, copper IUD, and diaphragm) do require a prescription and/or an office-visit with a clinician. See Table 104-2 and "Nonpharmacologic Therapy" section.

12. **C.** Mifepristone is commonly used with other agents such as misoprostol for pregnancy termination regimens. Depot medroxyprogesterone acetate, ethinyl estradiol, and drospirenone may be contained in various hormonal contraceptives and are not used for pregnancy termination. Refer to "Pregnancy Termination" section.

13. **A.** Hypothyroidism is not a contraindication for use of CHCs that include the contraceptive vaginal ring (Table 104-6). Smoking more than 15 cigarettes per day, along with being older than 35 years of age, is a contraindication to the use of contraceptives that contain estrogen. Migraines with aura and being less than 30 to 42 days postpartum are also contraindications to use of estrogen contraceptives due to increased risk of stroke and blood clots, respectively. In addition, if patients are having trouble with milk production, estrogen-containing contraceptives may decrease milk supply and are not recommended for those breastfeeding. See "Considerations with Combined Hormonal Contraceptive Use" and "Postpartum Use of CHCs" sections.

14. **D.** The ideal scenario would be to obtain a prescription for ulipristal acetate as it is labeled for use in patients who have had unprotected intercourse within 120 hours (5 days). OTC levonorgestrel is labeled for use within 72 hours of having unprotected intercourse. Levonorgestrel has an effectiveness up to 120 hours after intercourse, but the best option in this scenario is to obtain a prescription for ulipristal acetate if possible. There is also no concern with restarting hormonal contraception after using a levonorgestrel EC product; however, patients should be counseled to wait 5 days before restarting their hormonal contraception after taking ulipristal as hormonal contraceptives may interfere with the effectiveness of ulipristal. Another method of contraception should be used in the interim. Refer to "Emergency Contraception" section.

15. **B.** A long-acting reversible contraceptive (LARC) fits the criteria requested by the patient that includes high effectiveness, easy to use, and quickly reversible. Other LARC options include IUDs. Refer to "Subdermal Progestin Implants" and "Long-Acting Reversible Contraception" sections.