SEVENTH EDITION

Michèle G. Curtis
Silvia T. Linares
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Glass' Office Gynecology

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Wolters Kluwer Health

GLASS' OFFICE GYNECOLOGY

SEVENTH EDITION

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To Jessica, Rachael, Natalie, Matthew, and Ester who are the loves and lights of my life's journey.

–Michèle G. Curtis, MD, MPH, MML

To Norma, my mother*, for her eternal presence in my life, to Luis,* my husband*, for his support and encouragement, and to Martin,* my son*, happiness and awe every day.*

–Silvia T. Linares, MD

To Borys, my best friend and a true supporter of women. A life without you would be no life at all.

–Leah Antoniewicz, MD

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Preface

Clinical knowledge is estimated to double every 18 to 24 months and although this may appear to preclude the use of written textbooks, knowledge alone does not signify changes in clinical approaches, evaluations, or treatments. In addition, trying to piecemeal knowledge facts together to form a coherent story is not as effective as a collective summary of what is currently known, with the caveat that some things may have changed since the writing, editing, and final publication of the text.

As practitioners, it is abundantly clear that the role of technology in our practices is an ever expanding one with promises of incredible success, breakthroughs, and truly individualized medical care. At times, the breathtaking pace of advances in molecular "–omics," nanotechnology, computer modeling, data mining, and the diminishing size of diagnostic and surgical instruments is enough to make one feel almost obsolete. The appeal of these approaches lies in their underlying premise to get to the true root cause of illness and disease—a confirmation of the reductionistic approach that Western medicine is founded upon. It is enticing to think that if we could just know the exact genetic or proteomics trigger that has started the cascade of events leading to our patient's cancer, we could truly cure them.

But this approach alone is insufficient because it promotes such myopic foci that the issues of context get lost—the context of the patient's life, emotions, relationships, thought patterns, and value systems, all of which are integrated and interrelated in the creation of what is called health. Dr. David Lowe, a mentor of mine, once told me that health is a result of three things: who we are (genetics), where we live (environment), and how we live (lifestyle, daily living decisions). From this viewpoint, one is able to see the interaction of the macroenvironment outside of us with the scientifically seductive microenvironment that lies within us. In my opinion, it is this approach that will allow for the perfect marriage of public health with medical care and hopefully, will result in better health for all. One area with expanding awareness of the interdependent nature of macro and micro effects in women's health is in the fetal origins of disease and epigenetics, where effects may be traced back several generations not just one.

The practice of medical care is a subset of health care overall and the best practitioners; that is, the ones who can truly help their patients optimize their health, understand this, and seek to know more than just a litany of facts related to diagnosis and treatment alone. It is in knowing our patients, and the matrices of their lives both externally and internally, that we are best able to help them maintain their health or optimize it. The human touch we speak of embodies intuition, experience, empathy and compassion, and a willingness to develop a variety of communication skills and approaches so that patients truly know that their provider is listening and that they care. It is the true art of medicine and I believe that its value in impacting our patients' well-being is increasingly underappreciated and undervalued. If it truly has no significant role to play, then it is quite plausible that medical providers will simply become technicians with computers, assays, and technology taking on the role of "clinician."

As a physician who cares for and about a segment of patients that comprises a little over half of the world's population (women and girls), the importance of accurately assessing their health concerns and needs while getting to know them as the individuals they are is brought home in every patient encounter. The title of this book is *Office Gynecology*, but its contents reflect more than just selected gynecologic conditions. The chapters mirror the common issues seen by women's health providers every day and so the scope of this book includes more than just conditions that occur between the belly button and the knees. As we learn more about the interactions between the mind, body, and environment, there is no doubt that future topics we can only begin to imagine now will someday become almost fundamental chapters for textbooks such as this.

Acknowledgments

Identifying willing and expert authors to compose reviews of the issues and conditions we see in the practice of office gynecology is no easy feat—and that is only the first step in the process of producing a textbook. To the authors who did agree to participate—and even those who did not—in this project, I extend my sincere thanks and appreciation for doing so, or at least, considering it. Editing a book that seems to be exponentially increasing its chapter offerings with each edition is a herculean task—especially because it is done in the context of busy daily lives, professional and personal challenges and obligations, and the oh-so-human desire to just relax after a long day or week in lieu of engaging a text with critical and analytical thinking skills. This textbook would not have been possible without the incredible dedication and efforts of my fellow editors, particularly Dr. Leah Antoniewicz and Dr. Silvia T. Linares. They are amazing women as well as fabulous physicians. Then, there is the poor soul who receives the edited chapters, replete with highlights, markups, and ever changing references and tables and who then has to put it all together for the publisher. In this case, it was a woman with a great deal of patience and a strong sense of humor: Franny Murphy. Without her keeping us all on track and being able to learn our collectively different editing styles and approaches, this textbook would have not been possible.

This marks the third edition of *Glass' Office Gynecology* where I have served as the lead editor. It will also be my last. It is amazing to me how many life events can occur over the course of three editions, but through it all, the love of family remains and strengthens. I have reached the midway point of life and am currently reflecting on what it is I want to do for the next 20 years or so of my working life. I have told my friends and colleagues that if you only edit a book once, it may mean you did not do so well at it. If you edit it twice, you did do a good job the first time as reflected in the invitation to do it again. If you do it three times, you might want to consider an evaluation for a *DSM-5* diagnosis of some sort. For me, four times would be grounds for commitment and besides, it is time to do new things and develop new skill sets and perspectives. I hope these editions have been helpful to all of those providers who work to help women and their children and families. I hope there are further editions to come as well that will never lose sight of the fact that practicing medicine at both the macro and micro levels truly creates health care outcomes that are greater than just the sum of their component parts.

Michèle G. Curtis, MD, MPH, MML

SECTION

Common Gynecologic Conditions

CHAPTER 1

Contraception

Leah Antoniewicz

The use of contraception started since humans were able to associate coitus and pregnancy. Documents from 1850 BCE (the Kahun papyrus) describe several methods to create a hostile environment or a physical barrier for sperm. The Romans during the second century AD developed a spermicidal barrier using wool and an acidic vegetable mix.[1]

The voluntary control of fertility is of paramount importance to modern society and a central role of health care providers. To ensure suatainable development, countries need to plan population growth. More importantly, empowering women to control their reproductive capacity allows them to reach individual, familial, and societal goals, contributing to personal and collective well-being. Having freedom to decide over their sex life, procreation, and lifestyle is a fundamental right of women and is critical to achieving gender equality and women's autonomy. Unfortunately, depriving women of their sexual and reproductive rights is the main method used in many societies around the world to keep them from achieving their right place in society.

In the United States, 50% of all pregnancies are unintended, and approximately half of these end in abortion.[2] Of these, 50% of unintended pregnancies occurred despite the use of contraception. Although decreasing, adolescents have the highest unintended pregnancy rate. Disappointingly, the rate has increased for low-income and less educated women.[3]

Regulating fertility improves maternal and neonatal outcomes.[4] In developing countries, family planning programs prevent an estimated 187 million unintended pregnancies, including 60 million unplanned births, 105 million abortions, and averts an estimated 2.7 million infant deaths and 215,000 pregnancy-related deaths.[4] For a comparison of birth-related and method-related deaths, see Figure 1.1.[5]

The introduction of birth control methods that are easier to use and more effective provides women the opportunity to choose the one that better fits their personal preferences, health needs, and lifestyles. Contraceptives can be mechanical, hormonal, and behavioral. No method is 100% effective nor does any of them guarantee a perfect fit for every woman's needs. Each presents its own benefits, risks, and side effects. The decision of which method to use belongs to the patient. The role of the health care provider is to empower the patient by offering suggestions according to her health history, her personal lifestyle, psychological and social factors, the methods' correct use and side effects, and of course any contraindication that may apply to her case.

OVERVIEW OF CONTRACEPTION

Contraceptives are either hormonal or nonhormonal. Contraceptives can be taken orally, be injected, or be slowly released through direct contact with the body. Hormonal contraceptives use estrogen and/or progesterone and have several mechanisms of action. Estrogen prevents formation of the dominant follicle, potentiates progesterone, and stabilizes the endometrium. Ethynil estradiol (EE) is almost exclusively used as the estrogen component in hormonal contraceptives and is usually the component that is relatively or strongly contraindicated in some patients. Progesterone prevents ovulation, thickens cervical mucus, suppresses endometrial growth, and perhaps alters secretions and peristalsis of the fallopian tubes. The progestational compounds are varied, as are their side effect profiles. In the last two

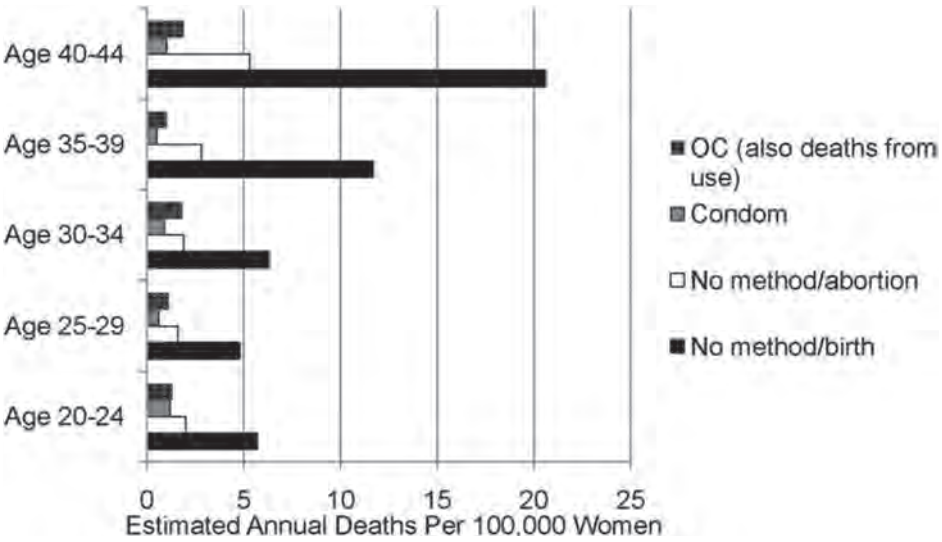

FIGURE 1.1 Estimated annual deaths per 100,000 women according to contraceptive use. (From Maguire K, Westhoff C. The state of hormonal contraception today: established and emerging noncontraceptive health benefits. *Am J Obstet Gynecol*. 2011;205:S4–S8.)

TABLE 1.1 Percentage of Women With Unintended Pregnancy During First Year of Typical Use and First Year of Perfect Use of Contraception and Percentage Continuing Use at End of First Year, United States

	% of Women Experiencing Unintended Pregnancy Within First Year of Use		% of Women Continuing Use at 1 Year[c]
Method (1)	**Typical Use[a] (2)**	**Perfect Use[b] (3)**	**(4)**
Chance[d]	85	85	
Spermicides[e]	26	6	40
Periodic abstinence	25		63
Diaphragm[f]	20	6	56
Withdrawal	19	4	
Condom (male)[g]	14	3	61
Pill	8		71
Ring	8	0.3	
Patch	8	0.3	
IUD			
Copper T380A	0.8	0.6	78
LNG 20	0.1	0.1	81
Depo-Provera	0.3	0.3	70
Levonorgestrel			
Implants (Implanon, Nexplanon)	0.4	0.4	88
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

[a]Among *typical* couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
[b]Among couples who initiate use of a method (not necessarily for the first time) and who use it *perfectly* (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.
[c]Among couples attempting to avoid pregnancy, the percentage who continue to use a method for 1 year.
[d]The percentages becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception to become pregnant. Among such populations, about 89% become pregnant within 1 year. This estimate was lowered slightly (to 85%) to represent the percent who would become pregnant within 1 year among women now relying on reversible methods of contraception if they abandoned contraception altogether.
[e]Foams, creams, gels, vaginal suppositories, and vaginal film
[f]With spermicidal cream or jelly
[g]Without spermicides
Adapted from Trussell J. Contraceptive efficacy. In Hatcher RA, Trussell J, Stewart F, et al, eds. *Update to Contraceptive Technology*. 19th ed. New York: Ardent Media, Inc; 2007.

TABLE 1.2 Strong Contraindications to Combined Hormonal Contraceptive Use

- Thrombogenic disorders (factor V Leiden, prothrombin mutations; protein C, S, or antithrombin deficiency)
- History of or current venous thromboembolism without anticoagulation
- Cerebral vascular or coronary artery disease
- Known or suspected estrogen-dependent neoplasm
- Abnormal uterine bleeding of unknown etiology
- Liver disease, including hepatic adenomas, carcinomas, benign liver tumors or acute infections (mononucleosis, hepatitis)
- Known or suspected pregnancy
- Conditions that increase the risk of myocardial infarction (smoker at age 35 years or younger, diabetes with complications)
- Migraine with aura
- Systemic lupus with complications or antiphospholipid antibodies
- In patients with conditions that predispose to hyperkalemia (renal insufficiency, adrenal insufficiency, hepatic dysfunction), YAZ and Yasmin should be used with caution because they contain drospirenone, an aldosterone antagonist.

decades, we have seen a decrease in both side effects and vascular complications of hormonal contraception as a result of lower doses of estrogen and progestins. In general, the estrogen-related contraindications are for those patients with cardiovascular disease, with thromboembolic disease or risks, and with liver disease. The most common contraindication for progestin-only methods is unwillingness or inability to accept irregular bleeding, including amenorrhea. With the exception of the copper-releasing intrauterine device (IUD) and sterilization, nonhormonal methods are far less cost-effective. This chapter begins with considerations of certain medical conditions at certain times of the reproductive spectrum. It continues with a detailed discussion of various reversible methods, starting with the most effective, followed by a discussion of permanent methods.

Contraception Concerns With Selected Medical Conditions and Special Populations

When considering that the hormone levels in pregnancy are far higher than those produced by combination (estrogen-progestin) hormonal contraceptives (oral contraceptives [OCs], the patch and the ring), there

TABLE 1.3 Relative Contraindications to Combined Hormal Contraceptive Use

- Controlled hypertension
- Multiple risk factors for cardiovascular disease (diabetes, obesity, hypertension, lupus, hypertriglyceridemia)
- Medicines that induce liver enzyme metabolism and decrease contraceptive efficacy
- History of cholestatic jaundice during pregnancy or active gallbladder disease
- Breast-feeding

TABLE 1.4 Strong Contraindications to Progestin-Only Methods

- Known or suspected progesterone-dependent neoplasm
- Known or suspected pregnancy
- Unwillingness/inability to have irregular bleeding or amenorrhea
- For both formulations of depo medroxyprogesterone acetate
  - Fragility fracture
  - Desire for pregnancy within a year
  - Current use of aminoglutethimide

are few absolute contraindications to combination hormone contraceptives (CHCs). Progestin-only methods and nonhormonal methods, such as the copper IUD, are a good option for women with relative or strong contraindications to estrogen. Depending on the patient's desires, sterilization may be the best option. For a complete list of strong and relative contraindications to CHCs (including the patch and ring), see Tables 1.1 and 1.2. Other disorders that are relative contraindications to the use of progestin-only methods are listed in Tables 1.3, 1.4, and 1.5.

Adolescents

Establishing confidentiality is of paramount importance with adolescents. Clinicians need to be familiar with how teens think and feel about sex and birth control, what their beliefs and emotions are, and how individual teens may make choices based on their lifestyles and social and affective circumstances. Oral CHCs and condoms are the most commonly used method by this age group, and concomitant use should be encouraged to protect against both pregnancy and sexually transmitted diseases (STDs). Long-acting reversible contraceptive (LARC) methods (IUDs and implants) are safe and effective and should be considered first line.[4]

Postpartum

Because of the higher risk of thrombosis after parturition, it is prudent to delay CHCs until 4 weeks postpartum. IUDs can be inserted immediately postpartum or anytime thereafter. The advantages to immediate insertion are obvious but there is evidence regarding increased expulsion

TABLE 1.5 Relative Contraindications to Progestin-Only Methods

- Controlled hypertension
- Multiple risk factors for cardiovascular disease (diabetes, obesity, hypertension, lupus, hypertriglyceridemia)
- Medicines that induce liver enzyme metabolism and decrease contraceptive efficacy
- History of cholestatic jaundice during pregnancy or active gallbladder disease
- Breast-feeding

rates for this approach, with the lowest expulsion rates occurring immediately postpartum.[5–7] Progestin-only pills can be given at 3 weeks in nonlactating women. Rarely, depo medroxyprogesterone acetate (DMPA) can cause metrorrhagia if given before 6 weeks postpartum but is otherwise safe to give at anytime in nonlactating women.

Lactation

Many authorities recommend nonhormonal or at least delaying hormonal contraceptives until 6 weeks postpartum. Because withdrawal of progesterone with delivery of the placenta is a lactogenic trigger and because estrogen has negative feedback on prolactin, it makes theoretical sense that these hormones could negatively impact lactation. Additionally, there are concerns of hormone transfer to the infant depending on the formulation. A Cochrane review found existing randomized controlled trials are insufficient to establish an effect of hormonal contraception on milk quality and quantity.[7] Therefore, if lactational amenorrhea or a nonhormonal option is not possible, a progesterone-containing contraceptive is recommended at 6 weeks postpartum. Earlier administration should be considered for certain situations.

Women Older Than Age 35 Years

Healthy women older than age 35 years who do not smoke and are not obese can safely take CHCs.

Perimenopause

The need for safe and effective contraceptive methods remains great in the perimenopausal period as evidenced by the high unintended pregnancy rate in this age group, often from a misconception that they do not think they are fertile. In fact, the pregnancy termination rate in women 40 to 50 years of age is exceeded only by those women younger than 15 years of age.[2]

The transition period of changing hormone patterns, or perimenopausal state, begins about 5 to 10 years before the actual menopause. Characteristics of the perimenopause are irregular cycles; changes in both the volume and the duration of bleeding; and for approximately half the women, the onset of variable vasomotor symptoms. The perimenopausal period is characterized by an increased incidence of anovulatory cycles, resulting in an unopposed estrogen state. This predisposes to dysfunctional uterine bleeding, possible endometrial hyperplasia, and a poorly documented, but frequently observed, accelerated growth of uterine myomata. CHC should be the method of choice for nonsmoking, nonobese women to regulate menstrual periods, provide contraception, control vasomotor symptoms, protect bone health, and reduce the risk of endometrial and ovarian cancers. These women often do well on the lowest estrogen dose of 20 mcg. Because there is no good test to confirm menopause, she can continue combined hormonal contraception until the age of 51 to 55 years, unless there is a change in her health status.

Cerebrovascular Disease

CHCs are contraindicated in the presence of cerebrovascular disease. They also increase the risk for stroke in women with other underlying risk factors.[8]

Migraine and Headache

Patients with a history of migraine headaches should use CHCs cautiously. Some patients will note an improvement, whereas some will notice no change; however, approximately 50% of patients will notice a worsening of their condition, especially during the hormone-free interval. One commonly accepted contraindication to the use of CHCs is a history of classic migraine (migraine with focal neurologic symptoms or aura lasting 5 to 60 minutes) due to an increased potential for stroke. It should be noted that women with a history of migraines have a two- to three-fold increased risk of ischemic stroke, regardless of CHC use.[8]

Seizure Disorder

CHCs have no impact on the pattern or frequency of seizures. However, some anticonvulsants can decrease serum concentrations of estrogen and thus may increase the likelihood of intermenstrual bleeding.[9] An increase in ovulation or accidental pregnancy has never been shown. Although there is no published data to support this, some clinicians start with a 50 mcg EE formulation. Starting with at least 30 to 35 mcg of EE does seem reasonable. If a woman has been started on a 30 mcg EE formulation and develops intermenstrual bleeding, switching to a 50 mcg EE pill may be helpful. Anticonvulsants that do not appear to decrease serum estrogen levels when used concurrently with a CHC include levetiracetam, valproic acid, ethosuximide, and zonisamide.[9] Gabapentin, lamotrigine, and tiagabine do not lower estrogen levels either but they have been studied at subclinical doses.[8]

Cardiovascular Disease

Almost all excess mortality in combined OC users is due to cardiovascular disease. Most of these deaths are due to myocardial infarction (MI). The cardiovascular disease risk is most prevalent in women older than 35 years of age who smoke.[12,13]

Venous Thromboembolism

Although not a major cause of morbidity and mortality, venous thrombotic disease and pulmonary emboli are

known side effects of CHC use. The dose of EE and type of progesterone influence this risk (desogestrel [DSG] and gestodene [GSD] are associated with a two-fold greater risk). Package labeling for certain progestin-only contraceptives list thromboembolism as a contraindication, but this is no supporting evidence for this claim.[13] The transdermal patch, however, did increase venous thromboembolism (VTE) by two-fold in one cohort study.[13] Coagulopathy screening is not cost-effective unless there is personal or family history. Unexplained VTE, hypercoagulable states, and VTE associated with pregnancy or exogenous estrogen are contraindications to combination OCs unless the patient is anticoagulated. Other risk factors for VTE should be considered.[2]

Obesity

Obesity (body mass index [BMI] greater than 30 kg/m^2), and even being overweight (BMI greater than 25 kg/m^2) are independent risk factors for VTE. In obese women ages 35 years or younger, CHC use is appropriate, although there is some evidence that with overweight or obese patients, the efficacy is less than with women with normal BMI.[9] Similarly, women weighing 90 kg or more had significantly higher failure rates with the transdermal patch. Obese women should be counseled regarding this possibility. The levonorgestrel IUD is an excellent choice because it circumvents potential problems related to EE and provides endometrial protection and stabilization.[8]

Hypertension

If a patient has hypertension, it should be controlled (to less than 140/90 mm Hg) prior to beginning combination OCs because they have the potential to aggravate this condition.[12,13]

Increases in blood pressure have been reported in women taking OCs, and follow-up evaluation of blood pressure in such patients is advised. If the blood pressure is controlled and no vascular disease is present, CHCs are not contraindicated. A history of pregnancy-induced hypertension does not preclude the use of CHCs as long as the blood pressure returns to normal postpartum.[13]

Dyslipidemia

Women younger than age 35 years, in the absence of uncontrolled hypertension, diabetes, or other OC contraindications, may consider CHC use. In general, estrogen decreases low-density lipoprotein (LDL), increases high-density lipoprotein (HDL), and increases triglycerides, but does not increase atherosclerosis.[13] This effect is seen with the transdermal patch and the vaginal ring. An OC with a less-androgenic progestin increases HDL more and triglycerides less. If a woman's triglycerides are above 350 mg/dL or in patients with familial hypertriglyceridemia, CHCs should be avoided because they may precipitate pancreatitis and/or adversely affect the patient's risk for cardiovascular disease.

Mitral Valve Prolapse

In general, CHCs can be safely used by women with mitral valve prolapse (MVP) who are symptom free. Use should be limited to MVP patients with an echocardiographic-confirmed diagnosis but without mitral regurgitation. A history of thrombotic complications would require another contraceptive method. Long-acting progestins such as injection or implants are safe to use and may provide increased fibrinolytic activity.

Diabetes

Young diabetic women who are free of retinopathy, nephropathy, hypertension, or other complicating vascular disease(s) are appropriate candidates for low-dose contraceptives. The progestin component of CHCs is believed to increase insulin resistance, although this has not had a verified clinical effect.[8] Women with a history of gestational diabetes during their last pregnancy can safely take low-dose CHCs. The incidence of frank diabetes developing within 3 years of pregnancy is no higher in women taking low doses of CHC than in those using nonhormonal contraceptive methods.[10]

Systemic Lupus Erythematosus

CHCs can be given to women with mild lupus (no vascular disease or nephritis) and no antiphospholipid antibodies.[12]

Sickle Cell Disease

Internationally, recommendations for women with sickle cell disease and CHC use vary widely. DMPA is an excellent choice, as it reduces painful crises.[8] In the United States, many clinicians think that the risks of pregnancy far outweigh the risks associated with CHC use in women with sickle cell disease. Thus, CHC are often prescribed for this population.[11,12]

Oral Contraceptives and Cancer

Breast Cancer

Fear of developing breast cancer has been a deterrent to the use of both hormonal contraceptives and hormone replacement therapy. The issue has been one of major debate for a number of years, and it is still unresolved.[13–15] Early studies suggested a slight association between OC use and breast cancers in *BRCA1/BRCA2* carriers. Results of the Women's Contraceptive and Reproductive Experiences (CARE)[15a] study showed no association between CHCs and DMPA and breast cancer in patients with benign breast disease or a family history

of breast cancer, including *BRCA1/BRCA2* mutations. Some recent studies have presented nonconclusive results that suggest a slightly increased risk for mutation carriers. Despite the failure to prove any decisive association between CHC use and breast cancer, the hypothesis is biologically plausible. Even a slight but hard to prove risk increase could be highly significant given the high incidence of breast cancer. Therefore, the controversy is likely to continue until larger longitudinal studies show more definitive results.

Cervical Cancer

OCs alone do not increase the risk of cervical cancer. However, there is strong evidence that recent use of CHC is associated with increased risk of human papillomavirus (HPV) infection independent of sexual behavior and cervical abnormalities.[16] Among HPV-infected women, those who used OCs for 5 to 9 years have approximately three times the incidence of invasive cancer, and those who used them for 10 years or longer have approximately four times the risk.[17] On the other hand, such association is not observed with progestin-only contraceptives (i.e., DMPA). The mechanism is probably related to CHC affecting host response, making her less likely to clear HPV infection rather than increasing the risk of HPV acquisition.[18]

Endometrial Cancer

Numerous studies have shown a decrease in the risk of endometrial cancer of about 50% in combination oral contraceptives (COC) users. The protective effect is greater with longer duration of CHC use and higher progestogen potency and persists for more than 20 years after cessation of the CHC. Because endometrial cancer is thought to be caused by unopposed estrogen stimulation, progestogen-containing contraceptives could protect against endometrial cancer. The reduction of inflammation in the endometrium produced by CHCs may be the cellular mechanism behind the lower incidence of endometrial carcinoma in CHC users.[19] Although CHCs can effectively reduce endometrial hyperplasia, it should be used only under certain circumstances in patients with or after endometrial cancer.[20]

Ovarian Cancer

Use of CHCs is associated with up to a 46% reduced risk of ovarian cancer compared with never use. As with endometrial cancer, protection from ovarian cancer may persist for up to 20 years after discontinuation of COCs.[17,19] The blockade of ovulation, follicular rupture, and ovarian production of steroids may explain the lesser incidence of ovarian cancer among CHC users. The degree of protection is directly related to the duration of use, with the most significant reduction seen in women using them for more than 8 years. A 20% reduction is seen for every 5 years of use, but some protection is conferred with as little as 3 to 6 months of use. There does not appear to be any diminution in protection with the use of low-dose combination OCs.[20] Furthermore, CHCs appear to reduce ovarian cancer for carriers of *BRCA1/BRCA2* mutations.[21]

Oral Contraceptives and Surgery

Estrogen-containing OCs significantly increase the likelihood of both idiopathic and postoperative venous thrombosis and pulmonary embolism. Although these effects were most marked with early, high estrogen content OCs, there is still risk with present-day preparations containing 30 to 50 mg estrogen. More selective choice of CHC users, reduced estrogen doses, and better surveillance of users appear to have diminished the risk of thromboembolic disease with CHC use. But unfortunately, there are no sure predictors of thromboembolic disease. Because the thrombotic effects of CHCs stop by 4 weeks after termination, it is recommended that CHC use be interrupted one cycle before elective surgery, but the risk of thrombosis should be balanced against the risk of pregnancy. If prolonged immobilization is expected, they should be discontinued. Heparin prophylaxis should be considered if they are continued.[22]

LONG-ACTING REVERSIBLE CONTRACEPTIVE METHODS

Contributing to the many reasons there is a high unintended pregnancy rate in the United States is the popular use of less effective methods (CHCs and condoms), which have high discontinuation rates. LARC methods (IUDs and implants) could help mitigate these factors, with very few contraindications. Several studies have shown that LARC methods reduced repeat adolescent pregnancy and repeat abortions.[3] In fact, expanding access to LARC has been declared a national priority by the Institute of Medicine.[23]

Although these contraceptive methods may have high cost initially, they have multiple advantages over other methods: They are not user-dependent, are highly cost-effective, have high continuation rates, and satisfaction and effectiveness are higher than other methods. They do not require additional visits for resupply or additional funding; furthermore, they offer a rapid return to fertility once discontinued.

Practitioners can increase LARC use in several ways: First, counseling all patients on these methods, including nulliparous and adolescent women[24,25]; second, avoiding unnecessary delays, such as screening for gonorrhea, chlamydia, or cervical cancer; third, avoiding waits for a follow-up visit after pregnancy (abortion, miscarriages, or term), especially in patients at risk for not returning.[25,26]

Intrauterine Devices

IUDs are highly effective with a pregnancy rate of less than 1% after 1 year. All IUDs are spermicidal by interfering with sperm transport and creating a sterile inflammatory environment in the uterus. Prefertilization properties constitute the primary mechanism of action, although the loss of the fertilized ovum may occur before implantation.[27] As previously stated, IUDs do not increase the rate of pelvic inflammatory disease or tubal occlusion. Cervical cancer and STI screening can be done just before insertion if indicated. If treatment for infection is necessary, the IUD should not be removed.[27] Return to fertility is immediate when removed.

Copper Intrauterine Devices

In addition to the mechanism above, copper is directly toxic to sperm, increasing its effectiveness. The TCu-380A (ParaGard) is currently approved for 10-year placement, but may be effective for 12 years. Because of this, it has the highest efficacy with the lowest cost. It is a good option for women who cannot or do not want to take hormones. It may also be used for emergency contraception. The copper IUD may cause dysmenorrhea and a 30 to 50% increase in menstrual flow, which can be mitigated with nonsteroidal anti-inflammatory drugs (NSAIDs). The discontinuation rates due to these two side effects is 12% so the patient should be asked ahead of time if dysmenorrhea and increase in menstrual flow would be acceptable.[28] Over time, copper IUDs are associated with stable ovulatory bleeding patterns, but prolonged bleeding is common in the first few months.[29] The 10-year cumulative failure rate is 2.1 to 2.8% (Fig. 1.2).

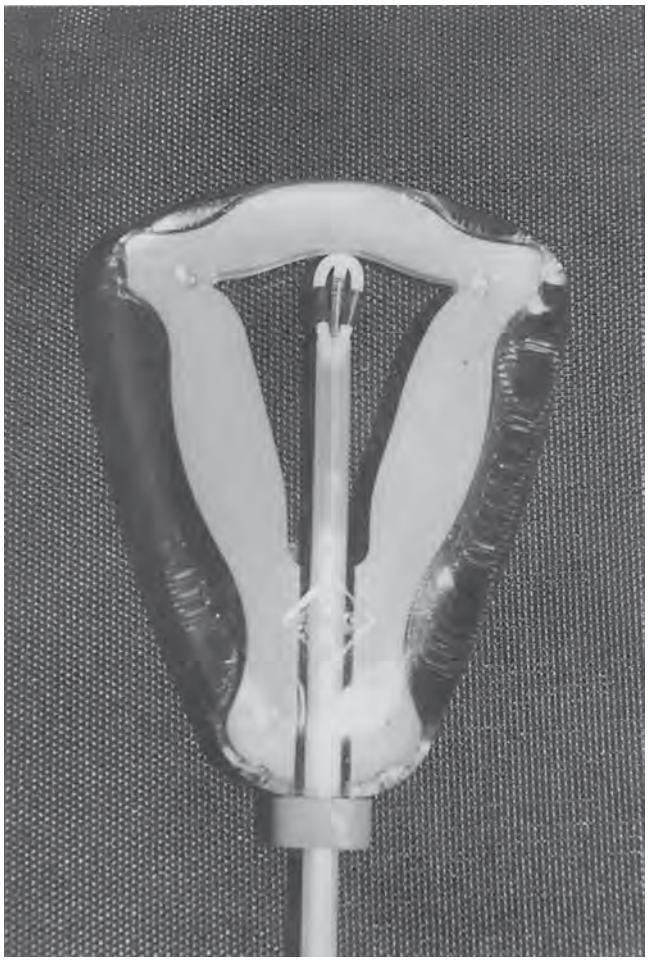

FIGURE 1.2 Copper IUD (ParaGard) readied for placement.

Levonorgestrel-Releasing Intrauterine Device

The levonorgestrel (LNG)-releasing IUD (Mirena) releases 20 mcg LNG daily. It inhibits sperm transport, thickens cervical mucus, partially inhibits ovulation, and causes reversible atrophy of the lining. These actions reduce menstrual flow by 70% at 6 months and by 90% at 12 months.[30] Amenorrhea is seen in 30% of users by 2 years of use.[31–33] The Mirena also improves dysmenorrhea so its use may be preferable in women experiencing heavy or painful periods. The Mirena IUD has been approved for 5 years of use but may be effective for up to 7 years. Two large clinical trials in Finland and Sweden with more than 1600 women and 45,000 cycles of use have demonstrated cumulative 5-year pregnancy rates of less than 0.7 per 100 women.[34]

Although irregular spotting or bleeding may occur in the first few months, this usually diminishes over time. The majority of women who continue to have cyclical menses with the LNG IUD have ovulatory progesterone levels, but only 58% of these women have normal growth and rupture of ovarian follicles on ultrasound exam. Of the women who do not have cyclical menses, 29% have growth and rupture of follicles.[35] It is not surprising then that women using the LNG IUD can develop large (greater than 3 cm) ovarian cysts. In one study, all these cysts spontaneously resolved over a 4-month period, and it is believed the formation of these cysts is of limited significance.[36] These findings are similar to what has been seen with the subdermal LNG implants.[37] As eluded to earlier, there are a host of noncontraceptive benefits with the LNG IUD. In addition to treatment for menorrhagia and dysmenorrhea, it can be used to protect the endometrium from effects of unopposed estrogen.

Complications Associated With IUD Use

The risk of pelvic inflammatory disease (PID) is about 1/1000 and occurs in the first 20 days postinsertion. Women at risk are those with bacterial vaginosis and cervicitis. These infections should be treated with the IUD in place. Uterine perforation is also 1/1000 and is more common with immobile or anteverted or retroverted uteri, lactating women, and inexperienced inserters.

LNG IUD expulsion is more common in younger women, women who have not had children, and when an IUD is inserted immediately after childbirth or abortion. There is a higher risk of expulsion for women who have never given birth.[38] LNG IUD expulsion rate is about 3% when used exclusively for contraception and 9 to 14% when used to control bleeding.[39,40] IUDs decrease the rate of ectopic pregnancy compared with no contraception. However, if pregnancy occurs, the risk of an ectopic pregnancy is increased and the patient should be evaluated immediately.

When pregnancy is diagnosed in the presence of an IUD, the location of the pregnancy (intra- or extrauterine) should be determined and the device removed as soon as possible in the first trimester. Septic abortion is greatly increased when pregnancy is complicated by IUD. Women who become pregnant with an IUD in place have a 50% increased rate of spontaneous abortion. After removal of the IUD, the spontaneous abortion rate decreases to about 30%. If it cannot be removed or she chooses not to have it removed, she should be counseled that in addition to the increased spontaneous abortion rate, the risk of preterm labor, delivery, and sepsis are increased. She can be reassured that there is no increase in congenital anomalies.

Removal of an IUD in an infected, pregnant uterus should be accomplished only after intravenous antibiotic blood levels have been achieved. The removal of the IUD should be done in a location where emergency measures are available, in case septic shock ensues.

The IUD can be inserted safely at any time after abortion or delivery. There is a higher rate of expulsion for the delayed postpartum insertions, although it can be prevented with high fundal placement. Additionally, the rate of expulsion is lower for immediate postpartum insertions (within 10 minutes of placental delivery) than for delayed insertions (within 48 hours of delivery).[22] Insertion of the IUD during the period of lactational amenorrhea has the advantage of significantly decreasing the spotting problem often encountered during the first cycle after insertion. Directions for placement of the copper and progesterone IUDs are found in Appendices 1.A and 1.B.

The patient should check for the IUD string monthly, and the practitioner should check for it at the time of gynecologic examination. If twirling a cytobrush in the cervical canal does not bring the strings into view, an ultrasound should be done to confirm intrauterine location. If the ultrasound does not show it, a flat plate abdominal radiograph can be taken, with an abdominal series to triangulate the location. If the IUD is intra-abdominal/extrauterine, it must be physically retrieved. An intra-abdominal IUD can cause serious problems, including bowel obstruction or perforation. Removal should be done as soon as possible after the diagnosis is made. Copper IUDs, in particular, elicit a strong inflammatory response that may make laparoscopic removal quite difficult. Perforation of the uterus usually occurs at the time of insertion, so it is important to identify the strings a few weeks afterward.

To remove an IUD, the strings are grasped with either a ring forceps or uterine dressing forceps and firm traction is exerted. If the string(s) cannot be seen, a cytobrush in the endocervical canal may help in extracting them. If ultrasound confirms intrauterine location, a paracervical block can be given before using alligator forceps or other instruments in the uterus. Visualization of the IUD with sonography or hysteroscopy may be necessary to facilitate removal.

Implants

Implanon, a single-rod subdermal implant the size of a matchstick, releases 68 mg of etonogestrel (metabolite of DSG) over 3 years. It releases about 40 mcg/day by the end of the first year and 25–30 mcg/day at the end of the third year. It is effective within 24 hours of insertion and prevents pregnancy by immediate thickening of cervical mucus, inhibition of ovulation, and endometrial atrophy. The Pearl index is less than 0.07 pregnancies per 100 woman-years if it is implanted in the *first 5 days* of the menstrual cycle.[38]

Implanon is convenient, has a high continuation rate, is rapidly reversible, does not affect bone density, and is easy to remove. Of note, the U.S. Food and Drug Administration (FDA) requires training to place or remove Implanon, and the manufacturer will not fill orders for physicians who are not trained. The procedure is very simple, requiring local anesthesia and a 2- to 3-mm incision between the bicep and tricep of the nondominant arm so that the distal end of the implant is 8- to 10-cm proximal to the medial epicondyle.

Side effects due to atrophy (irregular bleeding) were the most common reasons for discontinuation according to the package insert (11%). Other side effects such as headache and weight gain occurred in more than 5% of users but were not common reasons for discontinuation. Complications related to insertion and removal are much less common than with Norplant.[39] Implanon is contraindicated in patients being treated with CYP3A-inducing or CYP3A-inhibiting medications.

Jadelle, a two-rod subdermal implant was approved by the FDA for 5 years of use but is not currently marketed in the United States.

ORAL CONTRACEPTION

The development and widespread use of combination hormone contraceptives (CHC) was a major breakthrough in the 20th century. Many observers regard this development as second in importance only to the development and use of broad-spectrum antibiotics.

In choosing a CHC, the optimal formulation will comprise the lowest effective dose with acceptable bleeding profiles and minimal side effects. Certainly, there is a trend in lower estrogen doses, less androgenic progestins, and fewer total days of menstrual bleeding. CHCs impact protein, lipid, and carbohydrate metabolism, but this may not be clinically important. In the United States, CHCs with less than 50 mcg estrogen use EE as the estrogenic component. Lower doses are as effective and have less thrombotic risk and probably less side effects (nausea, breast tenderness, headache, hypertension). Combined hormonal contraceptives can be taken cyclically, by an extended regimen, or continuously.

Most women start CHCs containing 20 to 35 mcg EE. Some of the newer CHC formulations contain fewer placebo days or days with EE only. Some pills contain iron or folate and are chewable. Among the progestins, there are second-generation CHCs, which contain norethindrone (LNG, norgestimate), and third-generation CHCs, which contain DSG or GSD. Drospirenone and dienogest are the newest. Both DSG and norgestimate are less androgenic. The increase in thromboembolism reported in some studies with DSG and GSD may be due to confounding, as there is no biological evidence of this effect.[40] Clinicians can offer several options of CHCs to patients based on their individual characteristics, preference, and tolerance. For example, Yasmin and YAZ are both FDA approved for premenstrual dysphoric disorder (PMDD). These are also a good choice for polycystic ovarian syndrome, hirsuit, or hypertensive patients because drospirenone is antiandrogenic and a diuretic.

Benefits of Oral Contraception

Known benefits of CHC use include the prevention of unwanted and extrauterine pregnancies, reduction in pelvic inflammatory disease, recurrent ovarian cysts, ovulatory pain, premenstrual syndrome, PMDD, and blood loss/iron-deficiency anemia. They also decrease the rate of ovarian, endometrial, and colorectal cancers.[41] They may increase the pleasure of intercourse because it can be spontaneous and without worry of pregnancy. The efficacy of CHCs and other methods is depicted in Table 1.1.

Disadvantages of Oral Contraceptives

Unscheduled bleeding and side effects are a major source of patient noncompliance and discontinuation but tend to resolve after 3 months of use. Therefore, watchful waiting and reassurance is a more logical approach to CHC prescribing than continued switching from one formulation to another. The key to success is an informed patient. Breakthrough bleeding (BTB) is more common in women who smoke and with 20 mcg formulations. Make sure she is taking them regularly because this is the most common reason for BTB. If it persists, rule out pregnancy, infections, drugs that interfere with OCs, and cervical cancer. If the bleeding is just before the placebos, she can stop the pack and start again in 4 to 7 days (depending on the number of placebo pills normally in the pack). If it occurs midcycle, give 7 days of estrogen (EE 2 mg or conjugated estrogen 1.25 mg) while she is taking the OCs.[40] Alternatively, switch to a higher dose pill. Side effects (nausea, headache, breast tenderness, decreased libido) are markedly reduced with pills containing less than 50 mcg estrogen. When side effects do occur, they will usually decline after the first 3 months of OC use. Patients with refractory nausea may try taking the OC immediately after a meal rather than at night on an empty stomach. Changing to a lower dose pill may also help. Additionally, if side effects occur during the placebo pills, consider an extended or continuous cycle regimen.

A Cochrane review assessed 42 trials, including 3 placebo-controlled randomized clinical trials; none of the randomized trials showed a statistically significant difference in weight gain for CHC users compared with the placebo group.[42] Patients need to understand that pills offer no protection from sexually transmitted infections (STIs) and that condoms should be used in nonmonogamous relationships. Other complications include risk of MI, VTE, neoplasia (liver and adenocarcinoma of the cervix), and hypertension (HTN). Prescribe a 3-month supply, but discuss with the patient that monthly trips to the pharmacy may be required.

Clinical Decision Making

Dosing Choices

The World Health Organization (WHO) and FDA recommend using the lowest effective dose.[41] Traditional CHCs contain formulations using EE in combination with various types of progestins for 21 days with 7 days of placebo. Mestranol is used, rarely, and is equivalent to 35 mcg of EE. Clinical choices of a CHC may be based on either the type of progestin agent in the pill or the dose of EE. CHCs with EE may contain 50 mcg (first generation), 40 mcg, 30 mcg, 25 mcg, or 20 mcg. In general, the higher the dose of EE, the better the cycle control, although the type of progestin used in a formulation and the estrogen-progestin ratio may also effect cycle control.[43] In one large open-label study, a triphasic OC with 25 mcg EE and DSG (Cyclessa) was compared with a combination triphasic OC containing 35 mcg EE and norethindrone acetate (NETA). The triphasic combination containing 25 mcg EE and DSG had a significantly lower rate of intermenstrual bleeding and spotting (11%) in comparison to the triphasic combination with 35 mcg EE and NETA. These results may be due to the higher progestational activity of DSG compared with NETA, even though the dose of EE was higher in the NETA combination.[44] In a recent Cochrane review, second- and

third-generation progestins were superior to first-generation progestins for cycle control.[45] Multiphasic pills were created to decrease total hormone levels and side effects with increasing cycle control. So far, this has not been shown to be the case, but many studies were comparing different progestational agents. A recent prospective study in Iran compared LNG in a monophasic and triphasic formulation. There was no difference in side effects, but the triphasic pill was superior for cycle control.[46] Because we do not have enough evidence that triphasic pills have improved bleeding profiles, some experts recommend starting with the cheaper monophasic pills for new users.[47] Biphasic pills have the worst cycle control and are rarely used.[48]

Many newer CHCs also have an extended cycle regimens that have 24 to 28 hormone pills and typically use 20 to 25 mcg of EE. This decreases the chance of ovulation, decreases side effects of endogenous estrogen production, and decreases the days and amount of menstrual flow.[49] Theoretically, use of the additional EE would contribute to the stabilization of bleeding patterns even though the overall dose of EE is low, but in reality, studies have shown increases and decreases in BTB. Extended cycle or continuous CHCs are an option for women with hormone withdrawal symptoms, dysmenorrhea, endometriosis, menorrhagia, or women who simply desire fewer menstrual cycles. With continuous regimens, unscheduled bleeding is seen more frequently but it is reduced over time.

Use of CHCs containing 50 mcg estrogen should be reserved for women requiring additional estrogen to prevent intermenstrual bleeding (e.g., women using drugs that induce hepatic enzymes) or women who have recurring functional ovarian cysts while on OCs containing less than 50 mcg estrogen.

For first-time CHC users, it is best to see them 3 months after initiation of pills to monitor side effects, blood pressure, proper usage, etc.

TABLE 1.6 Drug Interactions With Hormonal Contraceptives

	Category				
Condition	**COC**	**P**	**R**	**CIC**	**Clarifications**
COC, combined oral contraceptives; **P**, combined contraceptive patch; **R**, combined contraceptive vaginal ring; **CIC**, combined injectable contraceptives					
Drug Interactions					
Antiretroviral Therapy					
a) Nucleoside reverse transcriptase inhibitors (NRTIs)	1	1	1	1	Clarification: Antiretroviral drugs have the potential to either decrease or increase the bioavailability of steroid hormones in hormonal contraceptives. Limited data (summarized in Annex 1) suggest potential drug interactions between many antiretroviral drugs (particularly some NNRTIs and ritonavir-boosted protease inhibitors) and hormonal contraceptives. These interactions may alter the safety and effectiveness of both the hormonal contraceptive and the antiretroviral drug. Thus, if a woman on antiretroviral treatment decides to initiate or continue hormonal contraceptive use, the consistent use of condoms is recommended. This is both for preventing HIV transmission and to compensate for any possible reduction in the effectiveness of the hormonal contraceptive. When a COC is chosen, a preparation containing a minimum of 30 mcg ethinylestradiol (EE) should be used.
b) Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	2	2	2	2	
c) Ritonavir-boosted protease inhibitors	3	3	3	3	
Anticonvulsant Therapy					
a) Certain anticonvulsants (phenytoin, carbamazepine, barbiturates, primidone, topiramate, oxcarbazepine)	3	3	3	2	Clarification: Although the interaction of certain anticonvulsants with COCs, P or R is not harmful to women, it is likely to reduce the effectiveness of COCs, P, or R. Use of other contraceptives should be encouraged for women who are long-term users of any of these drugs. When a COC is chosen, a preparation containing a minimum of 30 mcg of EE should be used. Clarification: The recommendation for lamotrigine does not apply when lamotrigine is already being taken with other drugs that strongly inhibit (e.g., sodium valproate) or induce (e.g., carbamazepine) its metabolism, since, in these cases, the moderate effect of the combined contraceptive is unlikely to be apparent.
b) Lamotrigine	3	3	3	3	
Antimicrobial Therapy					
a) Broad-spectrum antibiotics	1	1	1	1	Clarification: Although the interaction of rifampicin or rifabutin therapy with COCs, P, R, or CICs is not harmful to women, it is likely to reduce the effectiveness of COCs, P, R, or CICs. Use of other contraceptives should be encouraged for women who are long-term users of either of these drugs. When a COC is chosen, a preparation containing a minimum of 30 mcg EE should be used.
b) Antifungal	1	1	1	1	
c) Antiparasitics	1	1	1	1	
d) Rifampicin or rifabutin therapy	3	3	3	2	

1. A condition for which there is no restriction for the use of the contraceptive method
2. A condition where the advantages of using the method generally outweigh the theoretical or proven risks
3. A condition where the theoretical or proven risks usually outweigh the advantages of using the method
4. A condition which represents an unacceptable health risk if the contraceptive method is used.

Adapted from World Health Organization. *Medical Eligibility Criteria for Contraceptive Use.* 4th ed. Geneva, Switzerland: World Health Organization; 2009. http://whqlibdoc.who.int/publications/2010/9789241563888_eng.pdf. Accessed December 2, 2013.

Interactions With Other Drugs

With the exception of rifampicin (Rifampin) or rifabutin, broad-spectrum antibiotics have not been shown to decrease the effectiveness of CHCs. Certain anticonvulsants and certain antiretrovirals can reduce effectiveness. During rifampicin or rifabutin use, it is suggested that additional contraceptive measures be used. For select anticonvulsants, a higher dose CHC can be used. For certain antiretrovirals, a DMPA or an IUD is a better choice. A current drug history should be taken when prescribing OCs, and the user should report new medications. For a brief list of various drugs and their interactions with COCs, refer to Table 1.6.

Starting and Stopping the Pill

The patient may start on Sunday (Sunday start), on the first day of menses (first day start), or immediately (quick start). The quick start is recommended by many experts because it mitigates confusion about instructions, pregnancy before pills are started, or forgetting to fill the prescription. For a Sunday start, the patient is instructed to begin taking her pills on the first Sunday after the onset of menstruation, which avoids withdrawal bleeding on the weekends. If menstruation begins on a Sunday, the first tablet is taken that day. For the quick start and Sunday start methods, a negative pregnancy test and backup contraception for the first 7 days are required. For patients beginning a first day start, they are instructed to take their first pill on the first day of menses. Patients are also instructed to take their pills at the same time each day and to use some type of mnemonic or cue to avoid missing pills. Also, a discussion of emergency contraception is recommended for the possibility of imperfect use.

Missed Pills

If one pill is missed, the patient should take it as soon as possible and resume the rest of the pack as usual. Any time the patient misses two or more tablets, she should also use another method of contraception until she has taken a tablet daily for 7 consecutive days. If BTB occurs following missed tablets, it will usually be transient. The likelihood of ovulation occurring if only one or two tablets are missed is low. Newer formulations, with a decrease in the pill-free interval, decrease the likelihood of ovulation if pills are missed during the early part of the cycle. Further instructions for patients can be found in Table 1.7.

Discontinuation of the Pill

Return to fertility is rapid following discontinuation of today's low-dose CHCs. A recent review showed that the pregnancy rates after 12 months of discontinuation was similar to that of nonusers.[50] Allowing 2 to 3 regular cycles before attempting pregnancy is the ideal.

TABLE 1.7 Instructions for Patients Who Missed an Oral Contraceptive Pill

Consecutive Pills Omitted	Time in Cycle	Instructions to Patient
1	Any time	Take missed pills immediately and next one at regular time
2	First week	Take two pills every day for next 2 days, and then resume taking pills on regular schedule.[a,b]
2	Third week	Take one pill every day until last day of third week.[a] Dispose of placebos and begin new pack next day.
≥3	Any time	Take one pill every day until last day of that week. Dispose of placebos and begin new pack next day.[a]

In the event of vomiting, the dose must be repeated or inserted vaginally.
[a]Additional contraceptive measures should be used as soon as the omission of oral contraceptive pills is discovered. These additional measures should be used for at least 7 days.
[b]EC should be taken in the event of unprotected intercourse if two or more pills are missed in the first week.

STEROIDAL CONTRACEPTION: OTHER

Progestin-Only Contraceptive Pill

The progestin-only pill is an alternative for breast-feeding women and women with conditions that preclude the use of estrogen, yet they still retain many of the advantages of CHCs: decreased blood loss, menstrual cramping, and premenstrual syndrome symptoms.

All progestin-only contraceptives cause bleeding pattern changes.[51,52] Approximately 40% of patients will ovulate with the progestin levels achieved with a progestin-only regimen. Although the exact mechanism(s) of action are unknown, it is known that the cervical mucus becomes thick and hostile, rendering it relatively impermeable to sperm. In addition, the endometrium is out of phase, making nidation less likely.

Progestin-only contraceptives can be used by almost every woman and have few medical contraindications (active liver disease or liver tumor being one). Early postpartum administration may slow involution of the uterus after delivery and prolong postpartum spotting and bleeding. A major disadvantage is that they must be taken at the same time every day. Therefore, emergency contraception should be taken if there is a delay of 3 hours or more.

Injectables

Depo Medroxyprogesterone Acetate

DMPA is the only injectable contraceptive available in the United States, although Cyclofem and Mesigyna (combination injectables) are available in other countries.

The typical side effects of DMPA concern menstrual changes, particularly with episodes of unpredictable irregular bleeding during the first months of use. A review of several studies determined that 37.5% of users experienced irregular bleeding and 27.7% prolonged bleeding in the first 3 to 6 months of use.[52] With increasing duration of use, these episodes decrease and amenorrhea becomes common. If BTB persists, the next dose of DMPA can be given early or conjugated estrogens (1.25 mg) or EE (2 mg) may be given daily for 7 to 14 days for several cycles. Approximately 50% of women who use DMPA for 1 year report amenorrhea, and this is an advantage for women troubled with increased or irregular periods. By 3 years, approximately 80% of users are amenorrheic. Women may also complain of breast tenderness, weight gain, and/or depression.

Women with a history of long-term use of DMPA have lower bone mineral densities than nonusers, although this has not yet been associated with an increase in fracture rate, and numerous studies have shown this bone loss to be minimal and reversible.[53–56] It is recommended that this method not be continued for more than 5 years and that calcium intake be optimized. Bone mineral density scanning is not necessary and is a waste of resources.

Another concern with the use of injectable contraceptives is occasional delayed return of fertility following discontinuation. This is not related to the duration of use. After discontinuing DMPA (Depo-Provera) to become pregnant, 50% of women conceive promptly.[57] In a small proportion of women, fertility is not reestablished until as long as 18 months after the last injection. However, the use of DMPA has no permanent impact on the ability to conceive.[58] Counseling is required before initiation of this method, which is obviously not ideally suited for simple spacing of pregnancy.

In a placebo-controlled trial, there was no relationship between DMPA and weight change or in the balance of food intake and energy expenditure.[59] In other trials, weight gain was similar to women using other methods. However, in obese adolescents and Navajo women, weight gain was increased.[60]

Women with sickle cell anemia, congenital heart disease, fibroids, or those older than age 35 years who smoke are excellent candidates for DMPA. There is no increase in stroke risk or MI or VTE with use of DMPA.[59] There is no link with cervical cancer, no increase in breast cancer risk, and a decrease in the incidence of anemia and pelvic inflammatory disease.[62] Depo-Provera is an excellent choice for epileptics because the high progestin levels raise the seizure threshold.[63]

DMPA is not teratogenic and is safe for use in lactating women. Although it is preferable to delay for 4 to 6 weeks, it may be given immediately postpartum, even in women who are breast-feeding if the risk of immediate pregnancy is high. There is no good evidence that it exacerbates depression.[61]

A new subcutaneous formulation (DMPA-SC, 104 mg/0.55 mL) has the advantages of being less painful and the potential for patient administration. The efficacy and side effects are the same. Both formulations are effective within 24 hours; however, they should be initiated within 5 days of the last menstrual period or at anytime with a backup method for 7 days to err on the side of caution. Repeat injections should be given every 12 weeks but can be given as early as 11 weeks or late as 13 weeks.

Vaginal Contraceptive Ring

This is a vaginal delivery system for administering combination estrogen-progestin, which is changed monthly. The NuvaRing system consists of a flexible, nonbiodegradable vaginal ring containing etonogestrel and EE. In two clinical trials evaluating the safety and efficacy of the vaginal ring, pregnancy rates were between 1 and 2 per 100 woman-years of use.[64] It should be kept refrigerated before dispensing, and clinicians should be aware that it has a shelf life of only 4 months. The vaginal ring (outside diameter is 54 mm) is inserted by the woman and worn continuously for 3 weeks, after which it is removed for 1 week to allow for a withdrawal bleed. After this 1 week, a new device is inserted. The device can be inserted on days 1 to 5 of the menstrual cycle. In clinical trials, about 18% of the women and 30% of the men reported feeling the ring occasionally during intercourse. If this is a problem, the ring can be removed for intercourse but must be replaced within 3 hours. If the ring remains outside the vagina for longer than 3 hours, its efficacy may be compromised. If it is removed or expelled from the vagina for longer than 3 hours, a backup method of contraception for 1 week is recommended.[65] If displacement of the ring occurs, the patient may rinse it off and reinsert it within 3 hours of expulsion. If the ring is left in the vagina for more than 3 weeks, ovulation may continue to be inhibited for up to 2 weeks after the recommended-use period; therefore, it can be used continuously.[66]

The ring releases minimal amounts of EE into the circulation yet maintains efficacy and cycle control comparable to the OC. Clinically, there is less BTB with the ring than with any other hormonal contraceptive method, and although there appears to be no diminished efficacy with increasing body weight, it has not been studied in women weighing more than 200 lb.[67]

For noncontraceptive users starting use of the ring, an additional nonhormonal method of contraception is recommended for the first week following the first insertion. When backup nonhormonal contraception is used, diaphragms should be avoided because the contraceptive ring can preclude proper placement of the barrier contraceptive.

If switching directly from OCs, the ring can be inserted any time after the last active tablet is taken. When

switching from another method of birth control, the ring can be inserted when the previous method is discontinued.

On removal of the ring, follicle-stimulating hormone levels begin to rise almost immediately, and return to ovulation can be expected in several weeks.[68]

The most frequently reported side effects with the ring were vaginitis (13.7%), headache (11.8%), and leukorrhea (5.9%). It is believed that the ring has the same thromboembolic risk as CHCs. Discontinuation rates because of device discomfort are low (2.5%).[67]

Oil-based, local antifungal vaginal therapy has been shown to increase blood levels of the ring's active ingredients but should not have any effect on contraceptive efficacy. Tampons and water-based spermicides such as nonoxynol-9 (N-9) do not alter serum levels of the active hormones. There is no risk of toxic shock syndrome from the ring because the ethyl-vinyl-acetate ring is nonabsorbent.

Combination Hormonal Contraceptive Patch (Transdermal System)

The combination contraceptive transdermal system (Ortho Evra) consists of a 20-cm^2 matrix-type patch containing norelgestromin (the primary active metabolite of norgestimate) and EE. Due to its continuous delivery system, the patch is not associated with any peaks or valleys of serum hormonal concentrations, has overall higher levels of estrogen, and therefore may be more thrombogenic.

The Evra system uses a 28-day (4-week) cycle in which a new patch is applied each week for 3 weeks. There is a 7-day period in which no patch is worn (corresponding to the 7-day pill-free interval with OCs). In three large clinical trials with more than 22,000 cycles of use, the pregnancy rate (Pearl index) was approximately 1 per 100 woman-years of use.[69]

The recommendations for starting are the same as the pill. The start day is also referred to as the patch change day. A woman may change this day during the fourth week by applying a new patch early on the desired day. If a woman is in the first week of her cycle and has forgotten to apply a new patch, she should apply one as soon as she remembers but also use a backup method of contraception for the next 7 days. She should also note that her patch change day for successive weeks has also been changed. If she is in week 2 or 3 of her cycle, has forgotten to change the patch, and less than 48 hours have elapsed between her patch change day and recognition of the error, she simply needs to place a new patch. A backup method of contraception is not necessary, and her original patch change day remains the same. If more than 48 hours has passed, she should replace the patch, use a backup method of contraception, and note that her patch change date has changed.

If a woman is interested in changing from CHCs to the patch, she should apply the patch on the first day of her menses. No backup method of contraception is needed. If she is past the first day of withdrawal bleeding, she may apply the patch and use a backup method of contraception for the next week.

If the patch detaches (occurrence rate, 1.1%), it should be replaced immediately. Therefore, patient should be given a prescription for a replacement patch. Hormonal release from the patch is not significantly affected by treadmill exercise or exposure to cold water, whirlpool, or sauna. Efficacy and side effect profiles are not affected by the anatomic site of application (abdomen, buttocks, torso, or upper outer arm), although it should not be placed on the breasts.[70] Placement of the patch in an area where the skin stays taut (i.e., is not prone to wrinkle with movement or positions) is highly recommended. Makeup, lotions, or body oils should not be applied to where the patch will be placed, and on placement, the patch should be pressed firmly for 10 seconds to ensure complete adherence by all edges.

Efficacy of the contraceptive patch is lower in women weighing more than 198 lb or 90 kg, although this may not be completely related to the delivery system because a similar decrease in efficacy has been noted in women weighing more than 198 lb or 90 kg who are using combination OCs.[7,69] Clinical studies with the patch have shown a minimal effect on body weight with patch use.[71] Contraindications, warnings, and precautions are similar to combination OCs.

In the first two cycles of use, the patch was associated with a significantly higher incidence of breast discomfort (which was primarily mild to moderate in nature) in comparison to the CHC. By the end of the second cycle, there was no significant difference in breast discomfort between the two modalities.[72] The patch should not be applied to any skin disruptions (e.g., eczema or seborrheic lesions). The risk of VTE is the same at that for 35 mcg EE pills.[73]

BARRIER METHODS OF CONTRACEPTION

Patients using barrier methods should be instructed regarding use of emergency contraception.

Diaphragm

The diaphragm can be an effective method of contraception. Diaphragm failure rates for the first year are estimated at 13 to 23%.[74] When used faithfully, the failure rate is probably closer to 6%. The diaphragm is fitted by the practitioner in the office, preferably using actual diaphragms rather than rings. They are not a good choice for very anteverted or retroverted uteri. Sizes range from 50 to 105 mm in diameter, with most women using a size between 65 and 80 mm.

To fit the diaphragm, place the middle finger against the vaginal wall and posterior cul de sac. Lift the hand anteriorly until the index finger is against the back of the symphysis pubis. Mark this point with the thumb to approximate the necessary diameter of the diaphragm. Insert the corresponding ring or diaphragm. Both the practitioner and patient are to assess the fit. If it is too tight, a smaller size is chosen. If it is expelled with increased intra-abdominal pressure, a larger size is needed.

The diaphragm should be placed no more than 6 hours before intercourse. It should always be used with spermicide (about 2 teaspoons). It should be left in the vagina for about 6 hours, but no more than 24 hours, after coitus. Additional spermicide should be placed intravaginally without removing the diaphragm for each additional episode of intercourse. Oil-based lubricants should not be used with the diaphragm. After it is removed, it should be washed with soap and water, rinsed, and dried. Powders should never be used on the diaphragm. Periodic checks for leaks should be done. The diaphragm should not be exposed to light or extreme temperatures during storage.

The incidence of urinary tract infections (UTIs) among diaphragm users is about twice that of women using CHCs. This may be due to pressure on the urethra with the diaphragm in place or increased colonization of the vagina with *Escherichia coli*.[75,76] Voiding after intercourse is helpful in avoiding UTI. A single postcoital dose of prophylactic antibiotics may also be used. There are some parous women with relaxation of the anterior vaginal wall in whom proper fitting is difficult, although the flat metal spring diaphragm may be tried in such instances. Well-motivated, properly fitted, and instructed women find the diaphragm a very acceptable method of contraception. The diaphragm reduces the incidence of STIs, as well as cervical neoplasia, presumably by reducing acquisition of HPV and other pathogens.[77] However, women at high risk of acquiring HIV or who have the virus should also use condoms. With a change in weight greater than 10 lb or after each pregnancy, the postpregnant woman may need to be refitted with a diaphragm of another size.

Cervical Cap

Currently, the cervical cap devices approved for use in the United States include the cavity rim cervical cap, the Prentif, FemCap, and the Lea's Shield. Prentif comes in four sizes based on internal diameter size: 22, 25, 28, and 31 mm. FemCap is available in three sizes based on internal diameter size: 22, 26, and 30 mm. The Lea's Shield comes in only one size and does not require fitting by a clinician. Although Prentif is a latex cervical cap, FemCap and Lea's Shield are both made of medical-grade silicone. The silicone caps are advantageous for women with latex allergies, and silicone is believed to resist odor formation.

A practitioner experienced in the use of this device must fit the Prentif and FemCap to the size of the cervix. The dome of the cervical cap covers the cervix and the rim fits snugly into the vaginal fornices. The brim adheres and conforms to the vaginal walls. Approximately 50% of women can be properly fitted. Women with a long cervix, short cervix, small cervix, or one that is too anterior may not be suitable candidates for the cap. Unlike the diaphragm, the cervical cap may be used in women with relaxation of the anterior vaginal wall.

Women should be advised to check placement of the device prior to and after intercourse to confirm correct positioning; the possibility of emergency contraception in the event of dislodgment during intercourse should also be discussed. A follow-up exam after prescribing is recommended, and the patient should wear the device into the office so the clinician can confirm proper placement. If a speculum is used to determine proper placement, it should be inserted only halfway into the vagina to avoid inadvertent dislodgment of the cervical cap.

Prior to use, the cervical cap should be filled one-third with spermicidal jelly or cream, applied to the inside of the cap, which is then positioned over the cervix by hand or with a special applicator. The cap should be inserted no less than 20 minutes and no more than 4 hours prior to intercourse. It is advised that women insert the cervical cap prior to sexual arousal because lengthening of the vagina on arousal may make insertion and proper placement more difficult. After insertion and after each act of coitus, the cervix should be checked to ensure it is covered. The FemCap and Prentif should not be removed any less than 6 hours after intercourse and all cervical caps may be left in place for up to 48 hours. Removal of the Prentif or FemCap is done by exerting pressure on the rim to break the seal and easily removing it. Squatting seems to be the best position for removal of these devices. Cleaning of the device is best done with a mild soap. Heat, synthetic detergents, organic solvents, or sharp objects should not be used for cleaning purposes. The device should be inspected regularly for signs of puncture, perforation, or wear.

With FemCap, the past obstetric history can predict the necessary size about 85% of the time with nulliparous women most often using the small size, with parous women with abdominal modes of delivery requiring the medium, and with parous women with a history of vaginal delivery requiring the large size. In clinical trials with the FemCap, it was noted that the risk of pregnancy was twice as high for parous women using the large device in comparison to nulliparous women using the small device or parous women using the medium-size device. For this reason, parous women requiring the larger size should be strongly counseled about an increased risk for pregnancy when relying on the FemCap as the sole means of contraception.[78–80]

When used with a spermicide, Prentif first-year failure rates with perfect use are approximately 9%, but

with typical use, failure rates are estimated at 20% for nulliparous women and 26 to 40% for parous women.[81] Like other vaginal barrier methods, the cap is associated with increased incidence of UTIs, bacterial vaginosis, and vaginal candidiasis when used with a spermicide.[82] Cervical caps do not decrease the risk of transmission of STDs. They have been associated with disruption of the cervicovaginal epithelium, although the actual clinical ramifications of this are unclear.

The cervical cap should not be used in women with active vaginal, cervical, or pelvic infections or vaginal or cervical lesions. Use of the cap during menstruation is discouraged because of the possibility of an increased risk of toxic shock syndrome and endometriosis; this possibility is theoretical, and no clinical evidence exists to disprove or support this to date.

Sponge

The Today sponge is a physical and a chemical barrier that fits closely over the cervix, absorbs semen, and releases spermicide. It is available without a prescription. Another similar sponge that can be ordered via the Internet is the Protectaid sponge, which contains three spermicides, including a lower dose of N-9 that may reduce mucosal irritation. Whereas the Today sponge can be inserted immediately before coitus or up to 24 hours in advance, the Protectaid sponge should be inserted no more than 12 hours in advance. Both sponges should be left in the vagina for 6 hours after intercourse. The Today sponge can be used continuously for 24 hours.

Failure rates for the sponge are similar to use of spermicide alone and are higher than diaphragm use.[83] As with the cervical cap, parous women experience failure rates approximately double those of nulliparous women.[83,84]

Male Condom

Male condoms are the third most popular contraceptive method employed by married couples in the United States, following sterilization and OCs. First-year failure rates with condom use are reported to be 8 to 15%, although use of the condom by highly motivated couples has a failure rate of 2 to 4%.[85,86] Contraceptive failure rates are lower in women older than the age of 30 years, those who seek to prevent pregnancy rather than delay it, and women of higher socioeconomic-economic status and level of education.

Most current condoms are made of latex. There are also "natural skin" male condoms which are made of lamb's intestine. Newer materials such as polyurethane are also used for condoms. Allergic reactions to latex or chemicals in the latex can occur, either immediately or as delayed reactions.

Clinicians should never assume pre-existing knowledge on proper condom use on the part of their patients. It is important to place the condom on the penis before any genital contact occurs. Uncircumcised men must pull the foreskin back prior to placement. Before unrolling and applying the condom, air should be squeezed out of the reservoir and the tip of the condom should extend beyond the end of the penis. The condom must be withdrawn prior to loss of the erection. Condoms may break during vaginal intercourse or withdrawal; slipping and tearing are more common with polyurethane condoms than with latex ones, but polyurethane condoms are suitable for latex-sensitive users, and because they are thinner may offer enhanced sensitivity.[86] The principal disadvantage of the use of the condom relates to an interruption of sexual foreplay, which can be minimized by incorporating its application during foreplay.

Although water-based lubricants can be used with any type of condom, petroleum-based lubricants should not be used with natural skin or latex condoms because they markedly decrease the strength of condoms, even with only brief exposure times. Polyurethane condoms may be used with any type of lubricant.

Male condom use has risen since the mid-1980s in the United States primarily as an HIV protection method. A meta-analysis of 25 studies found that male condoms offered a protective efficacy of 84 to 87% to HIV infection.[81,87] The latex condom is the only male condom shown to effectively prevent HIV transmission; condoms made from lamb intestines are permeable to virus particles, such as HIV and herpes.[80] Theoretically, polyurethane condoms may offer similar HIV protection as the latex condoms, but this has not been clinically confirmed yet. Users must realize that to reduce the risk of HIV transmission, latex male condoms must be used with each and every act of sex.

In addition to the decreased transmission of HIV, latex condoms also offer good protection against other viral and bacterial STDs such as *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas* infections.[88] Debate exists as to the extent of protection they may offer in preventing transmission of the herpes and HPVs if virus particles are located on the groin or vulvar areas.[89,90]

Female Condom

The FDA approved the female condom in 1994 (Fig. 1.3). There are several studies that evaluated its use and effectiveness. One study included female employees of two hospitals in Cape Town, South Africa. Twenty-three of 52 participants used all 10 of the devices issued to them, 21 stated that they or their partner(s) did not enjoy using the method, and an additional 9 had other problems with it. One problem that has been reported is that the device is noisy. Sexual responsivity, however, was the same or better in 52%, and overall acceptability was 52%. Compared with the male condom, 50% of the women and 44% of their partners considered the device as good, or better than, the male condom.[91] In the initial

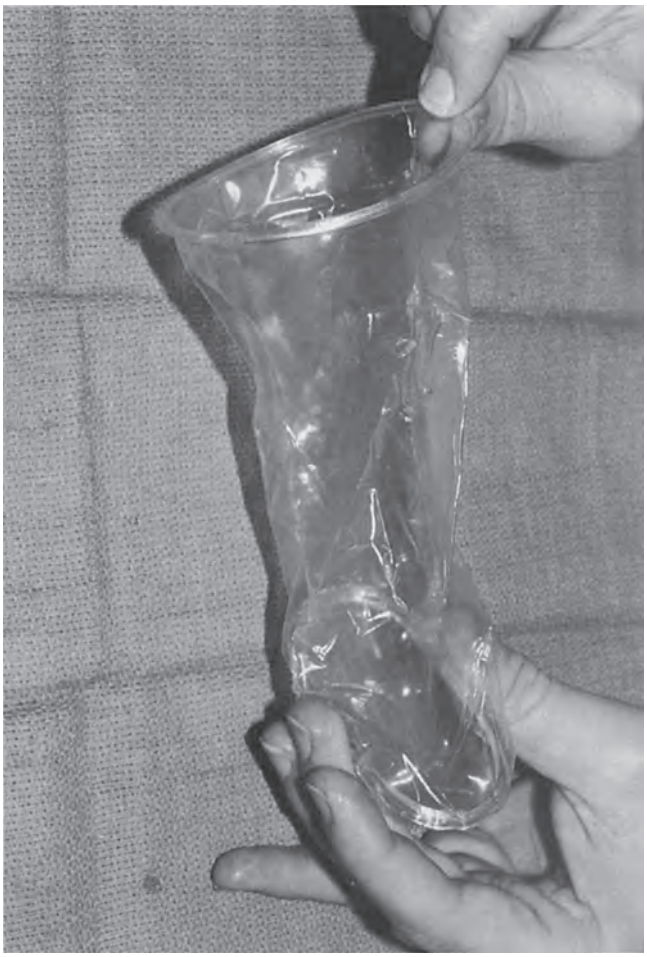

FIGURE 1.3 Female condom.

U.S. trial, there was a pregnancy rate of 15% in 6 months, although with perfect use the pregnancy rate is probably 3%.[92] The female condom should not be used with a male condom because this may increase slippage and/or breakage.[81]

Current experience shows that the female condom is an acceptable method for some couples. Although intended for single use only, some women reuse them for financial reasons. The female condom may be used for up to eight cycles of vaginal intercourse (and subsequent washing, drying, and relubrication with use) without any significant compromise to its structural integrity.[93] A clear advantage is that it is a female-controlled contraceptive that provides protection against STDs, including HIV. Directions regarding placement of the female condom can be found in Appendix 1.C.

SPERMICIDES

Spermicides are supplied as jellies, creams, foams, melting suppositories, foaming tablets, and soluble films. N-9 is the active ingredient in almost all spermicides available in the United States, and it works by disrupting the integrity of the sperm cell membrane.[81] Most spermicides employ N-9 in concentrations ranging from 3 to 20%. N-9 is not absorbed from the vagina. Other spermicides, such as octoxynol-9 or menfegol, are offered in some over-the-counter vaginal contraceptives, usually with 60 to 100 mg per vaginal application, but the FDA has stated that their efficacy and safety remain unproven.

Timing of the application of the spermicide is an important determinant of efficacy and although some must be inserted no more than 1 hour before coitus, others simply require enough time to melt or dissolve intravaginally prior to coitus. All must be reapplied for each act of intercourse. Aerosol foams offer better protection than the jellies, and melting suppositories provide poor intravaginal distribution.[94] The jelly, cream, and foam preparations are good for use up to 80 minutes prior to intercourse. The tablets and suppositories are good for 1 hour or less.

Efficacy of spermicides is highly product and user-dependent. Failure rates with perfect use are approximately 6%, whereas overall failure rates are approximately 26%. Unfortunately, the correct use of spermicides does not correlate with years of experience of use.[92]

Occasionally, spermicides may cause allergic reactions or yeast infections and may promote UTIs through alterations of the normal bacterial flora of the vagina.[81]

Since the mid-1980s, spermicides, including N-9, have been recommended for the prevention of STDs, including HIV. However, more recent studies indicate that N-9 causes an increase in genital ulcers and vaginal inflammation.[95,96] This raised concerns regarding the possibility of increasing the risk of HIV transmission. Several randomized trials have been performed more recently to evaluate the effectiveness of N-9 in prevention of STDs. Three different preparations of N-9 have been examined, including film, gel, and vaginal sponge. These investigators concluded that N-9 is not effective in preventing gonorrhea, chlamydia, trichomoniasis, syphilis, or HIV infection.[95,98,99] In addition, in one study using vaginal sponges with N-9, there was nearly a 50% increase in the transmission of HIV compared with the placebo group.[97] As a result of these findings, the Centers for Disease Control and Prevention (CDC) no longer recommends the use of spermicides containing N-9 for vaginal or anal intercourse.[99]

The use of spermicides does not increase the risk for spontaneous abortion, birth defects, or low birth weight.[100]

EMERGENCY CONTRACEPTION

Emergency contraception (EC), also known as postcoital contraception or the "morning after" pill, has been available for more than 30 years. These products delay ovulation and interfere with sperm transport but do not abort the zygote.

Three products—Preven, Plan B, and Ella—are currently approved by the FDA for the use of emergency contraceptive. Preven is simply the Yuzpe regimen (two doses of two COC tablets taken 12 hours apart, each with a combination of 50 mcg EE and 250 mcg LNG), which includes a pregnancy test and patient instructions. Plan B is a progestin-only formulation (LNG) that can be taken up to 72 hours after unprotected intercourse (but may be effective for up to 120 hours). Ella (30 mg ulipristal acetate, a selective progesterone receptor modulator) was recently approved and is effective up to 120 hours (5 days post risky intercourse).

A WHO-sponsored study demonstrated that the LNG regimen is more effective than the Yuzpe method. The proportion of pregnancies prevented in the LNG group was 85% (compared with the predicted rate that would have occurred with no EC), whereas the Yuzpe method prevented only 57% of pregnancies.[101] Ella had a similar efficacy to LNG in the first 72 hours.[102]

Treatment efficacy of EC is related in part to the timing of the first dose and the sexual exposure. The sooner after exposure the first dose of EC is administered, the greater the efficacy. For all regimens, the greatest protection against pregnancy is offered within the first 24 hours after unprotected sex. It is important that the patient understands if she continues to have unprotected sex, she may still become pregnant.

Side effects are also less with the LNG and ulipristal regimens. About 50% of users of the Yuzpe regimen experienced nausea and 20% report vomiting. In comparison, 23 and 6% had nausea and vomiting for the LNG regimen versus 15% and less than 5% for ulipristal.[102,103] As a proactive approach, it is recommended that an antiemetic be taken 1 hour prior to the first postcoital Yuzpe dose.[104] For all progesterone-only regimens, efficacy was less in women with a BMI greater than 30.

Both WHO and the International Planned Parenthood Federation find no absolute evidence-based contraindications to the use of EC, except for a known established pregnancy (e.g., a positive pregnancy test). The FDA-approved labeling in the United States does list clotting problems, ischemic heart disease, stroke, migraine, liver tumors, breast cancer, and breast biopsies as contraindications. Because the duration of therapy is short, the usual medical contraindications to long-term use of steroidal contraceptives are probably not applicable to EC.[105]

Other formulations marketed for use as combination hormonal methods have been studied for the use as emergency contraceptives. For additional information on other regimens that may be useful for EC, see Table 1.8.

Insertion of copper IUDs within 5 days of unprotected sex is another method of providing EC. An emergency IUD insertion reduces the risk of pregnancy by about 99%.

TABLE 1.8 Emergency Contraceptive Regimens (Other Than Ella or Plan B)

Conjugated estrogens (Premarin) 30 mg twice a day × 5 days *or* 10 mg four times a day × 5 days *or* 25 mg IV immediately and again 24 h later
Ethinyl estradiol (Estinyl) 2.5 mg twice a day × 5 days *or* 5 mg four times a day × 5 days
Oral contraceptive regimens[a]
Ovral two tablets immediately and again 12 h later
Levlen, Levora, Lo/Ovral, Nordette, Tri-Levlen, or Triphasil four tablets immediately and again 12 h later

[a]In the event of vomiting, the dose must be repeated.

NATURAL METHODS

Fertility Awareness–Based Methods

Fertility awareness–based (FAB) methods, also known as the rhythm method or periodic abstinence, encompass six techniques: the standard days method, the TwoDay method, the calendar rhythm method, the basal body temperature (BBT) method, the ovulation method, and symptothermal method. These methods are an option for the patient who does not want or cannot use other contraceptive methods. All are based on the fact that pregnancy is most likely to occur for only about 6 days of the menstrual cycle.[4] This is based on the ability of sperm to live in the female reproductive tract for 5 days and the ovum lack of viability for more than 24 hours. These methods also use physical changes, such as BBT and changes in cervical mucus (copious, watery, thin, stretchy), to determine the fertile window. These methods are contraindicated in women with irregular cycles, perimenopausal women, and women who recently gave birth, had an abortion, recently stopped another form of birth control, or are currently breast-feeding because these situations make it very difficult to predict ovulation.

The failure rate of FAB methods with typical use is usually estimated as 12 to 25% per year, with the TwoDay and standard days methods being most effective. There are several reasons for this. A principal reason is that sperm may survive for up to 5 days in the fallopian tube or in the pelvic peritoneal cavity.[107] Also, ovulation can occur before or after days 10 to 17 of the menstrual cycle. In addition, strict compliance with abstinence may be unreliable and misinterpretations of cervical mucus changes may occur. FAB methods can be supplemented with the use of over-the-counter ovulation predictor kits, especially ones that detect both estrone-3-glucoronide and luteinizing hormone (LH), to more accurately assess when abstinence is necessary.[106]

Standard Days Method

In women with menstrual cycles of at least 26 days and not more than 32 days, instructions not to have unprotected intercourse on days 8 to 19 of the cycle are given. This is the simplest method to teach and the one that has the fewest

number of days requiring abstinence or barrier contraception. CycleBeads have been shown to be very helpful.[108]

TwoDay Method

This method is a simple method based on the presence or absence of cervical mucus. Patients avoid unprotected intercourse all days with increased, thin, clear, stretchy cervical secretions. Unprotected intercourse may resume when there are no secretions for 2 consecutive days. It can be used in women with any cycle length.

Calendar Rhythm Method

The calendar technique requires the woman to record the length of her menstrual cycle for 6 months. She then subtracts 18 days from her shortest cycle and 11 days from her longest cycle to determine her fertile period and abstains from intercourse during that time. For example, if a woman's cycle averages 27 to 31 days, her fertile period would start on day 9 of her menstrual cycle (including the first day of her cycle in the count) (27 − 18 = 9) and end on day 20 of her menstrual cycle (including day one of her cycle in the count) (31 − 11 = 20). This method is not recommended for women whose cycle is less than or equal to 25 days or if it varies by more than 8 days between cycles. It is more successful if used in combination with other periodic abstinence methods.

Basal Body Temperature

The determination of temperature is a way of estimating the day of ovulation in each cycle. A special thermometer is available, making it easier to determine if there is a rise in BBT. With the rise in progesterone that follows ovulation, there is an increase in the BBT of 0.5 to 1°F. The woman must check her temperature on awakening, but *before* arising, and record the reading on a graph. Abstinence from intercourse starts on the first day of menses and continues until there is at least a 3-day duration, consecutively, of elevated BBT. This technique requires a fairly long period of abstinence. It is worth remembering that weekends, which often involve later hours and arising later, will tend to cause an elevation of the BBT that may approach 0.4 or 0.5°F, so that only persistence of the elevation in following days will be a certain determinant that ovulation has occurred. It is also useful to remember that the progesterone-induced temperature elevation begins only *after* ovulation, which is why its usefulness is mainly retrospective.

Ovulation Method

The time of ovulation can be identified by the amount and consistency of cervical mucus, and in this case, imminent ovulation can be anticipated before it occurs. Endogenous levels of estrogen and progesterone directly influence the quantity and quality of cervical mucus. Women are taught to recognize these changes. Abstinence is recommended during the menses, and then may occur every other day (as not to confuse semen with a change in secretions) until the first appearance of a larger amount of very thin, slippery mucus. After that, abstinence resumes until 4 days after the last day the almost liquid-like discharge was present. Unprotected sex must be avoided for 14 to 17 days out of each cycle. A different approach is to avoid intercourse until after ovulation has occurred (as noted by BBT or cervical mucus). Ovulation can also be determined in advance by urinary measurements of luteinizing hormone and estradiol, but this often requires the expense of three to four determinations per cycle.

Symptothermal Method

This method combines the use of BBT, changes in cervical secretions, and other physical changes, such as mittelschmerz and cervical texture. It can be used by women with any type of cycle. It is cumbersome, however, and unprotected intercourse must be avoided for 12 to 17 days.

Lactational Amenorrhea Method

The contraceptive effect of lactation has been long recognized. A 2003 Cochrane review reported that lactational amenorrhea was 98% effective when three conditions were present: there is amenorrhea, the baby is exclusively or almost exclusively breast-fed on demand, and that the method is not relied upon for more than 6 months. If any of these criteria are not met, another method must be used.[109] Pregnancy rates with supplementation are approximately 2.9 and 5.9% at 6 and 12 months, respectively.[110] It is obvious that if menstrual periods resume (at least 2 days of bleeding), the risk of conception is increased, but lactation still appears to provide some additional protection against pregnancy, perhaps by imperfect ovulation and/or endometrial response.

STERILIZATION

Female Sterilization

Sterilization is one of the most common methods of contraception in the United States. Most procedures are done in an outpatient surgical setting, although some are done in private offices. The mortality rate for sterilization is 1.5 per 100,000 procedures. This is lower than the mortality associated with childbirth (10 per 100,000).[111] The average failure rate in the first year is 0.5% for female sterilization and 0.1 to 0.15% for male sterilization, with the actual rate being operator, patient, and technique dependent.[112] Techniques that rely on more equipment have a higher failure rate secondary to technical problems.[113,114] Female patients younger than age 35 years have a higher failure rate, as do women who are not lactating at the time of the procedure.

With sterilization currently being readily available, careful consideration and counseling is in order. This is particularly true of women younger than age 30 years, and the procedure should generally be limited to the patient who is presumably in a long-term relationship.

These criteria are obviously not the case when a disease is present that could be worsened by the complication of subsequent pregnancy. The median age at sterilization is 30 years, and there is a higher incidence of regret in women sterilized before age 30 years and among those who divorce and remarry. In certain ethnic cultures, a woman incapable of bearing children may be considered "damaged" to some degree. The question needs to be asked, "What if something happened to your partner, or to one of your children—would this change your mind?" The decision should be regarded as irrevocable and unseemly optimism for the possibility of uncomplicated reversal should be faced with facts of insurance payments, the increase in risk of ectopic pregnancy, and the greatly diminished chance of success in the event of any type of cauterization procedure. An informed consent should state the risk of failure and the increased rate of ectopic pregnancy in that event.

Currently, the four most commonly used methods of sterilization in the United States include sterilization in conjunction with cesarean section or other abdominal surgery, immediate postpartum partial salpingectomy, minilaparotomy, or laparoscopy. An interval minilaparotomy approach would certainly be appropriate if the patient's history or pelvic findings suggested the possibility of significant pelvic adhesions and perhaps distortion of anatomy.

A more recently published, multicentered, prospective, cohort study involving 10,685 women was reported from the U.S. Collaborative Review of Sterilization (CREST). The CREST data show that failures continue beyond the first year: By 5 years, more than 1% of women had a sterilization failure, and by 10 years, 1.8% failed.[115] It is well known that the risk of ectopic pregnancy after tubal sterilization is greatly increased. Failures of sterilization are associated with a higher rate of ectopic pregnancies, with the incidence depending on the surgical procedure originally performed. Bipolar cauterization has a higher incidence of ectopic pregnancy associated with tubal failures than mechanical occlusion.[116] Another study found 7.3 tubal pregnancies per 1000 procedures, and found that bipolar tubal coagulation before the age of 30 years had a probability of ectopic pregnancy 27 times greater than women of similar age who underwent postpartum partial salpingectomy.[117] The same study also showed that a history of tubal sterilization does not rule out the possibility of ectopic pregnancy, even 10 years after the procedure.[117] The overall risk for ectopic pregnancy in sterilized women, however, is still lower than if they were not sterilized.

The first suggestion of a "post-tubal syndrome" was in 1951.[118] The CREST multicenter prospective study on this subject showed that of patients interviewed immediately prior and again poststerilization for up to 5 years, 35% report higher levels of menstrual pain, 49% reported very heavy increase in menstrual flow, and 10% reported increased spotting between periods, at the fifth year. During the first year, a lesser degree of pain and hypermenorrhea was found.[119] It is obvious that aging of the cohort may be a factor, as well as the fact that it takes such changes a significant time to develop. In similar, paired studies of poststerilization on women conducted several years apart, both Rulin and DeStefano showed an increased prevalence of pain in the latter studies.[120–123]

There have been anecdotal reports about the prevalence of hysterectomy after sterilization. Hillis et al. reported that the cumulative probability of undergoing hysterectomy within 14 years after sterilization was 17%.[124] The highest likelihood occurred among women who reported a history of endometriosis or noted prolonged bleeding prior to sterilization. Not surprisingly, women with gynecologic disorders were at greater risk of hysterectomy than were women without these disorders.[124] Women may be reassured that there is no detrimental effect on sexual response associated with tubal sterilization.[125]

A noncontraceptive benefit of tubal ligation is the reduction of ovarian cancer. Multiple small studies, flowed by a meta-analysis in 2011 have shown significant reductions for most types of ovarian cancer.[126] In fact, there has been evidence that bilateral salpingectomy alone reduced the cancer risk in *BRCA1/BRCA2* carriers.[127]

The FDA has approved two hysteroscopic methods of permanent female sterilization, the Essure in 2002 and Adiana in 2010. They can be performed in the office or outpatient. Both work after implants are placed in the fallopian tubes, inducing scar tissue formation and eventual occlusion. Women must use alternate forms of contraception at least for 3 months after the procedure and until proper implant placement is confirmed by hysterosalpingography. Because the Adiana procedure uses a silicone insert and radio-frequency ablation to occlude the tube instead of a nickel insert, evaluation of tubal occlusion can be more difficult. The Adiana insert is smaller and, theoretically, could cannulate tubes (with distal blockage or spasm) that the Essure could not. A notable difference is the resultant clinical pregnancy risk, with the Essure reporting no pregnancies in 643 women with confirmed occlusion for over 9 years. In contrast, the Adiana procedure has reported 12 pregnancies in 570 women over 5 years.[128] Bilateral placement rates were similar. However, bilateral occlusion was less with the Adiana system and more patients required a second procedure for bilateral occlusion with the Essure. Both procedures are tolerated well and have high satisfaction scores. At this point in time, the cost per patient is the same for the two procedures.[128]

Male Sterilization

Permanent surgical sterilization of men is done in the office and is safer, easier, and less expensive than surgical sterilization of women. In the "no scalpel" technique, a sharpened dissection forceps is used to pierce the skin and dissect the vas deferens. Complications are uncommon but may include some bleeding, hematoma formation, infection, or local reactions to anesthetics or sutures. A patent reanastomosis is achieved in approximately 86 to 97% of men seeking reversal of the vasectomy, although their fertility rates are considerably less due to a variety of issues.

CLINICAL NOTES

- In general, the estrogen-related contraindications are for those patients with cardiovascular disease, with thromboembolic disease or risks, and with liver disease. Hormone levels in pregnancy are far higher than those produced by contraceptive pills.
- Progestin-only methods and nonhormonal methods, such as the copper IUD, are a good option for women with relative or strong contraindications to estrogen.
- LARC methods (IUDs and implants) are safe and effective and should be considered first line, even in adolescent patients.
- Women should not be denied contraception because they do not have a recent Pap smear or STD screening.
- Healthy women older than age 35 years who do not smoke and are not obese can safely take CHCs.
- The need for safe and effective contraceptive methods remains great in the perimenopausal period as evidenced by the high unintended pregnancy rate in this age group.
- For perimenopausal women, CHCs or the vaginal ring should be the method of choice for nonsmoking, nonobese women to regulate menstrual periods, provide contraception, control vasomotor symptoms, protect bone health, and reduce the risk of endometrial and ovarian cancers.
- CHCs are contraindicated in the presence of cerebrovascular disease.
- CHCs are second-line in a patient with a history of classic migraine (migraine with focal neurologic symptoms or aura lasting more than 1 hour) due to an increased potential for stroke.
- There is no impact of CHCs on the pattern or frequency of seizures.
- Some anticonvulsants can decrease serum concentrations of estrogen and thus may increase the likelihood of intermenstrual bleeding among patients on CHCs but do not increase chance of pregnancy.
- Obesity is an independent risk factor for VTE and for contraceptive failure.
- For women with hypertension, if their blood pressure is controlled and no vascular disease is present, CHCs are not contraindicated.
- If a woman's triglycerides are above 350 mg/dL or in patients with familial hypertriglyceridemia, OCs should be avoided because they may precipitate pancreatitis and/or adversely affect the patient's risk for cardiovascular disease.
- In general, OCs can be safely used by women with MVP who are symptom free.
- Young diabetic women who are free of retinopathy, nephropathy, hypertension, or other complicating vascular disease(s) are appropriate candidates for low-dose contraceptives.
- Women with sickle cell anemia, congenital heart disease, or those older than age 35 years who smoke are excellent candidates for DMPA.
- Overall, the risk of breast cancer in women who take OCs until they are 55 years of age appears to be no different from that of nonusers.
- If prolonged immobilization is expected, stopping CHCs 1 month prior and use of a barrier method is advisable.
- The Mirena IUD releases 20 mcg LNG daily and has been approved for 5 years of use.
- The progesterone IUD may decrease blood flow by 40 to 50% and improve dysmenorrhea so its use may be preferable in women experiencing heavy or painful periods.
- The copper IUD has been approved for 10 years of use. It has the highest efficacy with the lowest cost.
- The copper IUD may increase menstrual flow up to 50% and can be mitigated by NSAID use. The increased menstrual flow subsides over time.
- If a pregnancy occurs with an IUD in place, the device should be removed as soon as possible, regardless of whether termination or pregnancy continuation is planned.
- Women who become pregnant with an IUD in place have an increased rate, approximately 50%, of spontaneous abortion. After removal of the IUD, the spontaneous abortion rate decreases to about 30%.
- Implanon, a single-rod subdermal implant the size of a matchstick, releases 68 mg of etonogestrel over 3 years. It does not affect bone mineral density.
- Few antimicrobial agents can interact with the pharmacokinetics and efficacy of sex steroid hormones present in OCs.
- In choosing a CHC, the optimal formulation will comprise the lowest effective dose with acceptable bleeding profiles and minimal side effects.
- Monophasic pills with 20 mcg EE are a good choice for new users.
- Yasmin and YAZ are both FDA approved for PMDD. These are also a good choice for polycystic ovarian syndrome, hirsuit, or hypertensive patients because drospirenone is antiandrogenic and a diuretic.
- The key to success in prescribing CHCs is an informed patient because unscheduled bleeding and side effects of are a major source of patient noncompliance and discontinuation.
- Extended cycle or continuous CHCs are an option for women with hormone withdrawal symptoms,

(continues)

dysmenorrhea, endometriosis, menorrhagia, or women who simply desire fewer menstrual cycles.
- Unscheduled bleeding is seen more frequently with continuous regimens but is reduced over time. Additional estrogen can be given to stabilize the endometrium.
- The quick start is recommended by many experts because it mitigates confusion about instructions, pregnancy before pills are started, or forgetting to fill the prescription.
- Although a third of women will experience irregular bleeding after the first 3 to 6 months of use, approximately 50% of women who use DMPA for 1 year and 80% for 3 years report amenorrhea.
- It is recommended that the DMPA method not be continued for more than 5 years and that calcium intake is optimized.
- A new subcutaneous formulation (DMPA-SC, 104 mg/0.55 mL) has the advantages of being less painful and the potential for patient administration.
- The NuvaRing system consists of a flexible, nonbiodegradable vaginal ring containing etonogestrel and EE that is worn for 3 weeks. The vaginal ring should be kept refrigerated before dispensing, and clinicians should be aware that it has a shelf life of only 4 months.
- There is less BTB with the vaginal contraceptive ring than with any other hormonal contraceptive method.
- The efficacy of the vaginal contraceptive ring has not been studied in women weighing more than 200 lb.
- The contraceptive patch system uses a 28-day (4-week) cycle in which a new patch is applied each week for 3 weeks. There is a 7-day period in which no patch is worn (corresponding to the 7-day pill-free interval with OCs).
- Hormonal release from the contraceptive patch is not significantly affected by treadmill exercise or exposure to cold water, whirlpool, or sauna nor is it affected by the anatomic site of application (abdomen, buttocks, torso, or upper outer arm), although it should not be placed on the breasts.
- Patients using barrier methods should be instructed regarding use of EC.
- Because there is evidence that N-9 may actually increase the risk of HIV transmission, the CDC no longer recommends the use of spermicides containing N-9 for vaginal or anal intercourse.
- EC delays ovulation and interferes with sperm transport. This can be achieved by insertion of a copper IUD, or by the Yuzpe, Preven, Plan B, or Ella regimens.
- The greatest protection against pregnancy is offered within the first 24 hours after unprotected sex.
- Fertility awareness–based (FAB) methods, also known as the rhythm method or periodic abstinence, encompass six techniques: the standard days method, the TwoDay method, the calendar rhythm method, the BBT method, the ovulation method, and symptothermal method.
- Lactational amenorrhea is 98% effective when three conditions were present: the method is not relied upon for more than 6 months, there is amenorrhea, and the baby is exclusively or almost exclusively breast-fed on demand.
- Progestin-only pills are preferred for lactating women seeking oral hormonal contraception.
- The average failure rate in the first year after transabdominal sterilization is 0.5% for women as opposed to 0.1 to 0.15% for vasectomy, with the actual rate being operator, patient, and technique dependent.
- Both the Adiana and Essure hysteroscopic sterilization procedures can be performed in the office and require additional contraception until the hysterosalpingogram (HSG) confirms bilateral occlusion 3 months postprocedure.
- The Essure hysteroscopic procedure has reported no pregnancies in 9 years of follow-up, making it the most effective of all sterilization methods.

Appendix 1.A
Placement of the Copper Intrauterine Device

1. Can be inserted whenever pregnancy has been reliably excluded, including immediately postpartum or after abortion.
2. Confirm uterine size and position on examination.
3. Clean cervix with antiseptic (optional).
4. Apply topical anesthesia or paracervical block to cervix; place tenaculum on anterior lip of cervix for traction (if uterus is extremely retroverted, placing tenaculum on posterior lip of cervix may be more helpful).
5. Sound the uterus; do not place IUD if uterus sounds to less than 6 cm or greater than 9 cm (excluding postpartum/postabortion).
6. Document IUD lot number in chart and open IUD package, keeping contents sterile.
7. Wear sterile gloves; load the IUD into the insertion tube with the arms of the "T" folded *downward* into tube; do not leave the IUD in the insertion tube with the arms folded for more than 5 minutes.
8. Insert solid tube into bottom of insertion tube until it touches the bottom of the IUD.
9. Adjust the flange of the insertion tube to depth of uterus and to the plane in which the arms will open.

Make sure the horizontal arms and long axis of the flange lie in the same horizontal plane.

10. Place insertion tube into cervix/uterus until it touches fundus of uterus. The flange should be at the cervix. Hold solid rod stationary and retract the insertion tube no greater than 0.5 inch to release the arms.
11. Hold insertion tube still and remove solid rod only. After the solid rod is out, remove the insertion tube. Cut threads 2.5 to 4 cm beyond and perpendicular to os. Measure and record the length of the strings.

Appendix 1.B
Placement of Levonorgestrel-Releasing Intrauterine Device

1. Can be inserted whenever pregnancy has been reliably excluded, including immediately postpartum or after abortion.
2. Confirm uterine size and position on examination.
3. Clean cervix and upper vagina with antiseptic (optional).
4. Apply topical anesthesia or paracervical block to cervix; place tenaculum on anterior lip of cervix for traction (if uterus is extremely retroverted, placing tenaculum on posterior lip of cervix may be more helpful).
5. Sound the uterus; do not place IUD if uterus sounds to less than 6 cm or greater than 9 cm (excluding postpartum or postabortion).
6. Document IUD lot number in chart and open IUD package, keeping contents sterile.
7. Release the threads, hold the slider in the furthest upward position and pull on the threads to pull the IUD into the inserter.
8. Adjust the flange to the sounded length of the uterus and secure the threads into the cleft.
9. Wear sterile gloves; with the number facing up, carefully insert into the cervix with countertraction on the tenaculum until the flange is 1.5 cm from the cervix.
10. Hold the inserter steady and open the arms of the IUD by pulling the slider back until it reaches the mark. Wait a few seconds.
11. Advance the inserter up to the flange so that the IUD is in the fundus.
12. Pull the slider all the way down and withdraw it. Cut threads 2.5 to 4 cm beyond and perpendicular to os. Measure and record the length of the strings.

Appendix 1.C
Placement of the Female Condom

1. After removing the condom from the package, check to ensure the lubrication is spread evenly inside the pouch from the bottom to the top. If more lubricant is necessary, add more from the additional lubricant that is supplied.
2. Check that the inner ring is at the bottom, closed end of the pouch.
3. Hold the condom with the open end hanging down toward the ground. Squeeze the inner ring with your thumb and middle finger. It should look like a long, narrow "O."
4. With the other hand, separate the labia so the vagina is accessible. The hand holding the condom pushes the inner ring and pouch up into the vagina until the entire inner ring is just behind the pubic bone. (This is the same placement one uses for a diaphragm.) The condom should be inserted straight into the vagina; in other words, it should not be twisted. About 1 inch of the open end should remain in place outside the vagina.
5. During sex, the outer ring may move from side to side, which is normal. However, if it begins to slide or slip or is noisy during sex, add more lubricant.
6. If the outer ring begins to be pushed into the vagina, the female condom should be replaced, with extra lubricant around the opening of the new pouch or on the penis.
7. To remove the condom, squeeze and twist the outer ring, keeping the sperm and semen inside the pouch. The condom is not designed to be flushed down a toilet—it must be placed in the trash. It should *not* be reused.
8. A new condom must be used with every act of sex.
9. The female condom should not be used at the same time as a male condom. If used simultaneously, neither product will stay in place.

REFERENCES

1. McLaren A. *A History of Contraception: From Antiquity to the Present Day*. Cambridge, MA: Basil Blackwell Ltd.; 1990.
2. Pazol K, Zane SB, Parker WY, et al. Abortion surveillance—United States, 2008. *MMWR Surveill Summ*. 2011;60(15):1–41.
3. Kost K, Singh S, Vaughan B, et al. Estimates of contraceptive failure from the 2002 National Survey of Family Growth. *Contraception*. 2008;77:10–21.
4. Amy J-J, Tripathi V. Contraception for women: an evidence based overview. *BMJ*. 2009;339:b2895.
5. Maguire K. The state of hormonal contraception today: established and emerging noncontraceptive health benefits. *Am J Obstet Gynecol*. 2011; 205(4):S4–S8.
6. American College of Obstetricians and Gynecologists Committee on Gynecologic Practice, Long-Acting Reversible Contraception Working Group. ACOG Committee Opinion no. 450: increasing use of contraceptive implants and intrauterine devices to reduce unintended pregnancy. *Obstet Gynecol*. 2009;114(6):1434–1438.

7. Grimes DA, Lopez LM, Schulz KF, et al. Immediate post-partum insertion of intrauterine devices. *Cochrane Database Syst Rev*. 2010;(5):CD003036.
8. Zakharova MY, Meyer RM, Brandy KR, et al. Risk factors for heart attack, stroke, and venous thrombosis associated with hormonal contraceptive use. *Clin Appl Thromb Hemost*. 2011;17(4):323–331.
9. Gaffield ME, Culwell KR, Lee CR. The use of hormonal contraception among women taking anticonvulsant therapy. *Contraception*. 2011;83(1): 16–29.
10. Kapp N, Curtis KM. Intrauterine device insertion during the postpartum period: a systematic review. *Contraception*. 2009;80(4):327–336.
11. Truitt ST, Fraser AB, Grimes DA, et al. Combined hormonal versus nonhormonal versus progestin-only contraception in lactation. *Cochrane Database Syst Rev*. 2003;(2):CD003988.
12. American College of Obstetricians and Gynecologists Committee on Practice Bulletins-Gynecology. ACOG practice bulletin. No. 73: use of hormonal contraception in women with coexisting medical conditions. *Obstet Gynecol*. 2006;107:1453–1472.
13. Shulman LP. The state of hormonal contraception today: benefits and risks of hormonal contraceptives: combined estrogen and progestin contraceptives. *Am J Obstet Gynecol*. 2011;205(4)(suppl):S9–S13.
14. Holt VL, Cushing-Haugen KL, Daling JR. Body weight and risk of oral contraceptive failure. *Obstet Gynecol*. 2002;99:820–827.
15. Kjos SL, Shoupe D, Douyan S, et al. Effect of low-dose oral contraceptives on carbohydrate and lipid metabolism in women with recent gestational diabetes: results of a controlled, randomized, prospective study. *Am J Obstet Gynecol*. 1991;163:1822–1827.

15a. Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med*. 2002;346:2025–2032.

16. Marks M, Gravitt PE, Gupta SB, et al. Theassociationof hormonal contraceptive use and HPV prevalence. *Int J Cancer*. 2011;128(12):2962–2970.
17. Moreno V, Bosch FX, Muñoz N, et al. Effect of oral contraceptives on risk of cervical cancer in women with human papillomavirus infection: the IARC multicentric case control study. *Lancet*. 2002;359(9312):1085–1092.
18. Marks M, Gravitt PE, Gupta SB, et al. Combined oral contraceptive use increases HPV persistence but not new HPV detection in a cohort of women from Thailand. *J Infect Dis*. 2011;204(10):1505–1513.
19. Maia H Jr, Casoy J, Pimentel K, et al. Effect of oral contraceptives on vascular endothelial growth factor, Cox-2 and aromatase expression in the endometrium of uteri affected by myomas and associated pathologies. *Contraception*. 2008;78(6):479–485.
20. Mueck AO, Seeger H, Rabe T. Hormonal contraception and risk of endometrial cancer: a systematic review. *Endocr Relat Cancer*. 2010;17(4): R263–R271.
21. Cibula D, Zikan M, Dusek L, et al. Oral contraceptives and risk of ovarian and breast cancers in BRCA mutation carriers: a meta-analysis. *Expert Rev Anticancer Ther*. 2011;11(8):1197–1207.
22. Goldzieher JW, Zamah NM. Oral contraceptive side effects: where's the beef? *Contraception*. 1995;52:327–335.
23. Freie HMP. Sickle cell diseases and hormonal contraception. *Acta Obstet Gynecol Scand*. 1983;62:211–217.
24. Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med*. 2002;346:2025–2032.
25. Figueiredo JC, Haile RW, Bernstein L, et al. Oral contraceptives and postmenopausal hormones and risk of contralateral breast cancer among BRCA1 and BRCA2 mutation carriers and noncarriers: the WECARE Study. *Breast Cancer Res Treat*. 2009;120:175–183.
26. Milne RL, Knight JA, John EM, et al. Oral contraceptive use and risk of early-onset breast cancer in carriers and noncarriers of BRCA1 and BRCA2 mutations. *Cancer Epidemiol Biomarkers Prev*. 2005;14:350–356.
27. Thomas DB. The WHO Collaborative Study of Neoplasia and Steroid Contraceptives: the influence of combined oral contraceptives on risk of neoplasms in developing and developed countries. *Contraception*. 1991;43: 695–710.
28. Jick SS, Walker AM, Jick H. Oral contraceptives and endometrial cancer. *Obstet Gynecol*. 1993;82:931–935.
29. Rosenberg L, Palmer JR, Zauber AG, et al. A case-control study of oral contraceptive use and invasive epithelial ovarian cancer. *Am J Epidemiol*. 1994; 139:654–661.
30. ACOG Practice Bulletin No. 110: noncontraceptive uses of hormonal contraceptives. *Obstet Gynecol*. 2010;115(1):206–218.
31. Institute of Medicine (US). *Initial National Priorities for Comparative Effectiveness Research*. Washington, DC: National Academies Press; 2009.
32. American College of Obstetricians and Gynecologists. ACOG committee opinion no. 392, December 2007. Intrauterine device and adolescents. *Obstet Gynecol*. 2007;110:1493–1495.
33. Grimes DA, Lopez LM, Schulz KF, et al. Immediate postabortal insertion of intrauterine devices. *Cochrane Database Syst Rev*. 2004;(4):CD001777. doi:10.1002/14651858.CD00177.pub2.
34. Grimes DA, Schulz KF, Van Vliet HH, et al. Immediate postpartum insertion of intrauterine devices. *Cochrane Database Syst Rev*. 2001;(2):CD003036. doi:10.1002/14651858.CD003036.
35. ACOG Committee on Practice Bulletins—Gynecology. ACOG practice bulletin no. 59. Intrauterine device. *Obstet Gynecol*. 2005;105:223–232.
36. Hatcher R, Hatcher RA, Zieman M, et al. *A Pocket Guide to Managing Contraception*. Tiger, GA: Bridging the Gap Foundation; 2007.
37. Suvisaari J, Lahteenmaki P. Detailed analysis of menstrual bleeding patterns after postmenstrual and postabortal insertion of a copper IUD or a levonorgestrel-releasing intrauterine system. *Contraception*. 1996;54:201–208.
38. O'Brien P, Marfleet CC. Frameless versus classical intrauterine device for contraception. *Cochrane Database Syst Rev*. 2005;(1):CD003282. doi:10.1002/14651858.CD003282.pub2.
39. Monteiro I, Bahamondes L, Diaz J, et al. Therapeutic use of levonorgestrel-releasing intrauterine systems in women with menorrhagia: a pilot study. *Contraception*. 2002;65:325–328.
40. Suvisaari J, Lahteenmaki P. Detailed analysis of menstrual bleeding patterns after postmenstrual and postabortal insertion of a copper IUD or a levonorgestrel-releasing intrauterine system. *Contraception*. 1996;54:201–208.
41. Luukkainen T, Toivonen J. Levonorgestrel-releasing IUD as a method of contraception with therapeutic properties. *Contraception*. 1995;52:269–276.
42. Sivin I, Stern J. Health during prolonged use of levonorgestrel 20 micrograms/d and the copper TCu 380Ag intrauterine contraceptive device a multicenter study. International Committee of Contraception Research (ICCR). *Fertil Steril*. 1994;61:70–77.
43. Mirena [package insert]. Wayne, NJ: Bayer HealthCare Pharmaceuticals Inc; 2009.
44. Barbosa I, Olsson SE, Odlind V, et al. Ovarian function after seven years' use of a levonorgestrel IUD. *Adv Contracept*. 1995;11:85–95.
45. Järvelä I, Tekay A, Jouppila P. The effect of a levonorgestrel-releasing intrauterine system on uterine artery blood flow, hormone concentrations and ovarian cyst formation in fertile women. *Hum Reprod*. 1998;13:3379–3383.
46. Shaaban MM, Segal S, Salem HT, et al. Sonographic assessment of ovarian and endometrial changes during long-term Norplant use and their correlation with hormonal levels. *Fertil Steril*. 1993;59:998–1002.
47. Sivin I, Schmidt F. Effectiveness of IUDs: a review. *Contraception*. 1987;36: 55–84.
48. Diaz J, Bahamondes L, Monteiro I, et al. Acceptability and performance of the levonorgestrel-releasing intrauterine system (Mirena) in Campinas, Brazil. *Contraception*. 2000;62:59–61.
49. Monteiro I, Bahamondes L, Diaz J, et al. Therapeutic use of levonorgestrel-releasing intrauterine systems in women with menorrhagia: a pilot study. *Contraception*. 2002;65:325–328.
50. Masimasi N, Sivanandy M, Thacker H. Update on hormonal contraception. *Cleve Clin J Med*. 2007;74:186–198.
51. Implanon [package insert]. Kenilworth, NJ: Schering-Plough Corporation; 2009.
52. Speroff L. Oral contraception. In: Speroff L, Fritz M, eds. *Clinical Gynecologic Endocrinology and Infertility*. 7th ed. Philadelphia: Lippincott Williams & Wilkins; 2005:861–942.
53. Hatcher R, Hatcher RA, Zieman M, et al. *A Pocket Guide to Managing Contraception*. Tiger, GA: Bridging the Gap Foundation; 2007.
54. Gallo MF, Grimes DA, Schulz KF, et al. Combination contraceptives: effects on weight [Cochrane Review]. In: *The Cochrane Library, Issue 2*. Oxford, UK: Update Software; 2003.
55. Cedars MI. Triphasic oral contraceptives: review and comparison of various regimens. *Fertil Steril*. 2002;77:1–14.
56. Kaunitz AM. Efficacy, cycle control and safety of two triphasic oral contraceptives: Cyclessa (desogestrel/ethinyl estradiol) and Ortho-Novum 7/7/7 (norethindrone/ethinyl estradiol): a randomized clinical trial. *Contraception*. 2000;61:295–302.
57. Kulier R, Helmerhorst FM, Maitra N, et al. Effectiveness and acceptability of progestogens in combined oral contraceptives—a systematic review. *Reprod Health*. 2004;1(1):1.
58. Kashanian M, Shahpourian F, Zare O. A comparison between monophasic levonorgestrel-ethinyl estradiol 150/30 and triphasic levonorgestrel-ethinylestradiol 50-75-125/30-40-30 contraceptive pills for side effects and patient satisfaction: a study in Iran. *Eur J Obstet Gynecol Reprod Biol*. 2010;150(1):47–51.
59. Van Vliet HA, Grimes DA, Lopez LM, et al. Triphasic versus monophasic oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2006;(3):CD003553.
60. Van Vliet HA, Grimes DA, Helmerhorst FM, et al. Biphasic versus triphasic oral contraceptives for contraception. *Cochrane Database Syst Rev*. 2006; (3):CD003283.

61. Spencer AL, Bonnema R, McNamara MC. Helping women choose appropriate hormonal contraception: update on risks, benefits, and indications. *Am J Med*. 2009;122(6):497–506.
62. Barnhart KT, Schreiber CA. Return to fertility following discontinuation of oral contraceptives. *Fertil Steril*. 2009;91:659–663.
63. D'Arcangues C. Management of vaginal bleeding irregularities induced by progestin-only contraceptives. *Hum Reprod*. 2000;15(suppl):24–29.
64. Meckstroth KR, Darney PD. Implantable contraception. *Obstet Gynecol Clin North Am*. 2000;27:781–815.
65. Fraser IS. Vaginal bleeding patterns in women using once-a-month injectable contraceptives. *Contraception*. 1994;49:399–420.
66. Cundy T, Reid IR, Roberts H, et al. Bone density in women receiving depot medroxyprogesterone for contraception. *Br Med J*. 1991;303:13–16.
67. Tang OS, Tang G, Yup PSF, et al. Further evaluation of long-term depot-medroxyprogesterone acetate use and bone mineral density: a longitudinal cohort study. *Contraception*. 2000;62:161–164.
68. Petitti DB, Piaggio G, Mehta S, et al. Steroid hormone contraception and bone mineral density: a cross-sectional study in an international population. *Obstet Gynecol*. 2000;95:736–744.
69. Scholes D, LaCroix AZ, Ichikawa LE, et al. Injectable hormone contraception and bone density: results from a prospective study. *Epidemiology*. 2002;13:581–587.
70. Schwallie PC, Assenze JR. The effect of depot-medroxyprogesterone acetate on pituitary and ovarian function, and the return of fertility following its discontinuation: a review. *Contraception*. 1974;10:181–202.
71. Kaunitz AM. Injectable contraception: new and existing options. *Obstet Gynecol Clin North Am*. 2000;27:741–780.
72. Pelkman CL, Chow M, Heinback RA, et al. Short-term effects of progestational contraceptive drug on food intake resting energy expenditure, and body weight in young women. *Am J Clin Nutr*. 2001;73:19–26.
73. Haider S, Darney PD. Injectable contraception. *Clin Obstet Gynecol*. 2007; 50(4):898–906.
74. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case-control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Contraception*. 1998;57:315–324.
75. Mattson RH, Cramer JA, Caldwell BV, et al. Treatment of seizures with medroxyprogesterone acetate. *Neurology*. 1984;34:1255–1258.
76. Roumen F. Contraceptive efficacy and tolerability with a novel combined contraceptive vaginal ring, NuvaRing. *Eur J Contracept Reprod Health Care*. 2002;7(suppl 2):19–24.
77. NuvaRing [package insert]. Roseland, NJ: Organon USA Inc; 2008.
78. Mulders TMT, Dieben TOM. Use of the novel combined contraceptive vaginal ring NuvaRing for ovulation inhibition. *Fertil Steril*. 2001;75: 865–870.
79. Roumen FJ, Apter D, Mulders TM, et al. Efficacy, tolerability and acceptability of a novel contraceptive vaginal ring releasing etonogestrel and ethinyl oestradiol. *Hum Reprod*. 2001;16:469–475.
80. Mulders TM, Dieben TO, Bennink HJ. Ovarian function with a novel combined contraceptive vaginal ring. *Hum Reprod*. 2002;17:2594–2599.
81. Zieman M, Guilegaud J, Weisberg E, et al. Contraceptive efficacy and cycle control with the Ortho Evra/Evra transdermal system: the analysis of pooled data. *Fertil Steril*. 2002;77:S13–S18.
82. Zacur HA, Hedon B, Mansour D, et al. Integrated summary of Ortho Evra/Evra contraceptive patch adhesion in varied climates and conditions. *Fertil Steril*. 2002;77:S32–S35.
83. Sibai BM, Odlind V, Meador M, et al. A comparative and pooled analysis of the safety and tolerability of the contraceptive patch (Ortho Evra/Evra). *Fertil Steril*. 2002;7(2)(suppl 2):S19–S26.
84. Audet M-C, Moreau M, Koltun WE, et al. Evaluation of contraceptive efficacy and cycle control of a transdermal contraceptive patch vs. an oral contraceptive: a randomized controlled trial. *JAMA*. 2001;285:2347–2354.
85. Jick SS, Hagberg KW, Kaye JA. ORTHO EVRA and venous thromboembolism: an update. *Contraception*. 2010;81(5):452–453.
86. Grady WR, Hayward MD, Yagi J. Contraceptive failure in the United States: estimates from the 1982 National Survey of Family Growth. *Fam Plann Perspect*. 1986;18:200–209.
87. Fihn SD, Lathan RH, Roberts P, et al. Association between diaphragm use and urinary tract infections. *JAMA*. 1986;254:240–245.
88. Hooton TM, Hillier S, Johnson C, et al. Escherichia coli bacteriuria and contraceptive method. *JAMA*. 1991;265:64–69.
89. Wright NH, Vessey MP, Kenward B, et al. Neoplasia and dysplasia of the cervix uteri and contraception: a possible protective effect of the diaphragm. *Br J Cancer*. 1978;38:273–279.
90. Mauck CK, Baker JM, Barr SP, et al. A phase I study of FemCap used with and without spermicide. Postcoital testing. *Contraception*. 1997;56:111–115.
91. Mauck C, Callahan M, Weiner DH, Dominik R. A comparative study of the safety and efficacy of FemCap, a new vaginal barrier contraceptive, and the Ortho All-Flex diaphragm. The FemCap Investigators' Group. *Contraception*. 1999;60:71–80.
92. U.S. Food and Drug Administration, Center for Devices and Radiological Health. *FemCap summary of safety and effectiveness data* [P020041]. March 28, 2003. http://www.fda.gov/cdrh/pdf2/P020041b.pdf. Accessed July 22, 2005.
93. Trussell J, Vaughan B. Contraceptive failure, method-related discontinuation and resumption of use: results from the 1995 National Survey of Family Growth. *Fam Plann Perspect*. 1999;31:64–72.
94. Gilliam MLL, Derman RJ. Barrier methods of contraception. *Obstet Gynecol Clin North Am*. 2000;27:841–858.
95. Trussell J, Vaughan B. Contraceptive failure, method-related discontinuation and resumption of use: results from the 1995 National Survey of Family Growth. *Fam Plann Perspect*. 1999;31:64–72.
96. Trussell J, Strickler J, Vaughan B. Contraceptive efficacy of the diaphragm, the sponge and the cervical cap. *Fam Plann Perspect*. 1993;25:100–105.
97. Trussell J, Hatcher RA, Cates W Jr, et al. Contraception failure in the United States: an update. *Stud Fam Plann*. 1990;21:51–54.
98. Cook L, Nanda K, Taylor D. Randomized crossover trial comparing the eZ-on plastic condom and a latex condom. *Contraception*. 2001;63:25–31.
99. Davis KR, Weller SC. The effectiveness of condoms in reducing heterosexual transmission of HIV. *Fam Plann Perspect*. 1999;31:272–279.
100. Centers for Disease Control and Prevention. Nonoxynol-9 spermicide contraception use—United States, 1999. *MMWR Morb Mortal Wkly Rep*. 2002;51:389–392.
101. Fleming DT, McQuillan GM, Johnson RE, et al. Herpes simplex virus type 2 in the United States, 1976–1994. *N Engl J Med*. 1997;337:1105–1111.
102. Armstrong GL, Schillinger J, Markowitz L, et al. Incidence of herpes simplex virus type 2 infection in the United States. *Am J Epidemiol*. 2001;153: 912–920.
103. Sapire KE. The female condom (Femidom)—a study of user acceptability. *S Afr Med J*. 1995;85:1081–1084.
104. Trussell J, Sturgen K, Strickler J, et al. Comparative efficacy of the female condom and other barrier methods. *Fam Plann Perspect*. 1994;26: 66–72.
105. Beksinska ME, Rees HV, Dickson-Tetteh KE, et al. Structural integrity of the female condom after multiple uses, washing, during and relubrication. *Contraception*. 2001;63:33–36.
106. Johnson V, Masters WH. Intravaginal contraceptive study. Phase II. Physiology. *West J Surg Obstet Gynecol*. 1963;71:144–153.
107. Roddy RE, Zekeng L, Ryan K, et al. A controlled trial of nonoxynol-9 film to reduce male-to-female transmission of sexually transmitted diseases. *N Engl J Med*. 1998;339:504–510.
108. Stafford MK, Ward H, Flanagan A, et al. Safety study of nonoxynol-9 as a vaginal microbicide: evidence of adverse effects. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;17:327–331.
109. Kreiss J, Ngugi E, Holmes K, et al. Efficacy of nonoxynol-9 contraceptive sponge use in preventing heterosexual acquisition of HIV in Nairobi prostitutes. *JAMA*. 1992;268:447–482.
110. Richardson BA, Lavreys L, Martin HL Jr, et al. Evaluation of a low-dose nonoxynol-9 gel for the prevention of sexually transmitted diseases. *Sex Transm Dis*. 2001;28:394–400.
111. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *MMWR Morb Mortal Wkly Rep*. 2002;51: 1–80.
112. Linn S, Schoenbaum SC, Monson RR. Lack of association between contraceptive usage and congenital malformation in offspring. *Am J Obstet Gynecol*. 1983;147:923–928.
113. Task Force on Postovulatory Methods of Fertility Regulation. Randomized controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet*. 1998;352:428–433.
114. Ella [package insert]. Morristown, NJ: Waston Pharma, Inc; 2010.
115. Trussell J, Elerston C, Stewart F. The effectiveness of the Yuzpe regimen of emergency contraception. *Fam Plann Perspect*. 1996;28:58–64, 87.
116. Raymond EG, Creinin MD, Barnhart KT, et al. Meclizine for prevention of nausea associated with use of emergency contraceptive pills: a randomized trial. *Obstet Gynecol*. 2000;95:271–277.
117. Webb A. How safe is the Yuzpe method of emergency contraception? *Fertil Control Rev*. 1995;4:16–18.
118. Roetzer J. Natural family planning and pregnancy outcome. *Int J Fertil*. 1988;33(suppl):40–42.

119. Brown JB, Holmes J, Barker G. Use of the home ovarian monitor in pregnancy avoidance. *Am J Obstet Gynecol*. 1991;165:2008–2011.
120. Rulin MC, Turner JH, Dunworth R, et al. Post-tubal sterilization syndrome—a misnomer. *Am J Obstet Gynecol*. 1985;151:13–19.
121. Rulin MC, Davidson AR, Philliber SG, et al. Changes in menstrual symptoms among sterilized in comparison women: a prospective study. *Obstet Gynecol*. 1989;74:149–154.
122. DeStefano F, Huezo CM, Peterson HB, et al. Menstrual changes after tubal sterilization. *Obstet Gynecol*. 1983;62:673–681.
123. DeStefano F, Pearlman JA, Peterson HB, et al. Long-term risk of menstrual disturbances after tubal-sterilization. *Obstet Gynecol*. 1985;152:835–841.
124. Hillis HD, March-Banks PA, Taylor GP. Tubal sterilization and long-term risk of hysterectomy findings from the U.S. Collaborative Review of Sterilization. The U.S. Collaborative Review of Sterilization Working Group (CREST). *Obstet Gynecol*. 1997;89:609–614.
125. Mosher WE, Pratt WF. *Contraceptive use in the United States, 1973–1988. Advance Data No. 182*. Hyattsville, MD: National Center for Health Statistics; 1990.
126. Cheng M, Wong YM, Rochat R, et al. Sterilization failure in Singapore: an examination of ligation techniques and failure rates. *Stud Fam Plann*. 1977;8:109–115.
127. Peterson HB, Jhisen X, Hughes JM, et al. A risk of pregnancy after tubal sterilization: findings from the U.S. Collaborative Review of Sterilization (CREST). *Am J Obstet Gynecol*. 1996;174:1161–1168.
128. McCausland A. High rate of ectopic pregnancy following laparoscopic tubal coagulation failure. *Am J Obstet Gynecol*. 1980;136:97–101.

CHAPTER 2

Uterine Abnormalities

Lubna Chohan

INTRODUCTION

History

As time has progressed, women's health issues have become increasingly important. Much of this can be contributed to the increased life expectancy of women and their added contribution to the work force. Life expectancy was 50 years of age for females in 1900.[1] In the United States in 2006, this increased to 80.2 years of age for females.[2] Women with excessive menstrual bleeding suffer both economic and psychosocial costs including discomfort and diminished quality of life. Work and school status can suffer from stained clothes, lost time, and extra cost of menstrual products. A survey of 2805 American women showed those that had increased menstrual flow during the prior year were more likely to be unemployed than women with a normal flow. It is estimated that the cost of this work loss is $1692 annually per woman.[3]

Definitions

Most definitions of normal menstruation include a cycle length of 21 to 35 days, duration of 7 days or less, and blood loss of less than 80 mL. These values come from a Swedish study done in 1966. About 500 women (ranging from adolescence through their 50s) were studied. Blood loss was estimated after collecting menstrual pads and tampons and using the alkaline hematin method. Median blood loss was 30 mL per month with 10% of women losing greater than 90 mL per month. Greater blood loss was found in perimenopausal women.[3]

Abnormal uterine bleeding is somewhat subjective as practitioners base their assessment on a patient's history. Even if a woman's menstrual blood loss is greater than 80 mL, many of them consider this to be normal. These patients oftentimes seek treatment once their quality of life is affected, not because of bleeding symptoms. For those with a blood loss of less than 80 mL per month, 25% of women will be anemic (hemoglobin less than 12 g/dL). For those with a blood loss of greater than 80 mL per month, 67% are anemic.[3] Table 2.1 includes other standard definitions regarding abnormal uterine bleeding. To note, heavy menstrual bleeding is a newer term for menorrhagia.[4]

Endocrinology and Pathology

The menstrual cycle is endometrial breakdown and remodeling in a cyclical fashion. This tissue has well-defined episodes of proliferation, differentiation, and breakdown. Menstruation occurs in response to the withdrawal of ovarian steroids. This causes the uterine functional layer (upper two-thirds of endometrium) to shed and regenerate on a regular basis. The functional layer is then replenished after menstruation by exposure to estradiol then progesterone.[5]

After menstruation, the vascular compartment of the endometrium comprising the spiral arteries and arterioles needs to be reconstructed. New endothelial cells are formed and growth begins of capillaries and smooth muscle cells to form larger vessels. The remodeling of the endometrial vasculature is a multifactorial and complex process.[5]

Prostaglandins have a role in endometrial pathology and subsequently abnormal uterine bleeding. Arachidonic acid is broken down into prostaglandins by cyclooxygenase (COX) and lipoxygenase (LOX). At the end of the menstrual cycle with progesterone withdrawal and shedding of the endometrial functional layer, there is an increase in COX-2 expression that lasts through the proliferative phase. Data suggests that prostaglandins produced by COX enzymes in the endometrium directly control endometrial angiogenesis.[5]

Treatment with COX enzyme inhibitors have been shown to reduce menstrual blood loss and points toward disturbances of prostaglandin pathways in menorrhagia.[5] With ovulatory abnormal uterine bleeding in the absence of underlying pathology (i.e., leiomyomas), there is no difference in circulating steroid hormones or endometrial histology when compared to women with normal menses. It has been shown that disturbances of arachidonic acid metabolism and angiogenic processes and elevated levels of prostaglandin E_2 (PGE_2) in endometrium are found in women with menorrhagia. A dual mode of action has been shown for COX inhibitors used in the treatment of menorrhagia: inhibition of prostaglandin synthesis and inhibition of PGE_2 binding to its receptor.[5]

Women with heavy menses have endometrial endothelial cells that proliferate more. Also, their spiral arterioles have less vascular smooth muscle cells. This then

TABLE 2.1 Definitions

Oligomenorrhea: Intervals between bleeding episodes vary from 35 days to 6 months
Amenorrhea: No menses for at least 6 months
Primary amenorrhea: Absence of menstruation in a 16-year-old with developed secondary sexual characteristics or in a 14-year-old with absent secondary sexual characteristics
Secondary amenorrhea: Absence of menses for 6 months in females with previously irregular menstrual pattern
Menorrhagia: Prolonged (more than 7 days) or excessive (greater than 80 mL) uterine bleeding occurring at regular intervals; also called **heavy menstrual bleeding**
Metrorrhagia: Uterine bleeding occurring at irregular but frequent intervals, the amount being variable
Intermenstrual bleeding: Bleeding of variable amounts occurring between regular menstrual periods
Polymenorrhea: Uterine bleeding occurring at regular intervals of less than 21 days
Dysfunctional uterine bleeding (DUB): Excessive uterine bleeding with no demonstrable organic cause (genital or extragenital). It is most frequent due to abnormalities of endocrine origin, particularly anovulation.

Data from Nelson AL. LNG-IUS: First-line therapy for idiopathic heavy menstrual bleeding. *The Female Patient*. 2010;35:39–43; Deligeoroglou E, Athanasopoulos N, Tsimaris P, et al. Evaluation and management of adolescent amenorrhea. *Ann N Y Acad Sci*. 2010;1205:23–32; Katz VL, Lentz GM, Lobo RA, et al. Abnormal uterine bleeding. In: Katz VL, Lentz GM, Lobo RA, et al, eds. *Comprehensive Gynecology*. 5th ed. St Louis, MO: Mosby Elsevier; 2007:915.

prevents proper vasoconstriction of these vessels and subsequent increased menstrual blood loss.[5]

ETIOLOGY

Anovulation

In adolescents, abnormal uterine bleeding is commonly related to anovulation from an immature hypothalamic-pituitary axis. This results in months to years of unpredictable ovulation after menarche.[6] For these first few years, normal cyclic progesterone production lags behind the normal development of GnRH and estrogen. In the first year after menarche, 85% of cycles are anovulatory. Four years after menarche, only 56% of cycles are ovulatory.[6] If menarche occurs earlier, there is a faster normalization of ovulation when compared to girls with a delayed menarche.[6]

Another source of anovulatory menstrual bleeding is polycystic ovarian syndrome (PCOS). This is thought to occur in up to 10% of adolescents[6] and 6 to 8% of reproductive-aged women.[7] Clinical features of PCOS include polycystic ovaries, anovulation causing menstrual irregularities, and hyperandrogenism causing hair growth and acne. It is also related to insulin resistance, obesity, and infertility. Reproductive and metabolic abnormalities of PCOS include overproduction of ovarian androgens, increased pituitary luteinizing hormone (LH) secretion, incomplete maturation of ovarian follicle development, and insulin resistance with compensatory hyperinsulinemia.[7] During times of chronic anovulation, there is prolonged unopposed estrogen which can lead to excessive endometrial proliferation. When the endometrial thickness grows beyond its available blood supply, the superficial layers slough and breakthrough bleeding occurs.[7]

Other causes of anovulation secondary to disturbances in the hypothalamic-pituitary-ovarian axis include stress, excessive exercise, eating disorders, thyroid disease, and menopausal transition.[8]

Hematologic Disorder

Bleeding disorders can cause abnormal uterine bleeding and should be evaluated, especially in the adolescent. It is estimated that bleeding disorders have a 2% community prevalence rate.[9] In women with heavy menstrual bleeding, bleeding disorders are reported at 10 to 20%[9] and even higher in adolescents (7 to 48%).[6] Other bleeding symptoms that are predictive of these diseases include bleeding after tooth extraction, epistaxis, prolonged bleeding after wounds, postoperative bleeding, postpartum hemorrhage, and family history of bleeding disorders. Platelet abnormalities (platelet function defects and thrombocytopenia) and von Willebrand disease (VWD) should be considered. The most common inherited bleeding disorder is VWD with a 1% incidence, but only 125 per million have a clinically significant bleeding disorder.[9]

Uterine Pathology

Leiomyomas

Leiomyomas (or myomas or fibroids) occur in 20 to 50% of women, making them the most common solid pelvic tumors in women.[10,11] Some studies show a prevalence of up to 80% in African American women and 70% in Caucasian women by 50 years of age.[11] This is the most common diagnosis for hysterectomy in the United States.[10] Myomas originate from smooth muscle cells of the uterus and are benign. They range in size, number, and location, including intramural (within the myometrium), subserosal (externally extending to the serosa), submucosal (internally impinging on the uterine cavity), and pedunculated. They are estrogen dependent and decrease in size during menopause and other hypoestrogenic conditions. There is a higher concentration of estrogen receptors in myomas than in adjacent myometrium. Fibroids bind 20% more estradiol per milligram of protein than myometrium.[10]

About 30% of fibroids become symptomatic (abnormal uterine bleeding and pelvic pressure).[11] Heavy menstrual bleeding occurs secondary to an obstructive effect of myomas on uterine vasculature and subsequent congestion in proximal myometrium/endometrium causing excessive bleeding during cyclic endometrial sloughing. Histologically, endometritis is often seen in tissue

overlying submucosal fibroids, which may also contribute to abnormal uterine bleeding.[10]

The transition of myomas to malignant tumors is extremely rare. It is thought that leiomyosarcomas may be unrelated to benign fibroids. In a study of about 1300 women with symptomatic fibroids undergoing myomectomy or hysterectomy, uterine sarcoma (leiomyosarcoma, endometrial stromal sarcoma, and mixed mesodermal tumor) was seen in 0.2%.[10] A more realistic percentage is likely much lower than 0.2% if you consider all women with fibroids; only a small percentage are symptomatic and require myomectomy or hysterectomy. As stated previously, fibroids decrease in size during menopause. If a rapid growth of myomas occurs in a menopausal patient, the concern for malignancy should arise.

Endometrial Hyperplasia and Cancer

As age increases, so does the risk of endometrial carcinoma. At the time of diagnosis, the median age is 61 years, with 75 to 80% of women being postmenopausal.[12] The prevalence of carcinoma in women age 40 years or younger varies from 2.9 to 14.4%.[12] In regards to endometrial hyperplasia, there is a 2 to 7% prevalence in premenopausal women.[12] The progression rate to endometrial cancer is 1% for simple hyperplasia (mean duration 10 years), 2 to 4% for complex hyperplasia (mean duration 10 years), 23% for atypical hyperplasia (mean duration 4 years), and 29% for complex atypical hyperplasia (mean duration 4 years).[12] Ninety-five percent of women with endometrial cancer present with postmenopausal bleeding as their only complaint. Of all women who have postmenopausal bleeding, 3 to 10% have endometrial cancer.[13]

Recommendations for endometrial sampling range widely from all women older than 35 years of age with abnormal uterine bleeding or those who do not respond to initial management in the United States to women older than 45 years of age with cyclical heavy bleeding, greater than 90 kg, or have other risk factors for carcinoma in New Zealand.[12] In one of the largest series studying the appropriate age for endometrial sampling, findings included atypical hyperplasia and carcinoma being significantly higher in women 45 to 50 years than in younger age women. They also found importance in distinguishing anovulatory abnormal uterine bleeding because this is more likely to lead to hyperplasia versus ovulatory bleeding. Other risk factors for hyperplasia and cancer included nulliparity; obesity (greater than 90 kg); polycystic ovaries with anovulation; family history of endometrial or colon cancer; tamoxifen treatment; and a triad of obesity, diabetes, and hypertension.[12]

Endometrial Polyps

Endometrial polyps are being diagnosed more frequently secondary to the improved quality of transvaginal ultrasound, saline-infusion ultrasounds, and hysteroscopy.[14] It is thought that estrogen stimulation of the endometrium plays a role in the creation of these polyps. Women who are symptomatic can have abnormal bleeding: intermenstrual bleeding, heavy menstrual bleeding, spotting, discharge, or postmenopausal bleeding. Asymptomatic premenopausal patients may have polyps that resolve spontaneously. Also, polyps less than 1 cm may resolve.[14]

In a systematic review and meta-analysis including 17 studies and over 10,000 patients, the association of menopause, abnormal bleeding, polyp size, and malignancy risk in regards to endometrial polyps were studied.[14] Endometrial neoplasia was found in 5.4% of postmenopausal patients compared to 1.7% of premenopausal patients. In regards to abnormal uterine bleeding, neoplasia was seen in 4.2% of women with symptomatic bleeding versus 2.2% of asymptomatic women. This review concluded that there is an increased risk of endometrial neoplasia in women with endometrial polyps who have symptomatic bleeding or are postmenopausal. Overall, an association with polyp size was not noted.[14]

In a smaller retrospective multicenter study, the malignant potential of endometrial polyps was studied in approximately 2000 postmenopausal women.[15] The prevalence of endometrial carcinoma was 0.1% for asymptomatic menopausal patients. This was 10 times lower than for symptomatic (any bleeding or spotting in the prior 6 months) patients. For asymptomatic women, the only variable significantly associated with cancer or hyperplasia was polyp diameter (larger than 18 mm).[15] Both of these studies conclude that there is a higher rate of cancer in women with symptomatic endometrial polyps.

Endocrine Disorder

Major endocrine causes of abnormal uterine bleeding and amenorrhea include polycystic ovarian syndrome, thyroid disease, and hyperprolactinemia. When prolactin is elevated, hypothalamic GnRH secretion is suppressed. This in turn can affect circulating estrogen levels and menstrual cycles. Causes of hyperprolactinemia include stress, thyroid disease, medications, and pituitary tumors. If prolactin is mildly elevated, this may be due to stress and the level should be remeasured. With hypothyroidism, the stimulating effect of thyrotropin-releasing hormone (TRH) in the pituitary gland can cause elevated prolactin. Prolactin is inhibited by dopamine. With antipsychotic drugs, these block dopamine receptors and subsequently increase prolactin. Also, with pituitary tumors, these place pressure on the pituitary stalk, obstruct dopamine flow, and cause prolactinemia. These patients are often treated with dopamine receptor agonists (i.e., bromocriptine or cabergoline).[16]

TABLE 2.2 Etiology of Abnormal Genital Bleeding

Cancer

Infection

Benign

Pregnancy

Uterus
- Polyps
- Endometrial hyperplasia
- Adenomyosis
- Leiomyomas

Cervix
- Polyps
- Ectropion
- Endometriosis

Vulva
- Skin tags
- Sebaceous cyst
- Condylomata
- Angiokeratoma

Vagina
- Gartner's duct cyst
- Polyps
- Adenosis

Trauma

Abuse

Foreign body

Pelvic trauma/straddle injury

Drugs

Contraception

Hormone replacement therapy

Anticoagulant

Tamoxifen

Corticosteroids

Chemotherapy

Dilantin

Antipsychotics

Systemic disease

Coagulation disorder
- von Willebrand disease
- Thrombocytopenia or platelet dysfunction
- Acute leukemia
- Factor deficiencies
- Advanced liver disease

Thyroid disease

Hyperprolactinemia

Polycystic ovarian syndrome

Chronic liver disease

Cushing syndrome

Hormone secreting adrenal and ovarian tumors

Renal disease

Emotional and physical stress

Smoking

Excessive exercise

Vulvar disease
- Crohn disease
- Behçet syndrome
- Pemphigoid
- Pemphigus
- Erosive lichen planus
- Lymphoma

Data from Goodman A. Initial approach to the premenopausal woman with abnormal uterine bleeding. UpToDate Web site. http://www.uptodate.com/contents/initial-approach-to-the-premenopausal-woman-with-abnormal-uterine-bleeding. Accessed December 2, 2013; DeSilva NK. Differential diagnosis and approach to the adolescent with abnormal uterine bleeding. UpToDate Web site. http://www.uptodate.com/contents/differential-diagnosis-and-approach-to-the-adolescent-with-abnormal-uterine-bleeding. Accessed December 2, 2013; Goodman A. Overview of causes of genital tract bleeding in women. UpToDate Web site. http://www.uptodate.com/contents/overview-of-causes-of-genital-tract-bleeding-in-women. Accessed December 2, 2013.

TABLE 2.3 Etiology of Abnormal Genital Bleeding by Age Group

Neonates
- Estrogen withdrawal

Premenarchal
- Foreign body
- Trauma/abuse
- Infection
- Urethral prolapse
- Sarcoma botryoides
- Ovarian tumor
- Precocious puberty

Early postmenarche
- Anovulation (hypothalamic immaturity)
- Bleeding diathesis
- Stress
- Pregnancy
- Infection

Reproductive years
- Anovulation
- Pregnancy
- Cancer
- Polyps
- Leiomyomas
- Adenomyosis
- Infection
- Endocrine dysfunction (polycystic ovarian syndrome, thyroid, pituitary)
- Bleeding diathesis
- Medications

Perimenopausal
- Anovulation
- Polyps
- Leiomyomas
- Adenomyosis
- Cancer

Menopause
- Atrophy
- Cancer
- Hormone replacement therapy

Data from Wilkinson JP, Kadir RA. Management of abnormal uterine bleeding in adolescents. *J Pediatr Adolesc Gynecol.* 2010;23(6)(suppl):S22–S30; Goodman A. Initial approach to the premenopausal woman with abnormal uterine bleeding. UpToDate Web site. http://www.uptodate.com/contents/initial-approach-to-the-premenopausal-woman-with-abnormal-uterine-bleeding. Accessed December 2, 2013; DeSilva NK. Differential diagnosis and approach to the adolescent with abnormal uterine bleeding. UpToDate Web site. http://www.uptodate.com/contents/differential-diagnosis-and-approach-to-the-adolescent-with-abnormal-uterine-bleeding. Accessed December 2, 2013.

Other endocrine disorders were discussed previously (i.e., PCOS).

In regards to causes of abnormal genital tract bleeding and causes by age groups, a more comprehensive list is included in Tables 2.2 and 2.3.

EVALUATION

Laboratory

A pregnancy test should be performed on patients with abnormal uterine bleeding. Other labs include complete blood cell count, thyroid-stimulating hormone, prolactin, LH, follicle-stimulating hormone, and liver and renal function tests.

When concerned about bleeding disorders, check a complete blood cell count, prothrombin time, activated partial thromboplastin time, factor VIII, and von Willebrand Factor (VWF) ristocetin cofactor and antigen. It is advised to screen for VWD before initiating hormonal therapy because exogenous estrogen can elevate VWF into a normal range, thus giving a false-negative result.[6] This is why pregnant women normalize their factor VIII, von Willebrand antigen level, and ristocetin cofactor activity and usually do not bleed during the pregnancy. However, they can start bleeding within a few days postpartum as these levels decrease.[9]

If clinical hyperandrogenism is present, also check testosterone and dehydroepiandrosterone sulfate (DHEA-S). If DHEA-S is elevated, then adrenal gland function should be investigated with 17OH-progesterone. If DHEA-S is greater than 700 mg/dL, consider late-onset type congenital adrenal hyperplasia as a diagnosis.[16] A list of laboratory tests to consider in the workup of abnormal uterine bleeding is included in Table 2.4.

Endometrial Sampling

There is not a worldwide consensus on when to perform an endometrial sampling. Some countries advocate endometrial sampling after 45 years or with risk factors for endometrial hyperplasia/carcinoma.[12] In the United States, with the American College of Obstetricians and Gynecologists (ACOG) support, the recommendation is

TABLE 2.4 Laboratory Workup for Abnormal Uterine Bleeding

Urine pregnancy test (or beta-hCG)
Complete blood cell count
Thyroid-stimulating hormone (TSH)
Prolactin
Follicle-stimulating hormone (FSH)
Luteinizing hormone (LH)
Liver functio n tests
Renal function tests
If concern for bleeding disorder:
Prothrombin time
Activated partial thromboplastin time
Factor VIII
VWF ristocetin cofactor and antigen
Studies of platelet aggregation and release
If clinical hyperandrogenism is present:
Testosterone
Dehydroepiandrosterone sulfate (DHEA-S)
17-OH progesterone

Data from Wilkinson JP, Kadir RA. Management of abnormal uterine bleeding in adolescents. *J Pediatr Adolesc Gynecol*. 2010;23(6)(suppl):S22–S30; Deligeoroglou E, Athanasopoulos N, Tsimaris P, et al. Evaluation and management of adolescent amenorrhea. *Ann N Y Acad Sci*. 2010;1205:23–32.

for endometrial sampling in women older than 35 years of age with abnormal uterine bleeding or those who do not respond to initial management.[12] In 2009, an ACOG Committee Opinion stated that postmenopausal patients with an endometrial echo of 4 mm or less (by transvaginal ultrasound) had a malignancy risk of 1 in 917 and did not require an endometrial biopsy. There are limitations of ultrasound and will be discussed in the following section.[17]

Radiology Studies

Ultrasonography and Sonohysterography

Transvaginal ultrasound has its limitations as it is a technical procedure and not all uteri will produce a reliable endometrial stripe. This can be affected by leiomyomas, prior surgery, obesity, adenomyosis, and axial orientation. For these patients, sonohystography could be used. This can help distinguish if no pathology is present, a thick endometrium, or abnormalities (i.e., polyp, submucosal fibroid).[17] Initial imaging of choice when evaluating leiomyomas is ultrasonography secondary to its availability and low cost. Limitations of transvaginal ultrasound include difficulty detecting small myomas and subserosal myomas. It is also difficult to map myomas in large uteri and when multiple fibroids are present.[18]

The timing of an ultrasound is also important. In women who are not menstruating (postmenopausal or premenopausal on birth control pills), ultrasonography can be done at any time because endometrial thickness does not vary. For menstruating women, the ideal time for imaging is after the bleeding cycle ends, when the endometrium is at its thinnest.[17]

With imaging studies readily available, we are seeing more cases of incidental findings. For asymptomatic (nonbleeding) postmenopausal patients with an incidental finding of a thickened endometrial echo, there is no validation for intervention.[17]

Magnetic Resonance Imaging

When evaluating fibroids, ultrasound has some limitations, as discussed previously. Magnetic resonance imaging (MRI) outperforms transvaginal ultrasonography in preoperative evaluation of location, number and size of myomas, and sensitivity for pedunculated submucosal and subserosal fibroids and large fibroids (>8.5 cm).[18] See Figures 2.1 and 2.2.

MRI is often the imaging study of choice for preoperative evaluation for laparoscopic (or robotic) myomectomies. With these surgeries, there is a lack of equivalent haptic perception compared to open surgery. For this reason, MRI is preferred for fibroid mapping.[19] This is also the imaging study chosen for uterine artery embolization, which will be discussed later in this chapter.

MANAGEMENT

Medical

There are a wide variety of medications that can be used to manage heavy menstrual bleeding. Medical treatment

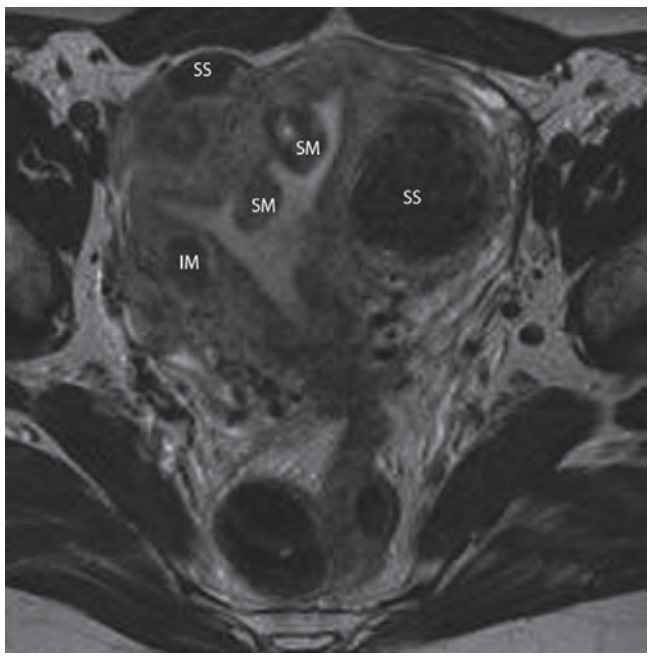

FIGURE 2.1 Coronal T2-weighted MRI shows multiple uterine submucosal (SM), subserosal (SS), and intramural (IM) fibroids. (From Griffin Y, Sudigali V, Jacques A. Radiology of benign disorders of menstruation. *Semin Ultrasound CT MR*. 2010;31[5]:414–432.)